TORTUGAS HASTA EL FONDO

Ciencia y mitos de las vacunas



Referencias

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Por ejemplo:

https://www.ncbi.nlm.nih.gov/pubmed/17469680

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- J. Durante la lectura, si encuentra un error en alguna de las referencias, tenga la amabilidad de ponerse en contacto con nosotros y comunicárnoslo.

Le deseamos una lectura agradable y provechosa.

Capítulo 1: Tortugas hasta el fondo: ensayos clínicos de vacunas

1-20

1	Nombre de la página: Vaccine Product Approval Process		
	Sitio web: FDA website http://www.fda.gov/biologicsbloodvaccines/deprovalprocess/biologicslicenseapplicationsblag 33096.htm		
	People		
	Sitio web: FDA website http://www.fda.gov/Drugs/ResourcesForYo u/Consumers/ucm143531.htm	Archivo: https://web.archive.org/web/201808251751 3/https://www.fda.gov/Drugs/ResourcesFor You/Consumers/ucm143531.htm	

2 Nombre del documento: Nombre del documento: ICH Harmonised Tripartite Guideline Choice Of Control Group And Related Issues In Clinical Trials E10 http://www.ich.org/fileadmin/Public Web Site/ICH Products/Guidelines/Efficacy/E10/Ste p4/E10 Guideline.pdf Autor/año: Archivo: https://drive.google.com/open?id=1IrAW9UYSFvIA8npBLKsA ICH Expert Working UZxft53cmhml Group, 2000 P 22 (28): It should be appreciated, however, that subjects receiving a new treatment are not receiving standard therapy (just as a placebo control group is not) and may be receiving an ineffective or harmful drug.

3	Nombre del artículo: U.S. advisory panel recommends Prevnar 13 vaccine for elderly	Fecha: Aug 14, 2014	
	Sitio web: Reuters http://www.reuters.com/article/us-pfizer-prevnar-idUSKBN0GD23I20140813		
	Archivo: http://archive.is/RfO2H		
	Por ejemplo: (Reuters) - An influential U.S. medical advisory panel on Wednesday recommended that people 65 and older be given Pfizer Inc's blockbuster Prevnar 13 vaccine to protect against pneumococcal bacteria that can cause pneumonia and other infections. []		
	Prevnar 13 and an older version of the vaccine known as Prevnar 7 have combined annual sales of almost \$4.5 billion, making them Pfizer's second-biggest franchise. Prevnar 13 is		

approved for children 6 weeks through 17 years of age, and for adults 50 and older.

4 Nombre del artículo: PMID: Placebo use in vaccine trials: 24768580 Recommendations of a WHO expert panel Archivo: https://www.ncbi.nlm.nih.gov/pmc/articles/P https://drive.google.com/open?id=1mX3Rr MC4157320/ To-Jg6eEC-H S1blgiDVfXYosUv Autor principal/año: Autor principal/año: Revista: Annette Rid, 2014 Vaccine

nothing).

Randomised, placebo-controlled trials are widely considered the gold standard for evaluating the safety and efficacy of a new vaccine. In these trials, participants are randomized to receive either the vaccine under investigation or a placebo (i.e. an inert substance such as a saline injection). Randomisation and the use of placebo interventions are designed to control for confounding effects, such that significant differences in disease incidence or adverse effects between the vaccine and control groups can likely be attributed to the vaccine.

5 PMID: Nombre del artículo: The clinical development process for a novel preventive 26732191 vaccine: An overview Archivo: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4944327/ http://archive.is/kPW8h Revista: Autor principal/año: Autor principal/año: Journal of Postgraduate Medicine K Singh, 2016 Phase III Studies [...] RCTs are considered the "gold standard," where participants are randomly allocated to receive either the investigational or the control vaccine (placebo, different vaccine, or

6 Nombre del documento: Nombre del documento: ICH Harmonised Tripartite Guideline Choice Of Control Group And Related Issues In Clinical Trials E10 http://www.ich.org/fileadmin/Public Web Site/ICH Products/Guidelines/Efficacy/E10/Ste p4/E10 Guideline.pdf Autor/año: Archivo: **ICH Expert Working** https://drive.google.com/open?id=1IrAW9UYSFvIA8npBLKsA Group, 2000 UZxft53cmhml P 13 (19): When a new treatment is tested for a condition for which no effective treatment is known, there is usually no ethical problem with a study comparing the new treatment to placebo. Nombre del documento: Nombre del documento: Expert consultation on the use of placebos in vaccine trials http://apps.who.int/iris/bitstream/handle/10665/94056/9789241506250 eng.pdf Autor/año: Archivo: WHO, 2013 https://drive.google.com/open?id=1vLHGu4pO0K2xUZmNsE4 RvxrbUtkq382v

A common model for the evaluation and deployment of a new vaccine, against a disease for which there is no existing vaccine, is that it is first tested in a placebo-controlled trial.

As a general rule, research subjects in the control group of a trial of a diagnostic, therapeutic, or preventive intervention should receive an established effective intervention.

	In some circumstances it may be ethically acceptable to use an alternative comparator, such as placebo or "no treatment". A placebo may be used: • when there is no established effective intervention;	
	Nombre del documento: Guidance for Industry E 10 Choice of Control Group and Related Issues in Clinical Trials https://drive.google.com/open?id=17LyWGbkC8dQRtcHfFjKMjs7xgxpU3CBp	
	Autor/año: FDA, 2001	
	P 15 (19): When a new treatment is tested for a condition for which no effective treatment is known, there is usually no ethical problem with a study comparing the new treatment to placebo.	

7	Expert consultatio	Nombre del documento: Expert consultation on the use of placebos in vaccine trials http://apps.who.int/iris/bitstream/handle/10665/94056/9789241506250_eng.pdf		
	Autor/año: WHO, 2013	Archivo: https://drive.google.com/open?id=1yLHGu4pO0K2xUZmNsE4RyxrbUtkq382y		
	P 12-13:there is uniformity on the use of placebos, i.e. that if a proven effective intervention exists, the trial intervention should generally be tested against it. Failure to do so deprives participants in the "control" arm of an intervention that is likely to benefit them.			

	ICH Harmonised Tripartite Guideline Choice Of Control Group And Related Issues In Clinical Trials E10 http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E10/Step4/E10_Guideline.pdf			
	Autor/año: ICH Expert Working Group, 2000	Archivo: https://drive.google.com/open?id=1IrAW9UYSFvIA8npBLKsAUZxft53cmhml		
	P 12 (18): A useful approach to the assessment of assay sensitivity in active control trials and in placebo-controlled trials is the three-arm trial, including both placebo and a known active treatment, a trial design with several advantages.			
	Nombre del artículo: Alternatives to Placebo-Controlled Trials https://www.cambridge.org/core/services/aop- cambridge- core/content/view/28A722D8EF2C2FCABB3A1 AC2477DFBB8/S0317167100005540a.pdf/altern atives_to_placebocontrolled_trials.pdf		PMID: 17469680	
			Archivo: https://drive.google.com/open?id=1uSF dSiRKhZex8QwuHiOmLjgxD3_Fi7vE	
	Autor principal/año:Autor principal/año: David L. Streiner, 2007		Revista: The Canadian Journal Of Neurological Sciences	
	P 41 (5): My recommendation would be that, when an existing therapy exists, and if certain conditions apply: * Studies should consist of three arms: the new drug, the existing drug, and a placebo group			

9 Nombre del documento:

ICH Harmonised Tripartite Guideline

Choice Of Control Group And Related Issues In Clinical Trials E10 http://www.ich.org/fileadmin/Public Web Site/ICH Products/Guidelines/Efficacy/E10/Ste p4/E10 Guideline.pdf

Autor/año: Archivo:

ICH Expert Working Group, 2000 https://drive.google.com/open?id=1IrAW9UYSFvIA 8npBLKsAUZxft53cmhml

Sección 2.5.2 - P 24-25 (30-31):

It is always difficult, and in many cases impossible, to establish comparability of the treatment and control groups and thus to fulfill the major purpose of a control group (see section 1.2). The groups can be dissimilar with respect to a wide range of factors, other than use of the study treatment, that could affect outcome, including demographic characteristics, diagnostic criteria, stage or severity of disease, concomitant treatments, and observational conditions (such as methods of assessing outcome, investigator expectations). Such dissimilarities can include important but unrecognized prognostic factors that have not been measured. Blinding and randomization are not available to minimize bias when external controls are used.

[...]

Control groups in a randomized study need to meet certain criteria to be entered into the study, criteria that are generally more stringent and identify a less sick population than is typical of external control groups. An external control group is often identified retrospectively, leading to potential bias in its selection.

10 Nombre del documento:

HAVRIX, Package Insert

https://drive.google.com/open?id=1XGppC-tPGSWvEZNGK8kRY15nGz76lxSA

Sección 6.1:

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine, and may not reflect the rates observed in practice.

11 Nombre del documento:

Guidelines for the Ethical Conduct of Studies to Evaluate Drugs in Pediatric Populations http://pediatrics.aappublications.org/content/pediatrics/60/1/91.full.pdf

Autor/año: Archivo:

https://drive.google.com/open?id=1sjvo 5OLgRv8ZCkh7lic-AAP, 1977

1Kih1gV1zEF

P 1-2:

The publication of these general guidelines and their implications for future drug development led the

FDA to request that the Academy's Committee on Drugs advise it about standards of ethical research which could be recommended to assure that children, and society in general, are served appropriately by studies carried out in pediatric populations without undue hazard or discomfort.

[...]

The Committee believes that it is unethical to adhere to a system which forces physicians to use therapeutic agents in an uncontrolled experimental situation virtually every time they prescribe for children. Furthermore, it is not only ethical but also imperative that new drugs to be used in children be studied in children under controlled circumstances so the benefits of therapeutic advances will become available to all who may need them.

12 Nombre del documento:

Ethical Considerations in Conducting Pediatric Research

Capítulo de libro de:

Pediatric Clinical Pharmacology

https://www.springer.com/gp/book/9783642201943

Autor principal/año:Autor principal/año:

Michelle Roth-Cline, 2011

A fundamental pillar of pediatric research is the ethical principle of "scientific necessity." This principle holds that children should not be enrolled in a clinical investigation unless necessary to achieve an important scientific and/or public health objective concerning the health and welfare of children. An "important scientific question" may be one that generates information that is necessary and timely for establishing the appropriate pediatric use of investigational therapeutics. A corollary is that children should not be enrolled in studies that are duplicative or unlikely to yield important knowledge applicable to children about the product or condition under investigation.

13 Nombre del documento:

Ethical Considerations in Conducting Pediatric Research

Capítulo de libro de:

Pediatric Clinical Pharmacology

https://www.springer.com/gp/book/9783642201943

Autor principal/año:

Michelle Roth-Cline, 2011

First, the risks to which children would be exposed must be low if there is no prospect of direct therapeutic benefit (PDB) to the enrolled children. Second, children should not be placed at a disadvantage by being enrolled in a clinical trial, either through exposure to excessive risks or by failing to get necessary health care. Consequently, the data necessary to initiate a pediatric investigation must demonstrate either an acceptably low risk of the experimental intervention or a sufficient PDB to justify the risks of the intervention.

Investigations involving children that pose more than low risk cannot be justified by the importance of anticipated knowledge. In pediatric studies, the allowable risk exposure for an intervention or procedure not offering a PDB must be restricted to low risk.

Nombre del documento:

MMR II Clinical Trials – FDA FOIA

https://drive.google.com/open?id=1GKahQSNG8LvCAnEG7SGNyYPUEiSJwfd8

An example from a form filled by investigators in vaccine trial in the late 1970s.

B. Describe the benefit to the subject or advancment of knowledge that will balance the risk involved.

C. Indicate measures proposed to minimize risk [...]

14 Nombre del documento:

Ethical Considerations in Conducting Pediatric Research

Capítulo de libro de:

Pediatric Clinical Pharmacology

https://www.springer.com/gp/book/9783642201943

Autor principal/año:Autor principal/año:

Michelle Roth-Cline, 2011

P 226-228:

FDA regulations also include a classification of "minor increase over minimal risk" (21 CFR 50.53, 2011). An intervention or procedure approved under this category must also involve "experiences to subjects that are reasonably commensurate with those inherent in their actual or expected... situations" and be "likely to yield generalizable knowledge about the subjects' disorder or condition that is of vital importance for the understanding or amelioration of the subjects' disorder or condition."

In assessing whether an intervention or procedure presents no more than a minor increase over minimal risk, there must be sufficient data that any research-related pain, discomfort or stress will not be severe and that any potential harms will be transient and reversible (Fisher et al. 2007). Even if the average risk associated with an intervention or procedure is thought to be low, if the risk estimate is unknown, reflects a large degree of variability, or has not been adequately characterized, then the risks of an intervention or procedure cannot be considered only a minor increase over minimal risk.

15 Nombre del documento:

VAQTA Package Insert

https://drive.google.com/open?id=1LuPKwCve8Pguo-GJOzbOm1b9Hgu0Zn15

In a double-blind, placebo-controlled efficacy trial (i.e. The Monroe Efficacy Study), 1037 healthy children and adolescents 2 through 16 years of age were randomized to receive a primary dose of 25U of VAQTA and a booster dose of VAQTA 6, 12, or 18 months later, or placebo (alum diluent)... There were no significant differences in the rates of any adverse events or adverse reactions between vaccine and placebo recipients after Dose 1.

16 Nombre del documento:

DAPTACEL Clinical Review

https://drive.google.com/open?id=1CFrePXwN-q5ywCnuflnwLjUwScsLPvBU

P 61, Tabla 50:

Rates for all hospitalizations, hospitalizations for acute otitis media, suspected bacterial respiratory infection, lower respiratory infection – no antibiotics, upper respiratory infection – no antibiotics, viral infection, gastroenteritis, urinary tract infection, seizures, trauma/intoxication, surgery were similar among vaccine groups.

17 Nombre del artículo: PMID: 17469680 Alternatives to Placebo-Controlled Trials https://www.cambridge.org/core/services/aopcambridge-Archivo: core/content/view/28A722D8EF2C2FCABB3A1AC24 https://drive.google.com/open?id 77DFBB8/S0317167100005540a.pdf/alternatives to p =1uSPdSiRKhZex8QwuHiOmLj lacebocontrolled trials.pdf gxD3 Fi7vE Autor principal/año:Autor Revista: The Canadian Journal Of Neurological Sciences principal/año: David L. Streiner, 2007

Streiner notes this problem in the context of measuring trial efficacy, but it's clear the same problem exists with the safety aspect, p 5:

However, there are many methodological problems when the comparison group consists of an active treatment: [...] (b) when the two arms yield comparable results, there is no guarantee that either one was effective in that particular trial;

And the proposed solution, p 5:

My recommendation would be that, when an existing therapy exists, and if certain conditions apply:

* Studies should consist of three arms: the new drug, the existing drug, and a placebo group.

18 Nombre del documento:

Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger

https://drive.google.com/open?id=1Bcb5L30zbAB4FGtzItrzUs_g1vJCv4lt

Autor/año:

CDC, 2020

19 Nombre del documento:

Pediarix Package Insert

https://drive.google.com/open?id=1rY3q-bXZDxIErcWTvm2th3hGm4zBRPAk

P 5, 6, 8

20 Nombre del documento:

Kinrix Package Insert

https://drive.google.com/open?id=1Ulz5HRP4ROFm49kQniiuqQ2vsRIFNH61

P 4

21-40

21 Nombre del documento:

INFANRIX Package Insert

https://drive.google.com/open?id=1fUUkPH8gHd5fiBFhyZhGBl56fwLtmcCf

Selected adverse events reported from a double-blind, randomized Italian clinical efficacy trial involving 4,696 children administered INFANRIX or 4,678 children administered whole-cell DTP vaccine (DTwP) (manufactured by Connaught Laboratories, Inc.) as a 3dose primary series are shown in Table 4.

[...]

In a German safety study that enrolled 22,505 infants (66,867 doses of INFANRIX administered as a 3-dose primary series at 3, 4, and 5 months of age), all subjects were monitored for unsolicited adverse events that occurred within 28 days following vaccination using report cards.

22 Nombre del documento:

The Immunological Basis for Immunization Series - Pertussis http://apps.who.int/iris/bitstream/10665/44311/1/9789241599337_eng.pdf Autor

Archivo:

principal/año:Auto r principal/año:

https://drive.google.com/open?id=1efbV0PaVOMSI6NcqbDtREba y JizPM2C

WHO, 2009

All aP vaccines are associated with significantly lesser side-effects, and thus the replacement of the wP vaccines was mainly driven by the safety-profile of these vaccines.

23 Nombre del documento:

Adverse Effects of Pertussis and Rubella Vaccines

http://www.nap.edu/read/1815/chapter/4#38

Autor/año:

IOM 1991

P 38:

In fact, since the first reports of serious adverse events following administration of pertussis and rubella vaccines (Madsen, 1933; Modlin et al., 1975), virtually no placebo-controlled or other experimental studies in humans of the adverse events covered in this report have been published.

24 Nombre del documento:

Adverse Effects of Pertussis and Rubella Vaccines http://www.nap.edu/read/1815/chapter/4#39

Autor/año:

IOM 1991

P 39:

A number of early studies of pertussis vaccine in the United States and the United Kingdom did include unexposed controls, but these studies were primarily concerned with efficacy and not with adverse events.

25 Enlace de búsqueda:

https://www.clinicaltrials.gov/ct2/results?term=Infanrix+safety&recr=Closed&rslt=&type= &cond=&intr=&titles=&outc=&spons=&lead=GlaxoSmithKline&id=&state1=&cntry1=&st ate2=&cntry2=&state3=&cntry3=&locn=&gndr=&age=0&phase=2&phase=3&rcv_s=&rcv_ e=&lup_s=&lup_e=

or

https://drive.google.com/open?id=14MfvK7yfw9M092-JHj3RB5_x7mjiPT_E

26 Nombre del documento:

Pentacel Package Insert

https://drive.google.com/open?id=1SB8zUchU9xp_i0eQTHent-znyta_oHec

P 10 (11)

27 Nombre del documento:

Pentacel Safety Review

https://drive.google.com/open?id=1u4ugyQjcQWZ43AMSop6-zSYugykHLoDK

P 75-76

28 Nombre del documento:

Quadracel Package Insert

https://drive.google.com/open?id=1qIjY0SVED2Q8WxXhJj8DAXDJ725F6NVa

P 5 (6)

29 Nombre del documento:

DAPTACEL Package Insert

https://drive.google.com/open?id=1mD GBQsmiGMO-VFpdRMqEdX6yMLVfFwn

P 10, 16-17, 21-22

30 Nombre del documento:

DAPTACEL Clinical Review

https://drive.google.com/open?id=1CFrePXwN-q5ywCnuflnwLjUwScsLPvBU

P 57, 61:

The Swedish trial (1992-1995) compared 4 groups: one of Infanrix by SmithKline Beecham (GSK), one CDPT (DAPTACEL) by Aventis-Pasteur (Sanofi), and one DTPwc – old generation vaccine by Aventis-Pasteur. The control group received a DT vaccine.

31 Nombre del documento:

Hiberix Package Insert

https://drive.google.com/open?id=1epLW5onHsW93NI2 qNxH-KaMvkcvATdc

P 4, 14

32 Nombre del documento:

ActHIB Package Insert

https://drive.google.com/open?id=1MeKZaNrIaVRjy_2VmtvBQ98t6syrVM14

P 13-16

33 Nombre del documento:

PedvaxHIB Package Insert

https://drive.google.com/open?id=10rwMmdmZ H3FE9v1oPPiByLqGbFegngS

P 7

34 Nombre del documento:

IPOL Package Insert

https://drive.google.com/open?id=1sWAblyncNXw-78rh8LtzkIKAmQfAkOK2

35 Nombre del documento:

IPOL FOIA FDA 2018

https://drive.google.com/open?id=1V7zf1YPJF2 V2KRRf-wUz-dCeKxMaUvz

P 90-93, 13-15

Nombre del documento: 36

PREVNAR-13 Package Insert

https://drive.google.com/open?id=1 iI7Np-BfDmUwkQzuJWp46rkSBZ-ow5i

The safety of Prevnar 13 was evaluated in 13 clinical trials in which 4,729 infants (6 weeks through 11 months of age) and toddlers (12 months through 15 months of age) received at least one dose of Prevnar 13 and 2,760 infants and toddlers received at least one dose of Prevnar active control.

37 Nombre del documento:

PREVNAR-13 Package Insert

https://drive.google.com/open?id=1 iI7Np-BfDmUwkQzuJWp46rkSBZ-ow5i

P 6:

Serious adverse events reported following vaccination in infants and toddlers occurred in 8.2% among Prevnar 13 recipients and 7.2% among Prevnar recipients.

[...]

The most commonly reported serious adverse events were in the 'Infections and infestations' system organ class including bronchiolitis (0.9%, 1.1%), gastroenteritis, (0.9%, 0.9%), and pneumonia (0.9%, 0.5%) for Prevnar 13 and Prevnar respectively.

38 Nombre del documento:

PREVNAR Package Insert

https://drive.google.com/open?id=1VLR6NluMGK0E4yXUZM18IpUpi MI7-MP

Revista:

P 3, 5, 15, 21

Nombre del artículo:

Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children

PMID: 10749457

Autor principal/año:Autor principal/año:

Pediatric Infectious Disease Journal

Steven Black, 2000

P 5

Overall 513 pneumococcal vaccine recipients and 579 controls were hospitalized within 60 days of receipt of a dose of vaccine.

[...]

Review of emergency room visits within 30 days of vaccination revealed 1188 visits in pneumococcal vaccine recipients and 1169 visits in controls.

40

Nombre del documento:

PREVNAR Package Insert

https://drive.google.com/open?id=1VLR6NluMGK0E4yXUZM18IpUpi MI7-MP

P 3. 15:

Efficacy was assessed in a randomized, double-blinded clinical trial in a multiethnic population at Northern California Kaiser Permanente (NCKP) from October 1995 through August 20, 1998, in which 37,816 infants were randomized to receive either Prevnar® or a control vaccine (an investigational meningococcal group C conjugate vaccine [MnCC]) at 2, 4, 6, and 12-15 months of age.

[...]

The majority of the safety experience with Prevnar® comes from the NCKP Efficacy Trial in which 17,066 infants received 55,352 doses of Prevnar®, along with other routine childhood vaccines through April 1998.

41-60

41

Nombre del documento:

ENGERIX Package Insert

https://drive.google.com/open?id=1aZ1MtPiO58lE6Pjg0Ee PZZ10c4iLjUs

P 7

Based on clinical trial symptom sheet data, the incidence of local side effects is 24% and of systemic side effects 8%; both local and systemic side effects occurred in approximately 13% of subjects. The incidence of local and systemic reactions was comparable to those of plasma derived hepatitis B vaccines.

42 Nombre del documento:

ENGERIX Package Insert

https://drive.google.com/open?id=1aZ1MtPiO58lE6Pig0Ee PZZ10c4iLjUs

P 7:

In a comparative trial in subjects from 11 years up to and including 15 years of age, the incidence of local and general solicited symptoms reported after a two-dose regimen of ENGERIX-B 20 μg was overall similar to that reported after the standard three-dose regimen of ENGERIX-B 10 μg.

43 Nombre del documento:

TWINRIX Package Insert

https://drive.google.com/open?id=1K0vRj8CXuYtdhYUys4EPj2cG_niylk0I

In a US study, 773 subjects (aged 18 to 70 years) were randomized 1:1 to receive TWINRIX (0-, 1-, and 6-month schedule) or concurrent administration of ENGERIX-B (0-, 1-, and 6month schedule) and HAVRIX (0- and 6-month schedule).

44 Nombre del documento:

Recombivax-HB Package Insert

https://drive.google.com/open?id=1LHJU WAhXqewxvZJwWpRCRT7f4pHFaPk

45 Nombre del documento:

HAVRIX Package Insert

https://drive.google.com/open?id=1XGppC-tPGSWvEZNGK8kRY15nGz76lxSA

P 5, 10

46 Nombre del documento:

VAQTA Clinical Review

https://drive.google.com/open?id=1IASUdLYQ1eUDFb8vXgFH61ZhJ9rJAfRd

P 12, 22

47 Nombre del documento:

VAQTA Package Insert

https://drive.google.com/open?id=1LuPKwCve8Pguo-GJOzbOm1b9Hgu0Zn15

P 11, paragraph 11. Description of the vaccine adjuvant. P 7 Table 5 (and table comments) – using the control group.

48 Nombre del artículo:

A controlled trial of a formalin-inactivated hepatitis A vaccine in healthy children http://www.nejm.org/doi/full/10.1056/NEJM1 99208133270702#t=article+Methods

PMID:

1320740

Archivo:

https://drive.google.com/open?id=1Wy 1j Dh1YVupEU7whmdE5VbKvyt y2Sk

Autor principal/año:Autor principal/año: Alan Werzberger, 1992

Revista:

The New England Journal of Medicine

Like the vaccine, each dose of the placebo — aluminum hydroxide diluent — contained 300 μg of aluminum and thimerosal at a 1:20,000 dilution.

49 Nombre del documento:

Varivax Package Insert

https://drive.google.com/open?id=1NnEIia3vR 01iqYnq2wNDRWz ZcvPo48

In a double-blind, placebo-controlled study among 914 healthy children and adolescents who were serologically confirmed to be susceptible to varicella, the only adverse reactions that occurred at a significantly (p<0.05) greater rate in vaccine recipients than in placebo recipients were pain and redness at the injection site {2}.

50 Nombre del artículo:

Live Attenuated Varicella Virus Vaccine Efficacy trial in healthy children

PMID: 6325909

Autor principal/año: Weibel, 1984

Revista: **NEJM**

P 1-2:

The placebo (Lot 909/C-H663) was identical in appearance to the vaccine in both lyophilized and reconstituted forms, but contained no virus material. The placebo consisted of lyophilized stabilizer containing approximately 45 mg of neomycin per milliliter.

51 Nombre del artículo:

Live Attenuated Varicella Virus Vaccine Efficacy trial in healthy children

PMID:

6325909

Autor principal/año:Autor

Revista: **NEJM**

principal/año: Weibel, 1984

P 5:

The minimal clinical reactivity reported in this trial confirms our previous experience with the vaccine. Among 914 initially seronegative children, only pain and redness at the injection site were reported more frequently among vaccine recipients than placebo recipients.

52 Nombre del documento:

ProQuad Package Insert

https://drive.google.com/open?id=13MxSgUKzQwZ59M2YZ 9Hwtc 217tSOVh

P 6, 8, 9-11

53 Nombre del documento:

MMR II Package Insert

https://drive.google.com/open?id=1IFm340mDs4z_GUMRASgVUWK8mzOnNpXx

54 Nombre del documento:

MMR II FOIA FDA

https://drive.google.com/open?id=1GKahQSNG8LvCAnEG7SGNyYPUEiSJwfd8

55 Nombre del documento:

MMR FOIA FDA

https://drive.google.com/open?id=16qovZioEkWxDF739XeUdwvAyRk7unWm5

56 Nombre del documento: Federal Register / Vol. 78, No. 142 https://drive.google.com/open?id=1Dml DhOUJWX5LlKr-9gM7olmHwlQVwFQ Autor/año: Federal Register, 2013 P 3-4

57 See the RotaTeq trial, top table Biological: Comparator: Placebo

https://clinicaltrials.gov/ct2/show/NCT00090233?term=rotavirus&rank=24

Archivo: http://archive.is/8eGQQ

For Rotarix, its noted: "The study has two groups: Group HRV and Group Placebo"

https://clinicaltrials.gov/ct2/show/NCT00140673?term=rotavirus&rank=65

Archivo: http://archive.is/LqCpd

58 Nombre del documento:

Rotarix Clinical Review

 $\underline{https://drive.google.com/open?id=1LNjfqQDrsaQEdaZ0MYNkc_YfIrOz2kto}$

P 24:

The placebo consisted of all components of Rotarix, but without any RV particles.

59 Nombre del documento:

Rotateq Clinical Review

https://drive.google.com/open?id=1T5ZQZYINtJhdrYGHrwSZ1M5HWFKf4dK8

P 37

60 Nombre del artículo: PMID:

Efficacy, Immunogenicity, and Safety of a Pentavalent Human-Bovine (WC3) Reassortant Rotavirus Vaccine at the End of Shelf Life

17200266

Autor principal/año: Revista: Stan L. Block, 2007 **Pediatrics**

P 2:

The placebo was identical to the vaccine except that it did not contain the rotavirus reassortants or trace trypsin.

61 - 70

61	Nombre del artículo: Safety and Efficacy of an Attenuated Vaccine against Severe Rotavirus Gastroenteritis https://www.nejm.org/doi/full/10.1056/NEMoa052434	PMID: 16394298 Archivo: https://drive.google.com/open?id=1BFeBU KyHVq9msLCtJLdY3bHJsIIQ4pS3
	Autor principal/año: Guillermo M. Ruiz-Palacios, 2006	Revista: The New England Journal of Medicine
	P 15-17	

62 Nombre del artículo: PMID: Safety and Efficacy of a Pentavalent 16394299 Human-Bovine (WC3) Reassortant Rotavirus Vaccine Archivo: https://www.nejm.org/doi/full/10.1056/NE https://drive.google.com/open?id=18tKqyoOx JMoa052664 5aSXdOCwFiSfffbqMzVIsY2W Autor principal/año: Revista: The New England Journal of Medicine Timo Vesikari, 2006 P 28-30 (6-8)

63 Nombre del documento:

ROTARIX Package Insert

https://drive.google.com/open?id=1b1rURgJfPiXgg3HGZtYzhpKnjv7ZW-P0

P 5:

No increased risk of intussusception was observed in this clinical trial following administration of ROTARIX when compared with placebo

64 Nombre del artículo: PMID: Postmarketing Surveillance of Intussusception 22695189 Following Mass Introduction of the Attenuated Human Rotavirus Vaccine in Mexico Autor principal/año: Revista:

F. Raúl Velázquez, 2012 The Pediatric Infectious Disease Journal

The attenuated human rotavirus vaccine was not found to be associated with an increased risk of intussusception in a large prelicensure placebo-controlled, clinical trial involving 63,225 infants in 11 Latin American countries and Finland.

Nombre del artículo:

Risk of Intussusception After Rotavirus Vaccination: Meta-analysis of Postlicensure Studies

https://journals.lww.com/pidj/fulltext/2015/07000/Risk of Intussusception After Rotavirus.18.aspx

PMID: 26069948

Archivo:

https://drive.google.com/open?id =172UmbRygo9WBW9iza1NlNk 3A0-7uV057

Autor principal/año: Revista: Dominique Rosillon, 2015

The Pediatric Infectious Disease Journal

No increased risk of serious adverse events, including intussusception, was detected in prelicensure clinical studies of either RV1 or RV5, including 2 randomized, controlled trials each involving over 60,000 infants.

65 Nombre del documento: Ethical Considerations in Conducting Pediatric Research Capítulo de libro de: Pediatric Clinical Pharmacology https://www.springer.com/gp/book/9783642201943 Autor/año: Michelle Roth-Cline, 2011 P 228:

In assessing whether an intervention or procedure presents no more than a minor increase over minimal risk, there must be sufficient data that any research-related pain, discomfort or stress will not be severe and that any potential harms will be transient and reversible.

66 Nombre del documento:

Declaration Of Helsinki – Ethical Principles For Medical Research Involving Human

https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-formedical-research-involving-human-subjects/

Archivo: Autor/año:

WMA, 1964 http://archive.is/4r8lC

Paragraph 18:

18. Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed. When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study.

Paragraph 28:

28. For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorised representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be performed with persons capable of providing informed consent, and the research entails only minimal risk and minimal burden.

67 Nombre del documento:

The Nuremberg Code

"Trials of War Criminals before the Nuremberg Military Tribunals under Control Council

https://drive.google.com/open?id=1zCEx9tvA 1vs4KycwYUU9uQ1GHC0mXp6

Autor/año:

U.S. Government, 1949

P 1 item 4:

The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

68 Nombre del documento:

Expert consultation on the use of placebos in vaccine trials

http://apps.who.int/iris/bitstream/handle/10665/94056/9789241506250 eng.pdf

Autor/año: Archivo:

WHO, 2013 https://drive.google.com/open?id=1yLHGu4pO0K2

xUZmNsE4RyxrbUtkq382y

The research must have a risk-benefit profile judged to be favourable, based on sufficient evidence from previous clinical and non-clinical studies (i.e. the expected benefits of conducting the research must outweigh any associated potential risks). There is an ethical obligation to introduce measures to reduce the risks to all trial participants.

69 Nombre del documento:

DAPTACEL Clinical Review

https://drive.google.com/open?id=1CFrePXwN-a5vwCnuflnwLiUwScsLPvBU

P 61 Tabla 50

70 The list of articles:

https://www.ncbi.nlm.nih.gov/pubmed/25371534 https://www.ncbi.nlm.nih.gov/pubmed/29443825 https://www.ncbi.nlm.nih.gov/pubmed/29239682 https://www.ncbi.nlm.nih.gov/pubmed/29217375 https://www.ncbi.nlm.nih.gov/pubmed/28720281 https://www.ncbi.nlm.nih.gov/pubmed/28522338 https://www.ncbi.nlm.nih.gov/pubmed/28498853

Capítulo 2: La ciencia de los efectos adversos de las vacunas

1-20

1	Nombre del documento: Immunization Safety Review: Measles-Mumps-Rubella Vaccine and Autism http://nationalacademies.org/hmd/reports/2001/immunization-safety-review-measles-mumps-rubella-vaccine-and-autism.aspx
	Autor/año: IOM, 2001

Nombre del documento:
Immunization Safety Review: Thimerosal - Containing Vaccines and Neurodevelopmental
Disorders
http://www.nationalacademies.org/hmd/reports/2001/Immunization-Safety-Review-Thimerosal---Containing-Vaccines-and-Neurodevelopmental-Disorders.aspx

Autor/año:
IOM, 2001

Nombre del documento:
Immunization Safety Review: Vaccinations and Sudden Unexpected Death in Infancy
http://www.nationalacademies.org/hmd/Reports/2003/Immunization-Safety-Review-Vaccinations-and-Sudden-Unexpected-Death-in-Infancy.aspx

Autor/año:
IOM, 2003

Autor/año:
IOM, 2004

Nombre del documento:
Immunization Safety Review Vaccines and Autism
https://www.nap.edu/catalog/10997/immunization-safety-review-vaccines-and-autism

6 Nombre del documento: Adverse Effects of Vaccines: Evidence and Causality http://nationalacademies.org/hmd/reports/2011/adverse-effects-of-vaccines-evidence-andcausality.aspx Autor/año: Archivo: IOM, 2011 https://drive.google.com/open?id=1nl18cdV y3TtQBzoCq0tS iuYmHF1 yYQ

7 Nombre del documento:

Adverse Effects of Vaccines: Evidence and Causality

http://nationalacademies.org/hmd/reports/2011/adverse-effects-of-vaccines-evidence-andcausality.aspx

Autor/año: Archivo: IOM, 2011 https://drive.google.com/open?id=1nl18cdV_y3TtQ BzoCq0tSiuYmHF1 yYQ

P 30 (59):

In 2009 HRSA requested that the IOM convene a committee of experts to review the epidemiological, clinical, and biological evidence regarding adverse health events associated with specific vaccines covered by the VICP. The committee was charged with developing a consensus report with conclusions on the evidence bearing on causality and the evidence regarding the biological mechanisms that underlie specific theories for how a specific vaccine is related to a specific adverse event.

8 Nombre abreviado: IOM 2011

P IX (10):

Following in this tradition, the task of this committee was to assess dispassionately the scientific evidence about whether eight different vaccines cause adverse events (AE), a total of 158 vaccine-AE pairs, the largest study undertaken to date, and the first comprehensive review since 1994.

9 Nombre abreviado: IOM 2011

P 18 (47):

The committee concluded the evidence convincingly supports 14 specific vaccine-adverse event relationships. In all but one of these relationships, the conclusion was based on strong mechanistic evidence with the epidemiologic evidence rated as either limited confidence or insufficient.

The committee concluded the evidence favors acceptance of four specific vaccine-adverse event relationships.

10 Nombre abreviado: IOM 2011

P 23 (52):

The committee concluded the evidence favors rejection of five vaccine-adverse event relationships.

[...]

The vast majority of causality conclusions in the report are that the evidence was inadequate to accept or reject a causal relationship.

2	2
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11	Nombre abreviado: IOM 2011
	P 19-21 (48-50)

12 Nombre abreviado: IOM 2011 P 630-632 (659-661)

13 Fecha: Nombre del artículo: Vaccine Safety: New Report Finds Few Adverse Events Linked Aug. 25, 2011 to Immunizations Sitio web: Time Magazine http://healthland.time.com/2011/08/25/vaccine-safety-new-report-finds-few-adverse-eventslinked-to-immunizations/ Archivo: http://archive.is/kV5ko Nombre del artículo: Fecha: Report Finds Few Side Effects For Vaccines Aug. 25, 2011 Sitio web: Forbes http://www.forbes.com/sites/matthewherper/2011/08/25/report-finds-few-side-effects-forvaccines/#2715e4857a0b41d59ef62b39 http://archive.is/X70SL Nombre del artículo: Fecha: IOM review ties few adverse effects to vaccines Aug. 25, 2011 Sitio web: **CIDRAP** http://www.cidrap.umn.edu/news-perspective/2011/08/iom-review-ties-few-adverse-effectsvaccines

14 Nombre del artículo:

Fecha:

Leading Dr.: Vaccines-Autism Worth Study

May 12, 2008

Sitio web:

Archivo:

CBS NEWS

https://www.cbsnews.com/news/leading-dr-vaccines-autism-worth-study/

Archivo:

http://archive.is/q82UH

http://archive.is/u3YmY

Bernadine Healy, a former top official in US Public Health bodies, told CBS News in 2008:

Healy goes on to say public health officials have intentionally avoided researching whether subsets of children are "susceptible" to vaccine side effects - afraid the answer will scare the public.

"You're saying that public health officials have turned their back on a viable area of research largely because they're afraid of what might be found?" Attkisson asked.

Healy said: "There is a completely expressed concern that they don't want to pursue a hypothesis because that hypothesis could be damaging to the public health community at large by scaring people.

15 Nombre abreviado:

IOM 2011

P 28 (57):

The overwhelming safety and effectiveness of vaccines in current use in preventing serious disease has allowed them to gain their preeminent role in the routine protection of health.

16 Nombre abreviado:

IOM 2011

P 49 (78):

It is important to note that mechanistic evidence can only support causation. Epidemiologic evidence, by contrast, can support ("favors acceptance of") a causal association or can support the absence of ("favors rejection of") a causal association in the general population and in various subgroups that can be identified and investigated, unless or until supportive mechanistic evidence is discovered or a rare, susceptible subgroup can be identified and investigated.

17 Nombre abreviado:

IOM 2011

PX(11):

Many of the case reports the committee reviewed simply cited a temporal relation between vaccine administration and an adverse event.

18 Nombre abreviado:

IOM 2011

P 440-442 (469-471)

19 Nombre abreviado: IOM 2011

P 154-156 (183-185)

20 Nombre de la página:

Acute Disseminated Encephalomyelitis (ADEM)

Sitio web:

WEBMD

https://www.webmd.com/brain/acute-disseminated-encephalomyelitis-adem#1

Archivo:

http://archive.is/8u53v

ADEM seems to be an autoimmune disease. That means your immune system attacks your body's own cells and tissues as if they were outside bacteria or viruses. Experts don't know exactly what triggers it, but it could be an overreaction to an infection. Most of the time, the attack happens when a child is getting over some common illness, like a cold or stomach

ADEM sometimes follows an immunization, particularly certain rabies shots and the vaccine for measles, mumps, and rubella. No direct connection has been made though. Other times, nothing out of the ordinary happens before symptoms appear.

21-34

21

Nombre de la página:

Optic neuritis

Sitio web:

Mayo Clinic

https://www.mayoclinic.org/diseases-conditions/optic-neuritis/symptoms-causes/syc-20354953

Archivo:

http://archive.is/A9RBl

The exact cause of optic neuritis is unknown.

22

Nombre de la página:

Guillain-Barre syndrome

Sitio web:

Mayo Clinic

https://www.mayoclinic.org/diseases-conditions/guillain-barre-syndrome/symptomscauses/syc-20362793

Archivo:

http://archive.is/2IgLm

The exact cause of Guillain-Barre syndrome isn't known.

23

Nombre de la página:

What is Transverse Myelitis?

Sitio web:

Johns Hopkins Medicine

http://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/transverse_myelit is/about-tm/what-is-transverse-myelitis.html

Archivo:

http://archive.is/CiqdA

The cause of 60% of TM cases may remain unknown despite the presence of inflammatory mechanisms. However, the remaining 40% is associated with autoimmune disorders such as multiple sclerosis, neuromyelitis optica, systemic lupus erythematous, Sjogren's syndrome and sarcoidosis among others. The term *idiopathic* — meaning the cause is unknown-has been used in the past in situations in which the cause cannot be determined. However, the lack of demonstration of a causative disorder, mechanism or agent may be the result of failure of an early diagnosis or the result of causative factors that disappears quickly such as in cases of viral infections or post-infectious disorders.

24

Nombre de la página:

Lupus

Sitio web:

Mayo Clinic

http://www.mayoclinic.org/diseases-conditions/lupus/basics/causes/con-20019676

Archivo:

http://archive.is/SY0oG

Lupus occurs when your immune system attacks healthy tissue in your body (autoimmune disease). It's likely that lupus results from a combination of your genetics and your environment.

It appears that people with an inherited predisposition for lupus may develop the disease when they come into contact with something in the environment that can trigger lupus. The cause of lupus in most cases, however, is unknown.

25

Nombre de la página:

Vasculitis

Sitio web:

Mayo Clinic

http://www.mayoclinic.org/diseases-conditions/vasculitis/basics/causes/con-20026049

http://archive.fo/DMh6g

The exact cause of vasculitis isn't fully understood. Some types are related to a person's genetic makeup. Others result from the immune system attacking blood vessel cells by mistake.

26

Nombre de la página:

Type 1 diabetes in children

Sitio web:

Mayo Clinic

https://www.mayoclinic.org/diseases-conditions/type-1-diabetes-in-children/symptomscauses/syc-20355306

Archivo:

http://archive.fo/TqdgF

The exact cause of type 1 diabetes is unknown. But in most people with type 1 diabetes, the body's immune system — which normally fights harmful bacteria and viruses — mistakenly destroys insulin-producing (islet) cells in the pancreas. Genetics and environmental factors appear to play a role in this process.

27

Nombre abreviado:

IOM 2011

P 14 (43)

28

Nombre abreviado:

IOM 2011

P XI (12):

Although the committee is optimistic that more can and will be known about vaccine safety in the future...

29

Nombre del documento:

Varivax Product Sheet

https://drive.google.com/open?id=1NnEIia3vR 01iqYnq2wNDRWz ZcvPo48

P 3 (4)

Vaccine-related adverse reactions reported during clinical trials were assessed by the study investigators to be possibly, probably, or definitely vaccine-related and are summarized below.

30 Nombre del documento: Engerix Clinical Review https://drive.google.com/open?id=1lt2scepRp3pTpbB4HQ3cYtE5bU3twD6o Of 55 SAEs reported during the active phase of the protocol and 12 reported during the 180 day extended safety follow-up, none were considered to be vaccine related. Nombre del artículo: PMID: Safety and Immunogenicity of Tetanus Diphtheria and 24794369 Acellular Pertussis (Tdap) Immunization During Pregnancy in Mothers and Infants Autor principal/año: Revista: Flor M. Munoz, 2014 **JAMA** Whether an adverse event was attributable to vaccination was judged by the investigators considering temporality, biologic plausibility, and identification of alternative etiologies for each event. [...] Serious adverse events were reported by 22 participants... None were judged to be attributable to Tdap vaccine. Nombre del artículo: PMID: Safety and Immunogenicity of the HPV-16/18 AS04-20413076 Adjuvanted Vaccine: A Randomized, Controlled Trial in Archivo: Adolescent Girls https://drive.google.com/o http://www.hu.ufsc.br/projeto hpv/Safety%20and%20Immun pen?id=1UyuQfB7G1uAL ogenicity%20of%20the%20HPV-1618%20AS04itDdnO-AZxJk7Tw1ojHX Adjuvanted.pdf Autor principal/año: Revista: Journal of Adolescent Health Doris M. Rivera Medina, 2010 No SAE in the HPV-16/18 vaccine group was considered related to vaccination or led to withdrawal. Nombre del artículo: PMID: Safety of a new conjugate meningococcal C 11668101 vaccine in infants Archivo: https://adc.bmj.com/content/archdischild/85/5/ https://drive.google.com/open?id=1hXmU 391.full.pdf hIcV38Y 1fGaUHJCL89rz6oaVUe7 Autor principal/año: Revista: R Lakshman, 2001 Archives of Disease in Childhood P 394 (4): 1755 (63%) subjects had adverse events that were considered not to have any causal relation

31 Nombre del documento:

with the vaccine.

PEDIACEL Package Insert

https://drive.google.com/open?id=18Bb7jBpmRTQHDJ JAYb7v1fpCK9-NboP

P 10:

The following additional adverse events have been spontaneously reported during the postmarketing use of PEDIACEL® worldwide. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Nombre del documento:

HAVRIX, Package Insert

https://drive.google.com/open?id=1XGppC-tPGSWvEZNGK8kRY15nGz76lxSA

In addition to reports in clinical trials, worldwide voluntary reports of adverse events received 136 for HAVRIX since market introduction of this vaccine are listed below. This list includes serious 137 adverse events or events which have a suspected causal connection to components of HAVRIX 138 or other vaccines or drugs. Because these events are reported voluntarily from a population of 139 uncertain size, it is not always possible to reliably estimate their frequency or establish a causal 140 relationship to the vaccine.

Nombre del documento:

ENGERIX Package Insert

https://drive.google.com/open?id=1aZ1MtPiO58lE6Pjg0Ee PZZ10c4iLjUs

P 8:

The following adverse events have been reported following widespread use of the vaccine. As with other hepatitis B vaccines, in many instances the causal relationship to the vaccine has not been established

32 Nombre del artículo:

International Consensus (ICON): allergic reactions to vaccines https://waojournal.biomedcentral.com/articles/10.1186/s40413 -016-0120-5

PMID: 27679682

Archivo:

http://archive.is/d1J1F

Autor principal/año: Revista:

Stephen C. Dreskin, 2016 World Allergy Organization Journal

All tests need to be interpreted carefully with appropriate positive and negative controls, recognizing that falsely positive skin test results may occur. These may be the result of true but clinically irrelevant IgE responses or to irritant effects of the vaccine.

33 Nombre del artículo (translated from Herbrew):

The 6-year-old's liver collapsed; His mother's lobe saved him

Fecha:

Nov 11, 2014

Sitio web:

https://www.ynet.co.il/articles/0,7340,L-4590167,00.html

Archivo:

http://archive.is/AbUmZ

In spite of all the intensive tests he has undergone, both hospitals have not been able to find out why the sudden and dramatic liver collapse. It is a rare condition. Once or twice a year, we have such a condition of a child with liver failure even though they are completely

"In this condition, they undergo tests to detect infectious, autoimmune or metabolic diseases, and often the cause is not found," explains Dr. Michael Gurevich, senior physician at the Schneider hospital transplant system, who was one of the surgeons.

One of the causes of the collapse, which was tested and ruled out is the flu vaccine he received the day before. "The medical literature does not describe a case where the flu vaccine caused liver inflammation or liver failure," Dr. Gurevich emphasizes. The mother also denies the possibility.

"The source of the problem is unknown and will probably never be known. All the possibilities were checked, all the tests were done, and do not know. We were told that it is a very rare condition for a child fully healthy to undergo a liver collapse. The best infectious disease specialists have said that if the child turned yellow within a day, then he was probably already sick. "

34 Nombre abreviado: IOM 2011

P 28 (57):

The overwhelming safety and effectiveness of vaccines in current use in preventing serious disease has allowed them to gain their preeminent role in the routine protection of health.

Capítulo 3: Diseñado para ser deficiente

1-20

1-2			
1	Nombre del artículo: Understanding vaccine safety information from the Vaccine Adverse Event Reporting System PMID: 15071280		
	Autor principal/año: Revista: The Pediatric Infectious D		sease Journal
	P 2: Clinical trials of new vaccines have typically involved a relatively small number of individuals (usually fewer than 10 000) and thus cannot usually detect uncommon adverse events.		
2	vaccination: the national Vac System (VAERS)	Post-marketing surveillance for adverse events after vaccination: the national Vaccine Adverse Event Reporting System (VAERS) http://www.fda.gov/downloads/Safety/MedWatch/UCM16849 https://drive.google.com/open?id=1e1suDwD92AF9 TfTW6yk89- PyMkgXqmFD	
	Autor principal/año: NIH/FDA, 1998		
P 1: Even the largest pre-licensure trials (>10,000 persons) are inadequate to as potential to induce rare but serious side effects.			equate to assess the vaccine's
_	T		
3	Nombre abreviado: Varricchio 2004		PMID: 15071280
	P 1		
4	Nombre de la página: About VAERS Sitio web: https://vaers.hhs.gov/about/index#objectives		<u>objectives</u>
5	Nombre de la página: Frequently Asked Questions (FAQs) Sitio web: VAERS website https://vaers.hhs.gov/faq.html		180825190718/https://vaers.h
6	Nombre abreviado: Varricchio 2004		PMID: 15071280
	P 2: VAERS is a passive surveillance, or spontaneous reporting, system. Passive surveil systems rely on health care professionals (or vaccinees) to voluntarily submit report illness after vaccination.		

VAERS

time, and is duplicative.

Nombre de la página: Guide to Interpreting VAERS Data Sitio web: VAERS website https://web.archive.org/web/20180209232915/https:// vaers.hhs.gov/data/dataguide.html "Underreporting" is one of the main limitations of passive surveillance systems, including

8	Nombre de la página: Information for Healthcare Providers	Archivo: https://web.archive.org/web/20171125064142/https://waers.h https://waers.h https://waers.h https://waers.h https://waers.h https://waers.h https://waers.h https://	
	Sitio web: VAERS website https://vaers.hhs.gov/resources/infoproviders.html		
	Nombre abreviado: Varricchio 2004		PMID: 15071280
	P 4: Only selected adverse events, as specified in the Reportable Events Table, are required by law to be reported by vaccine providers. The adverse events listed in the table have been shown to be potentially related to vaccination and therefore may be compensable through the Vaccine Injury Compensation Program (www.hrsa.gov/osp/vicp/) in the absence of an alternate cause.		

Nombre del documento: Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS) https://healthit.ahrq.gov/sites/default/files/docs/publication/r18hs017045-lazarus-final-report-2011.pdf Archivo: https://drive.google.com/open?id=1Uih_BuqrRJoaj4 o3otgqZiWiYgeBIH9H Autor principal/año: Ross Lazarus, 2011 P 6: New surveillance methods for drug and vaccine adverse effects are needed. Barriers to reporting include a lack of clinician awareness, uncertainty about when and what to report,

as well as the burdens of reporting: reporting is not part of clinicians' usual workflow, takes

10	Nombre del artículo: Post-marketing surveillance for adverse events after vaccination: the national Vaccine Adverse Event Reporting System (VAERS) http://www.fda.gov/downloads/Safety/MedWatch/UCM16849 7.pdf Autor principal/año: NIH/FDA, 1998 P 1-2: Thus, when the product leaves the controlled study environment into general clinical use by practitioners, the ability to determine adverse events is questionable.		Archivo: https://drive.google.com/open?id=1e1suDwD92AF9 TfTW6yk89- PyMkgXqmFD
	Nombre abreviado: Varricchio 2004		PMID: 15071280

P 4:

Therefore because VAERS functions primarily as a voluntary reporting system, reporting occurs for only a proportion of suspected adverse events, and this proportion varies depending on the vaccine and the type of event.

11 Nombre del artículo:

Introducing MEDWatch

http://www.fda.gov/downloads/Safety/MedWatch/UCM20141 9.pdf

Archivo:

https://drive.google.com/o pen?id=1 NEuU4vhWzPh 7ZTBVa aiIuTr3Eagcfv

Autor principal/año:

David A. Kessler, 1993

David Kessler, former head of FDA -

Only about 1% of serious events are reported to the FDA, according to one study.

Nombre del documento:

Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS)

https://healthit.ahrq.gov/sites/default/files/docs/publication/r1 8hs017045-lazarus-final-report-2011.pdf

Archivo:

https://drive.google.com/o pen?id=1Uih BuqrRJoaj4 o3otgqZiWiYgeBIH9H

Autor principal/año:

Ross Lazarus, 2011

P 6.

Adverse events from drugs and vaccines are common, but underreported. Although 25% of ambulatory patients experience an adverse drug event, less than 0.3% of all adverse drug events and 1-13% of serious events are reported to the Food and Drug Administration (FDA). Likewise, fewer than 1% of vaccine adverse events are reported.

12

Nombre abreviado:

Varricchio 2004

PMID:

15071280

Some studies have attempted to calculate incidence rates of adverse events with VAERS data along with the Biologics Surveillance Summaries that provide information on vaccine doses distributed in the United States. The most important limitation of the Biologics Surveillance Summaries is that they do not permit determination of the number of persons who actually received vaccine.

13

Nombre abreviado:

Varricchio 2004

PMID: 15071280

Because the VAERS database does not receive complete reporting of all adverse events and because many events it contains lack confirmed diagnoses and/or cannot be attributed to vaccines. VAERS cannot be used to calculate the incidence of adverse reactions after vaccination.

14 Nombre del artículo:

Post-marketing surveillance for adverse events after vaccination: the national Vaccine Adverse Event Reporting System (VAERS)

http://www.fda.gov/downloads/Safety/MedWatch/UCM16849 7.pdf

Archivo:

https://drive.google.com/o pen?id=1e1suDwD92AF9 TfTW6yk89-PyMkgXqmFD

Autor principal/año:

NIH/FDA, 1998

P 3:

Since VAERS receives an estimated 12,000 reports annually, it is difficult to ensure the accuracy and completeness of the database with available resources.

Nombre abreviado: Varricchio 2004

PMID: 15071280

P 2:

It is important to understand that submissions to VAERS are not formal case reports, but rather nonstandardized descriptions of symptoms and signs temporally associated with a vaccination or vaccinations. The information in a report is not necessarily complete, nor is it verified in most cases.

15 Nombre de la página:

Archivo:

Frequently Asked Questions (FAQs)

https://web.archive.org/web/20180825190718/https ://vaers.hhs.gov/faq.html

Sitio web:

VAERS website

https://vaers.hhs.gov/about/faqs#who_reports

16 Nombre del artículo:

PMID:

Postlicensure Safety Surveillance for Quadrivalent Human Papillomavirus 19690307 Archivo:

Recombinant Vaccine

https://drive.google.com/open?id=1MQ IcFiM-5POt66gfIdLaASCdgY9EZcDF

https://jamanetwork.com/journals/jama/fullarticle/ 184421

Autor principal/año: Barbara A. Slade, 2009 Revista: **JAMA**

17 Nombre abreviado: Archivo:

Slade 2009

https://drive.google.com/open?id=1MQIcFiM-

5POt66gfIdLaASCdgY9EZcDF

P 1

18 Nombre abreviado: Archivo:

Slade 2009

https://drive.google.com/open?id=1MQIcFiM-

5POt66gfIdLaASCdgY9EZcDF

P 3:

Of the 8471 manufacturer reports for qHPV AEFIs, 7561 (89%) had insufficient identifying information to permit clinical follow-up or review.

Nombre del artículo:

PMID: 26861066

Completeness of serious adverse drug event reports received by the US Food and Drug Administration in 2014

Revista:

Autor principal/año: Thomas J. Moore, 2016

Pharmacoepidemiology and drug safety

A similar condition exists for reporting of pharmaceutical drugs adverse events.

Overall, 21,595 (86.2%) of serious reports submitted directly to the FDA provided data for all four completeness variables, compared with 271,022 (40.4%) of manufacturer expedited reports and 24,988 (51.3%) of periodic reports. Among manufacturer serious reports, 37.9% lacked age and 46.9% had no event date. Performance by 25 manufacturers submitting 5000 or more reports varied from 24.4% complete on all variables to 67% complete. Patient death cases had the lowest completeness scores in all categories.

19	Nombre abreviado: Slade 2009	Archivo: https://drive.google.com/open?id=1MQIcFiM- 5POt66gfIdLaASCdgY9EZcDF
	P 7: However, VAERS data nee	ed to be interpreted with caution [] data limitations include

20	Nombre abreviado: Slade 2009	Archivo: https://drive.google.com/open?id=1MQIcFiM-5POt66gfIdLaASCdgY9EZcDF
	P 7:the extent of underrepor	ting to VAERS is not known.

21-40

21	Nombre abreviado: Slade 2009	Archivo: https://drive.google.com/open?id=1MQIcFiM-5POt66gfldLaASCdgY9EZcDF
	P 7: AEFI reporting rates also need cautious interpretation, because vaccine distribution data do not allow calculation of age-specific reporting rates and do not provide the numbers of doses actually administered	

22	Nombre abreviado: Slade 2009	Archivo: https://drive.google.com/open?id=1MQIcFiM- 5POt66gfldLaASCdgY9EZcDF
	P 3:	
	, , ,	December 31, 2008, VAERS received 12,424 reports of AEFIs
	following receipt of aHPV	(Table 1) an overall reporting rate of 53.9 reports per 100.000

22	Nombre abreviado:	Archivo:
	vaccine doses distributed.	
	Tollowing receipt of qHPV	(Table 1), an overall reporting rate of 55.9 reports per 100,000

23	Slade 2009	https://drive.google.com/open?id=1MQIcFiM- 5POt66gfIdLaASCdgY9EZcDF
	P 7: The postlicensure safety profile presented here is broadly consistent with safety data from prelicensure trials.	

24	Nombre del documento: GARDASIL Package Insert https://drive.google.com/open?id=1u3cOmn6ehXdR21bNuUQ7He3q6e2jFFxx
	P 8, Tabla 9

25

Nombre abreviado:

Archivo:

Slade 2009

https://drive.google.com/open?id=1MQIcFiM-5POt66gfIdLaASCdgY9EZcDF

P 2:

We also used proportional reporting ratio (PRR), another method to detect potential associations between reported AEFIs and a drug or vaccine, to compare the proportion of selected AEFI reports for qHPV with the proportion of selected AEFI reports for all other vaccines by age group and sex.

The PRR for deaths in 6- to 17-year olds was 1.4 (X^2 =0.42, P=.52). The PRR for deaths in 8- to 29-year-olds was 1.2 ($X^2=0.01$, P=.92). Neither of these met the screening criteria for signal detection.

26

Nombre abreviado: Varricchio 2004

PMID: 15071280

P 4-5:

Attempts to use the VAERS data to calculate internal "relative risks" of specific adverse events for a vaccine, using reports for another vaccine as a "control" group, raise a fifth methodologic issue. Relative risks represent a ratio of incidence rates, and incidence rates cannot be calculated from VAERS data as previously discussed. Relative reporting rates might be calculated, but elevated relative reporting rates calculated from VAERS data may be spurious, regardless of the results of statistical significance testing.

Relative reporting rates from VAERS should not be confused with data-mining methods that attempt to

identify adverse events reported more commonly after one vaccine (or group of vaccines) than after others. Three data-mining methods being applied increasingly to medical product safety data are the proportional reporting rate ratio (PRR), empiric Bayesian and neural network approaches.

[...]

PRR and other data-mining statistics can be biased by differences in usage and reporting of adverse events; thus elevated data-mining statistics do not necessarily reflect a causal relationship between a vaccine and an adverse event. PRR and other data-mining statistics should not be interpreted or presented as relative risks of specific vaccine adverse events. Such statistics should be used only as a hypothesis generation tool and are evaluated in the same manner as other hypotheses generated by VAERS.

27

Nombre abreviado:

Archivo:

Slade 2009

https://drive.google.com/open?id=1MQIcFiM-5POt66gfIdLaASCdgY9EZcDF

Most of the AEFI rates were not greater than the background rates compared with other vaccines, but there was disproportional reporting of syncope and venous thromboembolic events. The significance of these findings must be tempered with the limitations (possible underreporting) of a passive reporting system.

28

Nombre abreviado:

Archivo:

Slade 2009

https://drive.google.com/open?id=1MQIcFiM-5POt66gfIdLaASCdgY9EZcDF

P 7:

The VAERS reporting rate for qHPV is triple the rate for all other vaccines combined[...]

29 Nombre abreviado:

Archivo:

Slade 2009

https://drive.google.com/open?id=1MQIcFiM-5POt66gfIdLaASCdgY9EZcDF

P 7:

The VAERS reporting rate for qHPV is triple the rate for all other vaccines combined, perhaps reflecting greater public attention to HPV than the usual increased reporting following licensure of a new product ("Weber effect").

Reports of VTEs after aHPV immunization should be interpreted with caution due to the multiple limitations of a passive reporting system and the potential effect of widespread media coverage stimulating reporting.

30

Nombre abreviado:

Archivo:

Slade 2009

https://drive.google.com/open?id=1MQIcFiM-

5POt66gfIdLaASCdgY9EZcDF

P 7:

However, VAERS data need to be interpreted with caution, because not all reported events are systematically validated, and many may have only coincidentally followed vaccination. In addition, data limitations include underreporting, inconsistency in the quality and completeness of reported data, stimulated reporting due to extensive news coverage, and reporting biases.

[...]

A further limitation of VAERS reports after qHPV is that a large proportion (68%) come from the manufacturer and most of these reports (89%) do not include sufficient identifying information to allow medical review of the individual cases.

31 Nombre abreviado:

Archivo:

Slade 2009

https://drive.google.com/open?id=1MQIcFiM-

5POt66gfIdLaASCdgY9EZcDF

Most of the AEFI rates were not greater than the background rates compared with other vaccines

32

Nombre del artículo:

Fecha:

Study: HPV Vaccine Mostly Safe

Aug 19, 2009

Archivo:

http://archive.is/tIPgl

Sitio web:

NPR (National Public Radio)

https://www.npr.org/templates/story/story.php?storyId=112035659?storyId=112035659

It still appears that the vaccine is safe and that the benefits outweigh the risks.

Nombre del artículo:

HPV shot found safe, but some experts question its benefits

Fecha:

Aug 18, 2009

Archivo:

http://archive.fo/lOJ2M

Sitio web:

http://edition.cnn.com/2009/HEALTH/08/18/hpv.vaccine.safety/index.html?iref=24hours

"This continues to be a safe vaccine," says lead researcher Dr. Barbara A. Slade, a medical officer at the CDC.

33	Nombre de la página: Human Papillomavirus (HPV) Vaccine Safety	Archivo: http://archive.fo/lL2bv
	Sitio web: CDC website https://vaers.hhs.gov/resources/infoproviders.html	
	Nombre del documento: GACVS Safety update on HPV Vaccines http://www.who.int/vaccine_safety/committee/topics/hpv/130619HPV_VaccineGACVSstatement.pdf	Archivo: https://drive.google.com/open?id=1t WVoxULCHrmFbKCxNOLLFt6tc95 OhmoE
	Autor/año: GACVS, 2013	
	P3	

34 Nombre del documento:

Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS) https://healthit.ahrq.gov/sites/default/files/docs/publ ication/r18hs017045-lazarus-final-report-2011.pdf

Archivo:

https://drive.google.com/open?id=1U ih BuqrRJoaj4o3otgqZiWiYgeBIH9 H

Autor/año:

Ross Lazarus, 2011

P 6:

Adverse events from drugs and vaccines are common, but underreported. Although 25% of ambulatory patients experience an adverse drug event, less than 0.3% of all adverse drug events and 1-13% of serious events are reported to the Food and Drug Administration (FDA). Likewise, fewer than 1% of vaccine adverse events are reported. Low reporting rates preclude or slow the identification of "problem" drugs and vaccines that endanger public health.

35 Nombre de la página:

CDC > NNDSS > Data Collection and Reporting > History

Archivo:

http://archive.is/w2tuo

Sitio web:

CDC website

https://wwwn.cdc.gov/nndss/history.html

In 1879, a Congressional appropriation funded collecting and publishing reports of these notifiable diseases. The authority for weekly reporting and publishing of these cases was expanded by Congress in 1893 to include data from states and municipal authorities.

36 There are many examples. Two are brought here. Archivo: https://drive.google.com/open?i Nombre del documento: d=1114t rRuADPsjiQRNIE-Investigating a Pertussis Outbreak in Mississippi ZyOX7pkSP-QZ http://www.cdc.gov/washington/~cdcatWork/pdf/pertuss is outbreak.pdf Autor/año: CDC, 2007 Nombre de la página: Archivo: Notes from the Field: Measles Outbreak Among Members of a http://archive.is/nCKU Religious Community — Brooklyn, New York, March–June 2013 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6236a5.htm <u>3</u>

Sitio web:

CDC, Morbidity and Mortality Weekly Report (MMWR)

37 Nombre del documento:

Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS) https://healthit.ahrq.gov/sites/default/files/docs/publ ication/r18hs017045-lazarus-final-report-2011.pdf

Archivo:

https://drive.google.com/open?id=1U ih BuqrRJoaj4o3otgqZiWiYgeBIH9 H

Autor/año:

Ross Lazarus, 2011

P 1

38 Nombre abreviado:

Archivo: Lazarus 2011

https://drive.google.com/open?id=1Uih BuqrRJoaj4o3otgqZiW

iYgeBIH9H

To create a generalizable system to facilitate detection and clinician reporting of vaccine adverse events, in order to improve the safety of national vaccination programs.

This research project was funded to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS)

39 Nombre abreviado:

Archivo:

Lazarus 2011

https://drive.google.com/open?id=1Uih BuqrRJoaj4o3otgqZiW

iYgeBIH9H

P 6:

New surveillance methods for drug and vaccine adverse effects are needed. [...]

Proactive, spontaneous, automated adverse event reporting imbedded within EHRs and other information systems has the potential to speed the identification of problems with new drugs and more careful quantification of the risks of older drugs.

40 Nombre de la página:

Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ESP:VAERS) (Massachusetts)

https://digital.ahrq.gov/ahrq-funded-projects/electronic-support-publichealth-vaccine-adverse-event-reporting-system?nav=summaries

Archivo:

http://archive.is/w ip/BhpIK

Sitio web:

AHRQ Agency for Healthcare Research and Quality

This project served as an extension of the Electronic Support for Public Health (ESP) project, an automated system using electronic medical record (EMR) data to detect and securely report cases of statutory notifiable diseases to a local public health authority.

41-50

41	Nombre abreviado: Lazarus 2011	Archivo: https://drive.google.com/open?id=1Uih_BuqrRJoaj4o3otgqZiWiYgeBIH9H
	P 3-4	

42

Nombre abreviado:

Archivo:

Lazarus 2011

https://drive.google.com/open?id=1Uih BugrRJoaj4o3otgqZiW iYgeBIH9H

P 3:

Aim 3. Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data.

The draft was then widely circulated as an initial / working draft for comment by relevant staff in the CDC and among our clinical colleagues at Atrius. In addition to review by the internal CDC Brighton Collaboration liaison, this protocol has also received review & comment via the CDC's Clinical Immunization Safety Assessment (CISA) Network.

43

Nombre abreviado: Lazarus 2011

Archivo:

https://drive.google.com/open?id=1Uih BugrRJoaj4o3otgqZiW iYgeBIH9H

Unfortunately, there was never an opportunity to perform system performance assessments because the necessary CDC contacts were no longer available and the CDC consultants responsible for receiving data were no longer responsive to our multiple requests to proceed with testing and evaluation.

44

Nombre abreviado:

Archivo:

Lazarus 2011

https://drive.google.com/open?id=1Uih BuqrRJoaj4o3otgqZiW iYgeBIH9H

P 5:

The goal of Aim 3 was to comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data. We had initially planned to evaluate the system by comparing adverse event findings to those in the Vaccine Safety Datalink project—a collaborative effort between CDC's Immunization Safety Office and eight large managed care organizations. Through a randomized trial, we would also test the hypothesis that the combination of secure, computer-assisted, clinician-approved, adverse event detection, and automated electronic reporting will substantially increase the number, completeness, validity, and timeliness of physician-approved case reports to VAERS compared to the existing spontaneous reporting system; however, due to restructuring at CDC and consequent delays in terms of decision making, it became impossible to move forward with discussions regarding the evaluation of ESP:VAERS performance in a randomized trial, and compare ESP:VAERS performance to existing VAERS and Vaccine Safety Datalink data. Therefore, the components under this particular Aim were not achieved.

45

Nombre abreviado:

Lazarus 2011

https://drive.google.com/open?id=1Uih BuqrRJoaj4o3otgqZiW iYgeBIH9H

Preliminary data were collected from June 2006 through October 2009 on 715,000 patients, and 1.4 million doses (of 45 different vaccines) were given to 376,452 individuals. Of these doses, 35,570 possible reactions (2.6 percent of vaccinations) were identified. This is an average of 890 possible events, an average of 1.3 events per clinician, per month. These data were presented at the 2009 AMIA conference.

46 Nombre de la página:

Guide to Interpreting VAERS Data

Archivo:

https://web.archive.org/web/20180209232915/ https://vaers.hhs.gov/data/dataguide.html

Sitio web:

VAERS website

https://vaers.hhs.gov/data/dataguide.html

On the other hand, more serious and unexpected medical events are probably more likely to be reported than minor ones, especially when they occur soon after vaccination, even if they may be coincidental and related to other causes.

47 Nombre del artículo:

The Vaccine Safety Datalink: A Model for Monitoring Immunization Safety

http://pediatrics.aappublications.org/content/127/ Supplement 1/S45

Archivo:

21502240

PMID:

https://drive.google.com/open?id=16Yl Uk81p9MTRKh7erSEIzhdMIJF5ngM

Autor principal/año: James Baggs, 2011

Revista: **Pediatrics**

48 Nombre de la página:

Vaccine Safety Datalink

Archivo:

http://archive.is/TKFoi

Sitio web:

HCSRN website

http://www.hcsrn.org/en/Collaboration/Consortia/vsd.html

PI: Frank DeStefano, MD of the CDC Immunization Safety Office Funding agency: Centers for Disease Control and Prevention (CDC)

49 Nombre de la página:

Vaccine Safety Datalink (VSD)

Archivo:

http://archive.is/KtqCB

Sitio web:

CDC website

https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vsd/data-sharingguidelines.html

50

Nombre del documento:

Vaccine Safety Research, Data Access, and Public Trust

https://www.nap.edu/catalog/11234/vaccine-safety-research-data-access-and-public-trust

Autor/año:

IOM 2005

P 96:

One of the key goals of the Vaccine Safety Datalink (VSD) data sharing program should be maintenance of public trust in the use of the VSD to draw scientific conclusions about vaccine safety. Because of the contentious nature of some of the issues surrounding the VSD and the strained relationship between the Centers for Disease Control and Prevention (CDC) and some people who have been critical of CDC's vaccine safety activities, the committee recognizes that there may be public concerns about the role of CDC in reviewing proposals to use VSD data and in setting the VSD research agenda. A perception of bias in the VSD proposal-review process and in the priorities established for the VSD research plan could jeopardize public confidence in VSD activities. There are legitimate reasons for public concern about the independence and fairness of the review of VSD data sharing proposals and of determinations about when and how to release preliminary findings of VSD analyses.

The lack of transparency of some of those processes affects the trust relationship between the National Immunization Program (NIP) and some members of the general public.

P 97-98

The limitations of the VSD data sharing program and the limited ability of independent external researchers to conduct high-quality corroboration studies or studies of new hypotheses create a special need to involve the public in the priority-setting process for the VSD research plan. Only NIP-affiliated or MCO-affiliated researchers have access to VSD data for events before and after January 1, 2001, for corroboration studies and studies of new hypotheses, so independent external researchers may not be able to conduct studies that members of the public consider to have high priority.

[...]

In view of the limited ability of independent researchers to conduct high-quality VSD studies of new hypotheses and the limited ability of the public to provide input on which VSD studies should be pursued with federal tax dollars, there needs to be greater opportunity for input into the setting of priorities in the VSD research plan and greater transparency of the priority-setting process.

Capítulo 4: Primer curso de epidemiología

1-20

1	Nombre del artículo: The history of the discovery of the cigarettee-lung cancer link: evidentiary traditions, corporate denial, global toll https://tobaccocontrol.bmj.com/content/tobaccocontrol/21/2/87.full.pdf		PMID: 22345227 Archivo: https://drive.google.com/open?id=1YA WDfVhDNWb1O- SiwIRQDk9IF1jC7IUw
	Autor principal/año: Robert N Proctor, 2012	Revista: Tobacco Contro	ıl
	P 1: Lung cancer was still a very rare disease; so rare, in fact, that medical professors when confronted with a case sometimes told their students they might never see another.		

2	Nombre del artículo: Research on Smoking and Lung C Landmark in the History of Chron Epidemiology http://www.ncbi.nlm.nih.gov/pmc 89239/pdf/yjbm00061-0033.pdf	ic Disease	PMID: 2192501 Archivo: https://drive.google.com/open?id=1BW QHwQt9syfRTHCefTfRF1f6QblhOLk b
	Autor principal/año: Colin White, 1990	Revista: THE YALE JOURNAL OF BIOLOGY AND MEDICINE	
	P 3		

3	Nombre abreviado: White 1990	Archivo: https://drive.google.com/open?id=1BWQHwQt9syfRTHCefTfR F1f6QblhOLkb
	1	lture has made estimates of the average annual consumption of

tobacco products in the United States among persons aged 15 years and over, from 1900 to 1960. During this period the number of cigarettes marketed, per person, increased by a factor of about 80, from 50 to 3,900; the sale of pipe tobacco decreased from 1.6 to .6 pounds, and the number of cigars fell from 110 to 60, per person.

4	Nombre abreviado:	Archivo:
-	White 1990	https://drive.google.com/open?id=1BWQHwQt9syfRTHCefTfR
		F1f6QblhOLkb

P 2:

Speculation about these factors continued, but there was also much criticism of the view that the reported increase in lung cancer was credible. These criticisms led to debate throughout the forties and early fifties. An editorial in the British Medical Journal in 1942 stated "It is doubtful whether the higher incidence of cancer of the lung observed in recent years is real or only apparent". Factors which were listed as likely to be responsible for an artificial increase were better diagnosis of the disease and increased longevity of the population.

Nombre abreviado: White 1990 Archivo: https://drive.google.com/open?id=1BWQHwQt9syfRTHCefTffF1f6QblhOLkb
--

P 4:

Doll has noted that it had been known long before 1950 that smoking could cause disease, but it was "not until 1950 that a large amount of data was obtained in a sufficiently representative and responsible way to lead more than a handful of people to believe that smoking might actually be responsible for causing a material amount of disease" [28]. The two case-control studies in 1950 that were not only large but also well conducted were by Wynder and Graham in the United States [29] and by Doll and Hill in England

	wynder and Granam in the Officed States [29] and by Don and Hill in England.		
6	Nombre abreviado: White 1990	Archivo: https://drive.google.com/open?id=1BWQHwQt9syfRTHCefTfR F1f6QblhOLkb	
	P 5-6		
7	Nombre abreviado: White 1990	Archivo: https://drive.google.com/open?id=1BWQHwQt9syfRTHCefTfR F1f6QblhOLkb	
	P 6-7		
8	Nombre abreviado: White 1990	Archivo: https://drive.google.com/open?id=1BWQHwQt9syfRTHCefTfRF1f6QblhOLkb	
	P 9, 11		
9	Nombre abreviado:	Archivo:	

9	Nombre abreviado: Proctor 2012	Archivo: https://drive.google.com/open?id=1YAWDfVhDNWb1O-SiwIRQDk9lF1jC7IUw
	P 2	

10 Nombre abreviado: Archivo: White 1990 https://drive.google.com/open?id=1BWQHwQt9syfRTHCefTfR F1f6QblhOLkb

In 1958, by which time there was substantial epidemiologic evidence on smoking as a risk factor for lung cancer, the British Medical Journal commented as follows on this evidence: "The fact that experimental work has not provided complete and irrefutable proof has tended to hinder its wholehearted acceptance". A representative of the tobacco industry described this objection more forcefully, by stating that the search for chemical carcinogens in tobacco "has now been continued so long in the hands of so many able investigators and with such meager results that many scientists no longer believe it likely that tobacco smoke exerts any significant effect as a direct or specific carcinogen for human tissues". In 1962, Lancet summarized the results of the chemical analysis of tobacco products by noting "no carcinogen has been found in adequate concentration in tobacco smoke; no genuine lung cancers have been produced experimentally".

11

Nombre abreviado:

Archivo: Proctor 2012

https://drive.google.com/open?id=1YAWDfVhDNWb1O-

SiwIRQDk9lF1jC7IUw

P 2:

Tobacco industry laboratories conducted their own investigations: Brown and Williamson researchers identified benzpyrene in cigarette smoke in 1952, and by the end of the decade cigarette manufacturers had characterised several dozen carcinogens in cigarette smoke, including arsenic, chromium, nickel and a veritable zoo of polycyclic aromatic hydrocarbons (chrysene, methylcholanthrene, dibenzanthracene, dibenzacridene, etc). As Philip Morris research director Helmut Wakeham put it in 1961, carcinogens were found in 'practically every class of compounds in cigarette smoke'.

12

Nombre abreviado:

Archivo:

White 1990

https://drive.google.com/open?id=1BWQHwQt9syfRTHCefTfR

F1f6QblhOLkb

P 8:

The Surgeon General of the United States took a similar position: "The weight of the evidence is increasingly pointed in one direction: that excess smoking is one of the causative factors in lung cancer".

13

Nombre de la página:

Archivo:

Statistical Language - Correlation and Causation

http://archive.is/fZLZR

Sitio web:

Australian Bureau of Statistics

http://www.abs.gov.au/websitedbs/a3121120.nsf/home/statistical+language+-

+correlation+and+causation

Correlation is a statistical measure (expressed as a number) that describes the size and direction of a relationship between two or more variables. A correlation between variables, however, does not automatically mean that the change in one variable is the cause of the change in the values of the other variable.

Causation indicates that one event is the result of the occurrence of the other event; i.e. there is a causal relationship between the two events. This is also referred to as cause and effect.

14

Nombre de la página:

Archivo:

Emphysema

http://archive.is/WKTsi

Sitio web:

emedicinehealth

http://www.emedicinehealth.com/emphysema/article_em.htm

http://www.emedicinehealth.com/emphysema/page2 em.htm

The importance of cigarette smoking as a risk factor for developing emphysema cannot be overemphasized. Cigarette smoke contributes to this disease process in two ways. It destroys lung tissue, which results in the obstruction of air flow, and it causes inflammation and irritation of airways that can add to air flow obstruction.

15

Nombre de la página:

Archivo:

Epidemiology

http://archive.is/QP9g

Sitio web:

EXTOXNET

Extension Toxicology Network

http://pmep.cce.cornell.edu/profiles/extoxnet/TIB/epidemiology.html

Epidemiological studies can never prove causation; that is, it cannot prove that a specific risk factor actually causes the disease being studied. Epidemiological evidence can only show that this risk factor is associated (correlated) with a higher incidence of disease in the population exposed to that risk factor. The higher the correlation the more certain the association, but it cannot prove the causation

16 Título del libro: Publicador: **CAUSALITY** Oxford University Press

Autor principal/año: Phyllis Illari, 2014

P 32:

Rothman (1976) makes the point that in health situations what we call 'causes' are in fact components of sufficient causes, and are not sufficient in themselves. For instance, the measles virus is said to be the cause of measles, but in fact the 'complete sufficient cause' of measles also includes lack of immunity to the virus and exposure to the virus.

Rothman illustrates his ideas by means of 'causal pies'—see Figure 4.1—still used in epidemiology now. He thinks that a sufficient cause of a disease is generally not one single causal factor, but a complete 'causal mechanism'. Rothman takes a causal mechanism to be a minimal set of conditions and events that are sufficient for the disease to occur. In this perspective, no specific event condition or characteristic is sufficient, by itself, to produce the disease. So the definition of 'cause' does not describe a complete causal mechanism, but only a component of it.

17 Nombre de la página: Archivo: Research on Back Sleeping and SIDS http://archive.is/rZIPH

Sitio web:

NIH - Safe to Sleep

https://www1.nichd.nih.gov/sts/campaign/science/Pages/backsleeping.aspx

The single most effective action that parents and caregivers can take to lower a baby's risk of SIDS is to place the baby to sleep on his or her back for naps and at night.

Compared with back sleeping, stomach sleeping carries between 1.7 and 12.9 times the risk of SIDS. The mechanisms by which stomach sleeping might lead to SIDS are not entirely known. Studies suggest that stomach sleeping may increase SIDS risk through a variety of mechanisms, including:

Increasing the probability that the baby re-breathes his or her own exhaled breath, leading to carbon dioxide buildup and low oxygen levels; Causing upper airway obstruction; Interfering with body heat dissipation, leading to overheating.

Whatever the mechanism, evidence from numerous countries—including New Zealand, Sweden, and the United States—suggests that placing babies on their backs to sleep results in a substantial decline in the SIDS rate compared to placing babies on their stomachs to

18	Nombre de la página: Prospective study	Archivo: http://archive.is/zKOgQ
	Sitio web: The Free Dictionary	

Prospective study: an epidemiologic study in which the groups of individuals (cohorts) are selected on the bases of factors that are to be examined for possible effects on some

For example, the effect of exposure to a specific risk factor on the eventual development of a particular disease can be studied. The cohorts are then followed over a period of time to determine the incidence rates of the outcomes being studied as they relate to the original factors in question.

The term prospective usually implies a cohort selected in the present and followed into the future...

19 Nombre de la página:

Retrospective study

Archivo:

http://archive.is/tLNNW

Sitio web:

The Free Dictionary

https://medical-dictionary.thefreedictionary.com/retrospective+study

Retrospective study:

a study in which a search is made for a relationship between one (usually current) phenomen on or condition and another that occurred in the past. An example is a study of the family histories of young women diagnosed as having clear cell adenomas of the vagina, which yielded a relationship between the administration of diethy lstilbestrol to the mothers of the women during pregnancy and the development of the condition in the daughters.

20

Nombre de la página:

Archivo:

Types of Epidemiological Studies

http://archive.is/3Yd7R

Sitio web:

New Health Advisor

http://www.newhealthadvisor.com/Types-of-Epidemiological-Studies.html

21-29

21 Nombre del documento:

Reference Manual on Scientific Evidence https://www.nap.edu/read/13163/chapter/12#583

Autor principal/año:

Federal Judicial Center

National Research Council, 2011

P 583:

The second major reason for an invalid outcome in epidemiologic studies is systematic error or bias. Bias may arise in the design or conduct of a study, data collection, or data analysis. The meaning of scientific bias differs from conventional (and legal) usage, in which bias refers to a partisan point of view. When scientists use the term bias, they refer to anything that results in a systematic (nonrandom) error in a study result and thereby compromises its validity. Two important categories of bias are selection bias (inappropriate methodology for selection of study subjects) and information bias (a flaw in measuring exposure or disease in the study groups).

22 Nombre del artículo: PMID: Alcohol Consumption and Lung Cancer 11489747 http://cebp.aacrjournals.org/content/10/8/813.full Autor principal/año: Revista: Elisa V. Bandera, 2001 Cancer Epidemiology Biomarkers and prevention

23 Nombre de la página: Archivo:

Oxford Textbook of Global Public Health http://archive.is/bnzxf

Sitio web:

Oxford Medicine Online

http://oxfordmedicine.com/view/10.1093/med/9780199661756.001.0001/med-9780199661756-chapter-103

The 'art' of epidemiology is knowing when and how to apply the various epidemiological strategies creatively to answer specific health questions.

24 Nombre del artículo: PMID: Identifying and Avoiding Bias in Research 20679844

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2 917255/

Autor principal/año: Revista:

Christopher J. Pannucci, 2010 Plastic and Reconstructive Surgery

A general explanation of research biases.

Archivo: 25 Nombre del documento:

Adverse Effects of Vaccines: Evidence and Causality http://nationalacademies.org/hmd/reports/2011/adverse -effects-of-vaccines-evidence-and-causality.aspx

https://drive.google.com/open?id= 1nl18cdV y3TtQBzoCq0tSiuYm HF1 yYQ

Autor/año: IOM, 2011

P 17 (46):

Epidemiologic analyses also cannot identify with certainty which individual in a population at risk will develop a given condition.

26 Nombre abreviado: Archivo: IOM 2011

https://drive.google.com/open?id=1nl18cdV y3TtQBzoCq0tSiu YmHF1 yYQ

P 50 (79):

Mechanistic evidence, particularly that emerging from case reports, occasionally can provide compelling evidence of an association between exposure to a vaccine and an adverse reaction in the individual being studied, but it provides no meaningful information about the degree of risk to the population or even to other individuals who have the same predisposing characteristics.

27 Nombre abreviado: Archivo: IOM 2011 https://drive.google.com/open?id=1nl18cdV v3TtOBzoCq0tSiu YmHF1 yYQ

P 50 (79):

Epidemiologic analyses are usually unable to detect an increased or decreased risk that is small, unless the study population is very large or the difference between the groups (e.g., vaccinated vs. unvaccinated) at risk is very high... These studies also can fail to detect risks that affect a small subset of the population.

28 Nombre abreviado: Archivo: IOM 2011 https://drive.google.com/open?id=1nl18cdV_y3TtQBzoCq0tSiu YmHF1 yYQ

P 49 (78):

Epidemiologic evidence, by contrast, can support ("favors acceptance of") a causal association or can support the absence of ("favors rejection of") a causal association in the general population and in various subgroups that can be identified and investigated, unless or until supportive mechanistic evidence is discovered or a rare, susceptible subgroup can be identified and investigated.

29	Nombre abreviado: IOM 2011	Archivo: https://drive.google.com/open?id=1nl18cdV_y3TtQBzoCq0tSiu
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Capítulo 5: Ciencia intencionadamente sesgada

1-20

1 Nombre del documento:

DPT Vaccine Roulette 1982

https://www.youtube.com/watch?v=qpUsg4bDH5w

٥r

https://www.youtube.com/watch?v=VtOh6vFnWg4

2 Nombre del artículo:

The pertussis vaccine controversy in Great Britain, 1974-

1986

https://online.manchester.ac.uk/bbcswebdav/orgs/I3075-COMMUNITY-MEDN-1/DO%20NOT%20DELETE%20-

<u>%20PEP%20Quality%20and%20Evidence/QE-PEP-HTML5/media/F8430185-03E3-C538-8362-</u>

DE46812E97BE.pdf

Autor principal/año: Revista: Jeffrey P. Baker, 2003 Vaccine

P 1-2

3 Nombre del artículo:

Mercury, Vaccines, and Autism One Controversy, Three Histories

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2

376879/pdf/0980244.pdf

PMID:

18172138

Archivo:

https://drive.google.com/open?id=1ut2 gq2Ph7rf7z4pm-C2T8shDuxODqiBY

PMID:

12922137

Archivo:

https://drive.google.com/ope n?id=1RSZoULsPxrzRj13o7

MIlpzukCYJC-3z6

Autor principal/año: Revista:

Jeffrey P. Baker, 2008 American Journal of Public Health

"Autism and its Histories" chapter.

4 Nombre abreviado:

Archive

Baker 2008

https://drive.google.com/open?id=1ut2gq2Ph7rf7z4pm-

C2T8shDuxQDqiBY

P 7:

The events that would bring these three histories together began in 1997, when New Jersey Representative Frank Pallone, representing a district concerned about environmental mercury poisoning, appended a rider to the FDA Modernization Act of that year to assess all of the agency's products for mercury content. In response, the Center for Biologics Evaluation and Research (CBER) at the FDA initiated a formal risk assessment of thimerosal in vaccines beginning in April 1998.

[...]

Although acknowledging the many uncertainties involved, the FDA responded by inviting vaccine advisory bodies for consultation in June 1999. There followed a rapid series of meetings and conference calls involving representatives of the American Academy of Pediatrics and the Centers for Disease Control and Prevention (CDC), culminating in a joint statement released on July 9, 1999. Although noting that there was no evidence that the use of thimerosal as a vaccine preservative had caused any true harm, the groups agreed that

"thimerosal-containing vaccines should be removed as soon as possible" given the concerns raised by the Environmental Protection Agency's guidelines.

5 Nombre abreviado: Archivo: Baker 2008

https://drive.google.com/open?id=1ut2gq2Ph7rf7z4pm-C2T8shDuxODqiBY

Meanwhile, the third of the historical streams, represented by parents within the "alternative" autism community, rapidly entered the debate. As detailed by journalist David Kirby, it was in fact a group of parents of autistic children (rather than parental organizations critical of vaccination such as the National Vaccine Information Center) who first seized upon thimerosal as an explanation for the autism epidemic.

6 Nombre abreviado: Archivo: https://drive.google.com/open?id=1ut2gq2Ph7rf7z4pm-Baker 2008 C2T8shDuxODaiBY

P 7-8:

Parents organized effectively in the political realm as well. The self-designated "Mercury Moms" created an advocacy organization, Safe Minds. They were instrumental in persuading Congressman Burton to shift his focus from measles-mumps-rubella to thimerosal in his congressional hearings. And they organized successfully to oppose a rider to the Homeland Security Bill in 2003 that would protect thimerosal's manufacturer from legal action.

7 Nombre de la página: Archivo: No vaccine for the scaremongers http://archive.is/BAwsA

Nombre del artículo:

Bulletin of the World Health Organization

http://www.who.int/bulletin/volumes/86/6/08-030608/en/

Despite these successes, vaccine anxieties continue to periodically impede this highly effective public health measure. In certain industrialized countries, most notably the USA, public concern has shifted its focus from the diseases vaccination can prevent, to the risks of the vaccines themselves. The Internet has become a significant channel for anti-vaccination views. The popular video-sharing web site YouTube offers a plethora of anti-vaccination clips. The Internet has also become a forum for alternative medicine practitioners to present their anti-vaccination ideas and promote alternative products.

Anti-Vaccination Movement and Parental Refusals of Immunization of Children in USA	
https://ac.els-cdn.com/S0031393912000042/1-	Archivo:
<u>s2.0-S0031393912000042-</u>	https://drive.google.com/open?id=1zK
main.pdf? tid=5c8518f3-e7ca-4c27-9453-	ynoN4jsw_8X1RcstnPtUK4xOw- 6Wwr
70eb7f0defdf&acdnat=1537379447_77722dce80 b2060107f2ee77ed7af03d	OWWI
Autor principal/año: Marian Ołpinski, 2012	Revista: Pediatria Polska

PMID:

P 4:

The most influential medium for parents beliefs about immunizations seems to be Internet. Approximately 74% of Americans have Internet access. In 2006, 16% of users searched online for information on immunizations or vaccinations. Over half (52%) of users believe "almost all" or "most" information on health sites are credible, yet the availability of inaccurate and deceptive information online has labeled the Internet a "modern Pandora's box".

8	Nombre del artículo: Vanishing Vaccinations: Why Are So Many Americans Opting Out of Vaccinating Their Children?	PMID: 15568260
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Autor principal/año: Revista:

Steve P. Calandrillo, 2004 University of Michigan Journal of Law Reform

From the abstract:

The internet worsens fears regarding vaccination safety, as at least a dozen websites publish alarming information about the risks of vaccines. Increasing numbers of parents are refusing immunizations for their children and seeking legally sanctioned exemptions instead, apparently fearing vaccines more than the underlying diseases that they protect against. A variety of factors are at play: religious and philosophical beliefs, freedom and individualism, misinformation about risk, and overperception of risk. State legislatures and health departments now face a difficult challenge: respecting individual rights and freedoms while also safeguarding the public welfare.

9	Nombre del artículo: The Psychology of Anti-Vaxers: How Story Trumps Science	Fecha: Oct 19, 2014
	Sitio web: The Atlantic	Archivo: hhttp://archive.is/uOhEJ
	http://www.theatlantic.com/health/archive/2014/10/how-anti- vaccine-fear-takes-hold/381355/	

For example –

Jacklyn Smoot, a 26 year-old new mother from Orange, California, feels torn. Her son's pediatrician and the Centers for Disease Control and Prevention assure her that vaccines are safe and effective. Smoot hears personal stories from vaccine skeptics like her mother, some friends, and Internet bloggers, however, who warn that vaccines can cause injury or death. She wonders who is right.

Smoot's struggle began when she got a flu shot in December 2012. Her mother's reaction surprised her. "She said, 'What? But you're pregnant!' She scared me," Smoot says. "I found myself online for three hours trying to figure out if it was a good idea that I had gotten the flu shot while I was pregnant."

Then she got on the Internet.

Smoot downloaded the recommended immunization schedule from the CDC website. She looked up each vaccine on the schedule. Although she says she tried to look at a variety of trustworthy websites, she can only remember reading any information supporting vaccination on the CDC website. Smoot, however, says she does not trust doctors and scientists. "I know they're just going to tell me they're safe, and they're recommended, and this is what you're supposed to do," she says.

Dr. Neal Halsey is a professor at the Johns Hopkins Bloomberg School of Public Health and the School of Medicine. He runs the Institute for Vaccine Safety, providing independent assessment of and education on vaccine safety. "The vaccines we have available that are recommended for routine use in children are very safe vaccines," he says.

Dr. Diane Griffin, a virologist and chair of the molecular biology and immunology department at Johns Hopkins, agrees. "Oh, yes, vaccines are very safe," she says. According to the CDC, vaccines in the United States are the most safe and effective immunizations in history. The CDC's website says severe reactions to vaccines "occur so rarely that the risk is difficult to calculate."

"I probably find more information that says vaccines aren't safe," she says. "I think it's only because ..." She pauses. "Well, I don't really know. It could be maybe what I'm paying attention to more."

Nombre del documento:

Talking with Parents about Vaccines for Infants

https://www.cdc.gov/vaccines/hcp/patient-ed/conversations/downloads/talk-infants-coloroffice.pdf

Autor/año:	Archivo:
CDC. 2012	https://drive.google.com/open?id=1CmLPr0
	40TWioZcFMuyqifdm9GT9rsctH

10 Nombre del documento: Addressing Common Concerns of Vaccine-Hesitant Parents https://www.aap.org/en-us/Documents/immunization vaccine-hesitant%20parent final.pdf Archivo: Autor/año: https://drive.google.com/open?id=1-American Academy of Pediatrics, 2013 EzjdlPKRJgqy02o6xR WypH7unz6fq6 The document contains examples of "parental concerns" and studies who answer them.

11	Nombre del artículo: After \$1 billion, experts see progress on autism's causes	Fecha: Sep 4, 2012
	Sitio web: USA TODAY http://usatoday30.usatoday.com/news/health/story/2012-04-09/researchers-autism-causes/54129282/1	Archivo: http://archive.is/ixi6Z

More than \$1 billion has been spent over the past decade searching for the causes of autism. In some ways, the research looks like a long-running fishing expedition, with a focus on everything from genetics to the age of the father, the weight of the mother, and how close a child lives to a freeway.[...] The lion's share of money for finding a cause has been spent on

But even genetics enthusiasts acknowledge that genes are only part of the answer. Studies of identical twins have shown that autism can occur in one and not the other, meaning something outside a child's DNA is triggering the disorder in many cases. Some cases may be entirely due to other causes, Dawson said.

That broad "other" category means "environmental" influences — not necessarily chemicals, but a grab bag of outside factors that include things like the age of the father at conception and illnesses and medications the mother had while pregnant.

12	Nombre del artículo: Vaccination Patterns in Children A Diagnosis and in TheirYounger St https://relaped.com/wp-content/up	iblings		PMID: 29582071
	Autor principal/año: Ousseny Zerbo, 2018			
	P 2: The etiology of ASD is unknown for the vast majority of cases; however, study findings suggest that both genetic and environmental factors have a role.			
	Nombre de la página: Causes-Autism spectrum disorder (ASD) Archivo: http://archive		Archivo: http://archive.is/7	<u>kOxv</u>
	Sitio web: NHS website http://www.nhs.uk/Conditions/Autistic-spectrum-disorder/Pages/Causes.aspx			
	Most researchers believe that certain genes a child inherits from their parents could make them more vulnerable to developing ASD. Cases of ASD have been known to run in families. For example, younger siblings of children with ASD can also develop the condition, and it's common for identical twins to both develop ASD. No specific genes linked to ASD have been identified, but it may be a presenting feature of some rare genetic			

syndromes, including Fragile X syndrome, Williams syndrome and Angelman syndrome.

Nombre del artíc	culo:	Fecha:	
Autism's Tangled Varied Mutations	Genetics Full of Rare and	June 8, 2011	
Sitio web: Scientific America	an	Archivo: http://archive.is/jftAe	
of genes causes au families that had or responsible for the patient. Even some	Large genetic studies have ruled out the idea that the malfunction of a universal gene or set of genes causes autism. And the new papers, which assessed the genomes of about 1,000 families that had only one autistic child, revealed that the genetic mutations that are likely responsible for the disorder are exceedingly rare—sometimes almost unique to an individual patient. Even some of the most common point of mutations were found in only about 1 percent of autistic children.		
1 -	culo: disorders—A genetics	PMID: 21358411	
	http://www.nature.com/gim/journal/v13/n4/full/gim9201151a.html	Archivo: https://drive.google.com/open?id=1pK0vm5 TYvqNPFull_FgCyOFbKpQi4dM7	
Autor principal/a Judith H Miles, 20		Revista: Genetics in Medicine	
studies would lead most discoveries h	P 1: Although it was initially assumed that major genome-wide and candidate gene association studies would lead most directly to common autism genes, progress has been slow. Rather, most discoveries have come from studies of known genetic disorders associated with the behavioral phenotype.		

13	Nombre del artículo: Vaccine case draws new attention to autism debate	Fecha: Mar 7, 2008
	Sitio web: CNN http://edition.cnn.com/2008/HEALTH/conditions/03/06/vaccines.autism/index.html	Archivo: http://archive.is/qGAsI
	Numerous studies have shown no link between illness and the vaccines, public health officials have long contended.	

14	Nombre del artículo: Placebo use in vaccine trials: Recommendations of a WHO expert panel https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4 157320/		PMID: 24768580 Archivo: https://drive.google.com/open?id=1mX 3RrTo-Jq6eEC-H S1blqjDVfXYosUv
	Autor principal/año: Annette Rid, 2014	Revista: Vaccine	
	P 2: Randomised, placebo-controlled trials are widely considered the gold standard for evaluating the safety and efficacy of a new vaccine.		

15	Pages dedicated to Marie Curie, Alexander Fleming and Louis Pasteur:
_	http://lib.cet.ac.il/pages/item.asp?item=7936 Archivo: http://archive.is/Uiya1
	http://lib.cet.ac.il/pages/item.asp?item=7935 Archivo: http://archive.is/xNcNK
	http://lib.cet.ac.il/pages/item.asp?item=7931 Archivo: http://archive.is/2DQgz

16 Nombre del documento:

Responsible Science, Volume I

https://www.nap.edu/catalog/1864/responsible-science-volume-i-ensuring-the-integrity-ofthe-research

Archivo: Autor/año:

https://drive.google.com/open?id=1782CN NAS, 1992 gkLfXgxmkd3NtBj0diDm8PJjBb5

P 36:

Until the past decade, scientists, research institutions, and government agencies relied solely on a system of self-regulation based on shared ethical principles and generally accepted research practices to ensure integrity in the research process. Among the very basic principles that guide scientists, as well as many other scholars, are those expressed as respect for the integrity of knowledge, collegiality, honesty, objectivity, and openness. These principles are at work in the fundamental elements of the scientific method, such as formulating a hypothesis, designing an experiment to test the hypothesis, and collecting and interpreting data. In addition, more particular principles characteristic of specific scientific disciplines influence the methods of observation; the acquisition, storage, management, and sharing of data; the communication of scientific knowledge and information; and the training of younger scientists. How these principles are applied varies considerably among the several scientific disciplines, different research organizations, and individual investigators.

17 Nombre del documento:

Responsible Science, Volume I

https://www.nap.edu/catalog/1864/responsible-science-volume-i-ensuring-the-integrity-ofthe-research

Archivo: Autor/año:

https://drive.google.com/open?id=1782CNg NAS, 1992 kLfXgxmkd3NtBi0diDm8PJiBb5

P 95:

Regardless of the incidence, the panel emphasizes that even infrequent cases of misconduct in science are serious matters. The number of confirmed incidents of misconduct in science, together with the possibility of underreporting and the results presented in some preliminary studies, indicate that misconduct in science is a problem that cannot be ignored. The consequences of even infrequent cases of misconduct in science require that attention be given to appropriate methods of treatment and prevention.

18	Nombre del artículo: The 7 biggest problems facing science, according to 270 scientists	Fecha: Sep 7, 2016
	Sitio web: VOX	Archivo: http://archive.is/FvXSC
	http://www.vox.com/2016/7/14/12016710/science-challeges-research-funding-peer-review-process	

19	Nombre de la página: Budget	Archivo: http://archive.is/QP9Wz
	Sitio web: NIH website https://www.nih.gov/about-nih/what-we-do/budget	

20	Nombre de la página:	Archivo:
	Government Funding of Scientific Research	http://archive.is/xYL6g

Sitio web:

NSF website

https://www.nsf.gov/nsb/documents/1997/nsb97186/nsb97186.htm#federal

Within the Federal budget, there should be an overall strategy for research, with areas of increased and areas of decreased emphasis... To ensure the most effective use of Federal discretionary funding it is essential that agreement be reached on which fields and which investment strategies hold the greatest promise for new knowledge that will contribute most effectively to better health, greater equity and social justice, improved living standards, a sustainable environment, a secure national defense, and to extending our understanding of nature.

A Yale scientist confesses about "funding biases" he performed in some of his studies, funded by commercial as well as government agencies, and explains that pressure system under which governmental bodies funding research are operating.

Fecha: June 13, 2014

Nombre del artículo:

Research Funding: When Is the Money Dirty?

Archivo:

Sitio web: **Huffington Post**

https://www.huffingtonpost.com/david-katz-md/researchfunding-when-is- b 5493613.html

http://archive.is/Mz2fY

All research starts with biased funders and researchers — because in the absence of such bias, it would be research no one would bother doing. I don't think anyone runs studies in the absence of hopes and preferences pertaining to the outcomes.

So, too, do all funders. While the NIH does not generally manufacture and sell the interventions it studies, it certainly does care about the outcomes. NIH, too, must justify its existence, and budget — just not to shareholders. NIH and all federal agencies are accountable to Congress, and by extension to us, in our tax-paying multitudes. NIH competes in the federal budget with other societal priorities (and, no doubt, pork-barrel boondoggles); and perhaps more intensely, the various institutes compete with one another for slices of the common pie. Too many negative study results tend to suggest that an institute is not spending money all that well and wisely — and affect the outcome of that competition. Even NIH program officers are biased about study outcomes.

21-40

	21	Nombre del artículo: Follow the Funding	Fecha: May 1, 2015
		Sitio web:	Archivo:
		The Scientist http://www.the-	http://archive.is/Wpcec
		scientist.com/?articles.view/articleNo/42799/title/Follow-the-	
1		Funding/	

A few years ago, David Sinclair's lab was slipping through his fingers. With grant money running dry and the outlook for overall federal research budgets bleak, the Harvard geneticist was losing lab members because he couldn't support them with funding from the National Institutes of Health (NIH), as he had done in years past. Sinclair says his 18person-strong group dwindled to just four or five people. "And that was painful," he recalls. "I had to let people go for lack of money."

And Sinclair says he's not alone. "Even at a place like Harvard, I know [other] labs that have downsized dramatically and even closed down," he says. "So it's hit across the board." 22

A few articles from the scientific literature, demonstrating the high importance of submitting a research proposal.

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0133061#pone.0133061.ref 012

Archivo: http://archive.is/B5y7y

http://www.bmj.com/content/317/7173/1647

Archivo: http://archive.is/ao0fc

http://www.apa.org/gradpsych/2016/01/research-funding.aspx

Archivo: http://archive.is/R4iUH

23

Dr. Boyd Hally desribes how the NIH stopped funding his research on Alzheimer disease when he wanted to investigate mercury exposure as a possible cause.

https://www.youtube.com/watch?v=8AQxkIcXrt0

24

Nombre de la página:

What are the Chances of Getting Funded?

Archivo:

http://archive.is/wiTtL

Sitio web:

NIH website

https://nexus.od.nih.gov/all/2015/06/29/what-are-the-chances-of-getting-funded/

According to NIH data, only 20-30% of applying researchers are granted funding of their research proposals.

25

Nombre del documento:

Financing Vaccines in the 21st Century: Assuring Access and Availability https://www.nap.edu/catalog/10782/financing-vaccines-in-the-21st-century-assuring-accessand-availability

Archivo: Autor/año:

https://drive.google.com/open?id=15 AilgxcXk IOM. 2004 feOJaNbCgScTr2MbeuMTuD

P 116:

The major contributors to vaccine research in the United States are companies conducting industrial research, government agencies (the National Institutes of Health [NIH] and the Department of Defense [DoD]), and the academic institutions they fund.

Nombre del artículo:

PMID:

United States vaccine research: a delicate fabric of public and private collaboration. National Vaccine Advisory Committee.

9411380

Autor principal/año: Revista: **NVAC 1997 Pediatrics**

Tabla 2 on P 2:

Source	Estimated Amoun in Millions
Taxpayers NIH	\$ 500 (36%)
Intramural Grants to academia	
Vaccine sales	\$ 650 (46%)
Large companies (15 to 20% sales)	
Risk capital	\$ 250 (18%)
Large companies (15 to 20% sales) Risk capital	
Small companies Total	\$1400 (100%)

26 One example of many -Archivo: http://archive.is/pfgvJ Nombre de la página: GlaxoSmithKline to Plead Guilty and Pay \$3 Billion to Resolve Fraud Allegations and Failure to Report Safety Data Sitio web: US Department of Justice, Office of Public Affairs https://www.justice.gov/opa/pr/glaxosmithkline-plead-guilty-and-pay-3-billion-resolvefraud-allegations-and-failure-report

27	Nombre del artículo: Whistleblower on Medical Research Fraud: 'Positive Results Are Better for Your Career'	Fecha: Sep 10, 2015
	Sitio web:	Archivo:
	Spiegel Online	http://archive.is/PA2Th
	http://www.spiegel.de/international/zeitgeist/spiegel-	
	<u>interview-with-whistleblower-doctor-peter-wilmshurst-a-</u>	
	<u>1052159.html</u>	

SPIEGEL: How exactly did they offer it to you? They probably didn't say: "Here's a bribe for you."

Wilmshurst: No, of course not! Initially we were talking about the results that I'd obtained: That the drug that I had been testing for them did not work and had dangerous side effects. Then the company representatives asked me to leave some of the patients out of the data analysis. Without these patients, the study result would have been positive. When I said I couldn't do that, they asked me not to publish the data. And to compensate me for the work I had done in vain, they said, they would offer me this amount of money.

28	Nombre del artículo: As drug industry's influence over research grows, so does the potential for bias	Fecha: Nov 24, 2012
	Sitio web: Washington Post https://www.washingtonpost.com/business/economy/as-drug-industrys-influence-over-research-grows-so-does-the-potential-for-bias/2012/11/24/bb64d596-1264-11e2-be82-c3411b7680a9_story.html	Archivo: http://archive.is/eFJxM
	When the company is footing the bill, the opportunities for bias	are manifold. Company

When the company is footing the bill, the opportunities for bias are manifold: Company executives seeking to promote their drugs can design research that makes their products look better. They can select like-minded academics to perform the work. And they can run the

statistics in ways that make their own drugs look better than they are. If troubling signs about a drug arise, they can steer clear of further exploration.	
Nombre del artículo: Many Antidepressant Studies Found Tainted by Pharma Company Influence	Fecha: Oct 21, 2015
Sitio web: Sceintific American http://www.scientificamerican.com/article/many-antidepressant-studies-found-tainted-by-pharma-company-influence/	Archivo: http://archive.is/cxvEV

Nombre de la página:
Ten Great Public Health Achievements -- United
States, 1900-1999

Sitio web:
CDC website
http://archive.is/ZQXW

Ten Great Public Health Achievements -- United States, 1900-1999:
Vaccination [...]

Nombre del artículo: Straight Talk about Vaccination Sitio web: Sceintific American http://www.scientificamerican.com/article/straight-talk-about-vaccination/ Archivo: http://archive.is/gFzXa

This sad state of affairs exists because parents have been persistently and insidiously misled by information in the press and on the Internet and because the health care system has not effectively communicated the counterarguments, which are powerful.

[...]

The key facts parents need to know, though, are that vaccines prevent potentially fatal diseases, that vaccines have a high degree of safety, and that their safety is constantly evaluated and reevaluated in a system operating independently from the pharmaceutical companies that make vaccines.

31	Nombre del artículo: How Many Scientists Fabricate and Falsify	PMID: 19478950
	Research? A Systematic Review and Meta- Analysis of Survey Data https://www.ncbi.nlm.nih.gov/pmc/articles/P MC2685008/pdf/pone.0005738.pdf	Archivo: https://drive.google.com/open?id=1qOwU Wd9WRgChSUN-jNC8AJjaaT2yuEBR
	Autor principal/año: Daniele Fanelli, 2009	Revista: PLOS One

P 1

A pooled weighted average of 1.97% [...] of scientists admitted to have fabricated, falsified or modified data or results at least once –a serious form of misconduct by any standard– and up to 33.7% admitted other questionable research practices. In surveys asking about the behaviour of colleagues, admission rates were 14.12% [...] for falsification, and up to 72% for other questionable research practices.

[...]

Considering that these surveys ask sensitive questions and have other limitations, it appears likely that this is a conservative estimate of the true prevalence of scientific misconduct.

32	Nombre del artículo: A Population-Based Study Of Measles, Mumps, And Rubella Vaccination And Autism http://www.nejm.org/doi/pdf/10.1056/NEJMoa021134	PMID: 12421889 Archivo: https://drive.google.com/open?id=1Yr4-bZH0ybUOZcp52BHoxzR_A1gjSSG6
	Autor principal/año: Kreesten Meldgaard Madsen , 2002	Revista: NEJM

33	Nombre abreviado: Madsen 2002	Archivo: https://drive.google.com/open?id=1Yr4-bZH0ybUOZcp52BHoxzR_A1gjSSG6
	P 1: This study provides strong evidence against the hypothesis that MMR vaccination causes autism	

34	Nombre del artículo: Study Finds No Link Between MMR Vaccine and Autism	Fecha: Nov 7, 2002
	Sitio web: LA Times http://articles.latimes.com/2002/nov/07/science/sci-autism7	Archivo: http://archive.is/K80dM
	Nombre del artículo: Danish Study Finds No Links Between Vaccine and Autism	Fecha: Nov 6, 2002
	Sitio web: Wall Street Journal http://www.wsj.com/articles/SB103661903159271588	Archivo: http://archive.is/bXtrs
	Nombre del artículo: The Autism-Vaccine Myth	Fecha: Sep 5, 2014
	Sitio web: PBS http://www.pbs.org/wgbh/nova/body/autism-vaccine-myth.html	Archivo: http://archive.is/QNv9e
	The New England Journal of Medicine publishes "A population mumps, and rubella vaccination and autism" by Madsen et al. T describe "strong arguments" against the hypothesis that the MM based on an analysis of data from 537,303 children in Denmark,	hese authors R vaccine causes autism,

35	Nombre de la página: Vaccines Do Not Cause Autism	Archivo: http://archive.is/SCAqJ	
	Sitio web: CDC website http://www.cdc.gov/vaccinesafety/concerns/autism.html		
	Nombre de la página: Do Vaccines Cause Autism? Archivo: http://archive.is/4VNXR		
	Sitio web: Johns Hopkins University School of Public Health - Institute for Vaccine Safety http://www.vaccinesafety.edu/vs-autism.htm		

the MMR vaccine.

Nombre de la página: Archivo: Vaccine Safety: Examine the Evidence https://drive.google.com/open?id=111B FNOu118F7xhM8z7zhmohkVYgoJfs Sitio web: AAP, 2013 https://www.aap.org/en-us/Documents/immunization vaccine studies.pdf Nombre del documento: Information Sheet Observed Rate Of Vaccine Reactions Measles, Mumps And Rubella Vaccines Archivo: Autor/año: https://drive.google.com/open?id=12JOo WHO, 2014 DTvzr3qlbq93QChZP8a vhOSn9J5 http://www.who.int/vaccine_safety/initiative/too ls/MMR vaccine rates information sheet.pdf P 3, 9

36 Nombre del documento: Adverse Effects of Vaccines: Evidence and Causality http://nationalacademies.org/hmd/reports/2011/adverse-effects-of-vaccines-evidence-andcausality.aspx Archivo: Autor/año: https://drive.google.com/open?id=1nl18cdV_y3TtQBz IOM, 2011 oCa0tSiuYmHF1 vYO P 145(174)

37 Nombre del artículo: Fecha: Denmark scientist accused of stealing autism research Apr 13, 2011 money Sitio web: Archivo: Reuters http://archive.is/h1qLN

A scientist in Denmark has been indicted by a federal grand jury in Atlanta for allegedly stealing \$1 million in grant money that the Centers for Disease Control and Prevention had earmarked for autism research. U.S. prosecutors on Wednesday said they are seeking to extradite Poul Thorsen, 49, accused of wire fraud and money laundering. He used the stolen money to buy a home in Atlanta, a Harley Davidson motorcycle and two cars, prosecutors said. [...] Thorsen, a visiting scientist at the Atlanta-based CDC in the 1990s, helped two government agencies in Denmark obtain \$11 million in research grants. He moved back to Denmark in 2002 to be principal investigator for the program. Prosecutors said he was also in charge of administering the research dollars, earmarked in part to study the relationship

between autism and exposure to vaccines.	
Nombre del artículo: Dane indicted for defrauding CDC	Fecha: Apr 13, 2011
Sitio web: Atlanta Business Chronicle http://www.bizjournals.com/atlanta/news/2011/04/13/da ne-indicted-for-defrauding-cdc.html	Archivo: https://web.archive.org/web/2080919220752/https://webcachgoogleusercontent.com/search=cache:sU81j6AiPG8J:https://ww.bizjournals.com/atlanta/nes/2011/04/13/dane-indicted-fodefrauding-cdc.html+&cd=1&hl=en&ct=nk≷=il&client=firefox-b

Thorsen worked in the 1990s as a visiting scientist at the CDC Division of Birth Defects and Developmental Disabilities, when the CDC was soliciting grant applications for research related to infant disabilities. Thorsen promoted the idea of awarding the grant to Denmark and provided input and guidance for the research. From 2000 to 2009, the CDC awarded more than \$11 million to two governmental agencies in Denmark to study the relationship between autism and exposure to vaccines... Nombre de la página: Fugitive Profiles Sitio web: Archivo: http://archive.is/wip/4qVfg Office of Inspector General, HHS https://oig.hhs.gov/fraud/fugitives/profiles.asp#other-<u>fugitives</u>

38	Nombre del artículo: Association Between Thimerosal-Containing Vaccine and Autism	PMID: 14519711
	Autor principal/año: Anders Hviid, 2003	Revista: JAMA
	Nombre del artículo: Measles-Mumps-Rubella Vaccination and Asthma-like Disease in Early Childhood	PMID: 18845551
	Autor principal/año: Anders Hviid, 2008	Revista: American Journal of Epidemiology
	Nombre del artículo: Autism and Thimerosal containing vaccines: lack of consistent evidence for an association.	PMID: 12880876
	Autor principal/año: Paul Stehr-Green, 2003	Revista: American Journal of Preventive Medicine
	Nombre del artículo: Thimerosal and the Occurrence of Autism: Negative Ecological Evidence From Danish Population-Based Data	PMID: 12949291
	Autor principal/año: Kreesten M. Madsen, 2003	Revista: Pediatrics

Nombre abrev Madsen 2002	Nombre abreviado: Madsen 2002	Archivo: https://drive.google.com/open?id=1Yr4- bZH0ybUOZcp52BHoxzR_A1gjSSG6
	Article title, P 1	

	40	Nombre abreviado: Madsen 2002	Archivo: https://drive.google.com/open?id=1Yr4-bZH0ybUOZcp52BHoxzR_A1gjSSG6
P 6: Supported by grants fromthe National Vaccine Program Office Immunization Program, Centers for Disease Control and Prever		Supported by grants from.	

41-60

41 Nombre de la página: Archivo: Vaccines Do Not Cause Autism http://archive.is/SCAqJ Sitio web: CDC website http://www.cdc.gov/vaccinesafety/concerns/autism.html There is no link between vaccines and autism

42 Nombre del documento:

Adverse Effects of Vaccines: Evidence and Causality

http://nationalacademies.org/hmd/reports/2011/adverse-effects-of-vaccines-evidence-andcausality.aspx

Archivo: Autor/año: https://drive.google.com/open?id=1nl18cdV_y3TtQBz IOM, 2011 oCq0tSiuYmHF1 yYQ

P 50 (79):

Epidemiologic analyses are usually unable to detect an increased or decreased risk that is small, unless the study population is very large or the difference between the groups (e.g., vaccinated vs. unvaccinated) at risk is very high... These studies also can fail to detect risks that affect a small subset of the population.

43	Nombre abreviado: Madsen 2002	Archivo: https://drive.google.com/open?id=1Yr4-bZH0ybUOZcp52BHoxzR AlgiSSG6
	P 2: We performed an extensive record review for 40 children with autistic disorder	

44	Nombre abreviado: Madsen 2002	Archivo: https://drive.google.com/open?id=1Yr4-
		bZH0ybUOZcp52BHoxzR_A1gjSSG6

P 2:

We determined MMR-vaccination status on the basis of vaccination data reported to the National Board of Health by general practitioners, who administer all MMR vaccinations in Denmark.

45	Nombre abreviado: Madsen 2002	Archivo: https://drive.google.com/open?id=1Yr4-bZH0ybUOZcp52BHoxzR_A1gjSSG6

We assume that the data on MMR vaccination are almost complete, since general practitioners in Denmark are reimbursed only after reporting immunization data to the National Board of Health.

46 Nombre abreviado: Archivo:

Madsen 2002 https://drive.google.com/open?id=1Yr4bZH0ybUOZcp52BHoxzR A1gjSSG6

Data obtained from Tabla 2

Madsen 2002

Table 2. Adjusted Relative Risk of Autistic Disorder and of Other Autistic-Spectrum DISORDERS IN VACCINATED AND UNVACCINATED CHILDREN.

VACCINATION	Person-Years†	Auтıs	AUTISTIC DISORDER		OTHER AUTISTIC-SPECTRUM DISORDERS	
		NO. OF CASES	ADJUSTED RELATIVE RISK (95% CI)	NO. OF CASES	ADJUSTED RELATIVE RISK (95% CI)	
Total Vaccination	2,129,864	316		422		
No Yes	482,360 1.647.504	53 263	1.00 0.92 (0.68-1.24)	77 345	1.00 0.83 (0.65-1.07)	

Researchers Calculations

MMR Status Person Years No. Autistic Kids Adjusted Relative Risk

Unvaccinated 482,360 1,647,504 263 0.92 Vaccinated Conclusion Vaccinated kids have lower autism risk

Calculation without Adjustments

MMR Status Person Years **Autistic Children** Years/Child Relative Risk Unvaccinated 482,360 53 9,101 1.00 1,647,504 263 1.45 Vaccinated 6,264 Vaccinated kids have higher (45%) autism risk Conclusion

47 Nombre abreviado: Archivo:

> Madsen 2002 https://drive.google.com/open?id=1Yr4-

> > bZH0vbUOZcp52BHoxzR A1giSSG6

3/pdf

We calculated the relative risk with adjustment for age, calendar period, sex, birth weight, gestational age, mother's education, and socioeconomic status.

48 Nombre del artículo: Increasing Exposure to Antibody-Stimulating Proteins and Polysaccharides in Vaccines Is Not Associated with Risk of Autism http://www.jpeds.com/article/S0022-3476(13)00144-

PMID: 23545349

Archivo:

https://drive.google.com/open?id= 1LVEHpSumks-

XGbdd7DujwX2hDOP4ltVl

Autor principal/año: Revista:

Frank DeStefano, 2013 The Journal Of Pediatrics

49 Nombre abreviado: Archivo: DeStefano 2013

https://drive.google.com/open?id=1LVEHpSumks-

XGbdd7DujwX2hDOP4ltVl

Study Title P 1:

Increasing Exposure to Antibody-Stimulating Proteins and Polysaccharides in Vaccines Is Not Associated with Risk of Autism

50	Nombre abreviado: DeStefano 2013	Archivo: https://drive.google.com/open?id=1LVEHpSumks- XGbdd7DujwX2hDOP4ltVI
	P1	

51 Few examples –

No link between vaccines and autism

https://www.ncbi.nlm.nih.gov/pubmed/17928818

No link between Type 1 diabetes and vaccines of the childhood program

https://www.ncbi.nlm.nih.gov/pubmed/11731639

No link between vaccines and asthma

https://www.ncbi.nlm.nih.gov/pubmed/12182372

No link between thimerosal in vaccines and neurological disabilities

https://www.ncbi.nlm.nih.gov/pubmed/14595043

Influenza and H1N1 vaccines are safe

https://www.ncbi.nlm.nih.gov/pubmed/21767718

52 Archivo: http://archive.is/bh8oL

53	Nombre abreviado: DeStefano 2013	Archivo: https://drive.google.com/open?id=1LVEHpSumks-
	Desterano 2013	XGbdd7DujwX2hDOP4ltVI
	P 1	

54	Nombre del artículo: New study finds no link between 'too many vaccines' and autism	Fecha: Mar 29, 2013
	Sitio web: NBC http://vitals.nbcnews.com/_news/2013/03/29/17516929-new-study-finds-no-link-between-too-many-vaccines-and-autism	Archivo: http://archive.is/oDjiE

55	Nombre del artículo: New study finds no link between 'too many vaccines' and autism	Fecha: Mar 29, 2013	
	Sitio web:	Archivo:	
	NBC	http://archive.is/oDjiE	
	http://vitals.nbcnews.com/_news/2013/03/29/17516929-new-		
	study-finds-no-link-between-too-many-vaccines-and-autism		

"This study looked into the concern that receiving too many vaccines at one doctor's visit or too many vaccines during the first two years of life may be linked to the development of autism," the report's lead author, Dr. Frank DeStefano told NBC chief medical editor Dr. Nancy Snyderman. "We found they're not related."

DeStefano hopes the new research will convince parents that it's safe to follow CDC vaccination schedules.

[...]

"The number of vaccines in the current immunization schedule is what's needed to protect children," he said. "It's not too many for a child's immune system."

56	Nombre del artículo: Vaccines Not Linked To Autism. Again.	Fecha: Mar 29, 2013
	Sitio web: Forbes http://www.forbes.com/sites/emilywillingham/2013/03/29/vaccines-not-linked-to-autism-again/#5b452ca95166	Archivo: http://archive.is/QVEo0
	Nombre del artículo: Multiple Vaccines Not Linked To Autism Risk	Fecha: Mar 30, 2013
	Sitio web: Medical News Today http://www.medicalnewstoday.com/articles/258414.php	Archivo: http://archive.is/Tsbin
	Nombre del artículo: Number Of Early Childhood Vaccines Not Linked To Autism	Fecha: Mar 29, 2013
	Sitio web: NPR http://www.npr.org/sections/health-shots/2013/03/29/175626824/the-number-of-early-childhood-vaccines-not-linked-to-autism	Archivo: http://archive.is/V8Xst
	Nombre del artículo: No link found between autism and number of vaccines	Fecha: Mar 29, 2013
	Sitio web: CBS News http://www.cbsnews.com/news/no-link-found-between-autism-and-number-of-vaccines/	Archivo: http://archive.is/TKUmJ
	Nombre del artículo: Multiple Vaccinations on Same Day Does Not Raise Autism Risk	Fecha: Mar 29, 2013
	Sitio web: Time Magazine http://healthland.time.com/2013/03/29/multiple-vaccinations- on-same-day-does-not-raise-autism-risk/	Archivo: http://archive.is/eB8AB

DeStefano 2013 https://d		Archivo: https://drive.google.com/open?id=1LVEHpSumks-XGbdd7DujwX2hDOP4ltV1	
	For example, P 2: we evaluated the associations between the total cumulative exposure to antibody stimulating proteins and polysaccharides from childhood vaccinations and ASD outcomes		
	or P 7: however, we found no asso infancy and the developme	ociation between exposure to antigens from vaccines during nt of ASD with regression.	

58	Nombre abreviado: DeStefano 2013	Archivo: https://drive.google.com/open?id=1LVEHpSumks-
		XGbdd7DujwX2hDOP4ltVl

P 1:

A recent survey found that parents' top vaccine-related concerns included administration of too many vaccines during the first 2 years of life, administration of too many vaccines in a single doctor visit, and a possible link between vaccines and learning disabilities, such as autism.

59 Nombre abreviado: Archivo: DeStefano 2013 https://drive.google.com/open?id=1LVEHpSumks-XGbdd7DujwX2hDOP4ltVl

P 1:

Using the number of antibody-stimulating proteins and polysaccharides contained in vaccines as a measure, we evaluated the association between the level of immunologic stimulation received from vaccines during the first 2 years of life and the risk of developing an autism spectrum disorder (ASD), including specific ASD subtypes.

60 Nombre abreviado: Archivo: DeStefano 2013 https://drive.google.com/open?id=1LVEHpSumks-XGbdd7DujwX2hDOP4ltVl P 2, Tabla 1

61-80

61	Nombre abreviado: DeStefano 2013	Archivo: https://drive.google.com/open?id=1LVEHpSumks-XGbdd7DujwX2hDOP4ltV1

Admittedly, this approach assumes that all proteins and polysaccharides in a vaccine evoke equivalent immune responses, whereas some proteins actually may be more likely than others to stimulate an immune response. Moreover, the calculations do not take into account the number of epitopes per antigen or the immunologic strength of each epitope.

62	Nombre abreviado: DeStefano 2013	Archivo: https://drive.google.com/open?id=1LVEHpSumks-XGbdd7DujwX2hDOP4ltVl
	P 4: Nonetheless, we believe that our estimates provide a valid relative ranking of the antigen	

63 Nombre abreviado: Archivo: DeStefano 2013 https://drive.google.com/open?id=1LVEHpSumks-XGbdd7DujwX2hDOP4ltVl

P 4:

content of vaccines.

The immunization schedule in effect during the years in which our study children were vaccinated included some, such as diphtheria, tetanus, and whole-cell pertussis, that were cruder and more antigenic than current vaccines, and also caused more side effects. Removal of whole-cell pertussis vaccine from the childhood vaccination schedule has substantially decreased the antigenic load from vaccines.

64	Nombre abreviado: DeStefano 2013	Archivo: https://drive.google.com/open?id=1LVEHpSumks-XGbdd7DujwX2hDOP4ltVl
	P 2, Tabla 1	

65 Nombre del artículo (traducido del hebreo): Are vaccines a burden on the immune system?

(Answer: no)

Fecha: Mar 17, 2018

Archivo:

http://archive.is/OfpPN

Sitio web:

Davidson institute, Educational arm of Weizmann Institute for Science, Rehovot, Israel

(Traducido del hebreo)

A 2013 study [DeStefano 2013] looked at another question – is there an association between the number of anigens and the risk for autism [...] Like many other studies done since, this 2013 study also concluded there is none.

66 Nombre del artículo:

> Autoimmune disorders and quadrivalent human papillomavirus vaccination of young female subjects http://onlinelibrary.wiley.com/doi/10.1111/joim.12155/ pdf

PMID:

24206418

Archivo:

https://drive.google.com/open?id= 1dSrBeFU P-

ZKrSaMwoaow6Pc9rst9isY

Autor principal/año:

L. Grimaldi-Bensouda, 2014

Revista:

Journal of Internal Medicine

67 Nombre abreviado: Archivo:

Grimaldi-Bensouda 2014

https://drive.google.com/open?id=1dSrBeFU P-

ZKrSaMwoaow6Pc9rst9isY

P 9:

Funding

funded by an unrestricted grant from Sanofi Pasteur MSD

Merck and Sanofi-Pasteur closed their joint company in 2016. 68

http://www.msd.com/about/featured-stories/spmsd/index.html

Archivo:

https://web.archive.org/web/20180907083210/http://www.msd.com/about/featuredstories/spmsd/index.html

69 Nombre abreviado:

Archivo:

Grimaldi-Bensouda 2014

https://drive.google.com/open?id=1dSrBeFU P-

ZKrSaMwoaow6Pc9rst9isY

P 9:

Funding

The Scientific Committee for the study received honoraria from Sanofi Pasteur MSD

70

Nombre abreviado:

Archivo:

Grimaldi-Bensouda 2014

https://drive.google.com/open?id=1dSrBeFU P-ZKrSaMwoaow6Pc9rst9isY

P 8:

Conflict of interest statement

71

The LA-SER (LASER ANALYTICA) company was purchased in 2018 from another company. Due to this, the company website (http://www.la-ser.com) is no longer available. These excerpts were copied from the company's website, when it was still online. 5 of the top 8 major pharma manufacturers and 15 mid-size companies and biotechs already use PGRx

http://www.la-ser.com/services-2/data-solutions/

We provide cutting edge outcomes research designed to demonstrate the benefit to patients that products and health technologies provide.

http://www.la-ser.com/services-2/real-world-evidence/

Founded by one of the world's pioneers and leaders in pharmacoepidemiology and public health, Professor Lucien Abenhaim, who directed the famous McGill

Pharmacoepidemiology Education Program for several years, LASER ANALYTICA offers unique consulting capabilities in these domains.

http://www.la-ser.com/services-2/real-world-evidence/

A news story about LA-SER acquiring Analytica:

http://myemail.constantcontact.com/LA-SER-Group-Grows-Worldwide-Healthcare-Economics-Consulting-Capabilities.html?soid=1102157698477&aid=K05zKxx4Z4c Archivo: http://archive.is/U0iWM

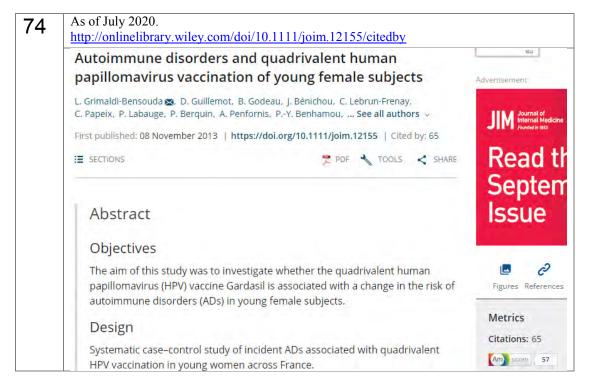
A news story about LA-SER being acquired by Certara:

https://www.certara.com/pressreleases/certara-acquires-analytica-laser-a-leader-in-marketaccess-health-economics-and-outcomes-research-heor-and-real-world-evidence-solutions?/

Archivo: http://archive.is/TtBdC

72	Nombre del documento: MMWR Vol. 63, No. 5 https://www.cdc.gov/mmwr/pdf/rr/rr6305.pdf	
	Autor/año: CDC, 2014	Archivo: https://drive.google.com/open?id=1KF2xY aHnQs8NrjCW1owte8XUMs2NOM
	P 28 (30)	

73	Nombre del documento: HPV Vaccine is Safe — (Gardasil) https://www.cdc.gov/vaccinesafety/pdf/data-summary-hpv-gardasil-vaccine-is-safe.pdf	
	Autor/año: CDC, 2016	Archivo: https://drive.google.com/open?id=1HxmM kj j9UedaLjabAkHNH05f2Ma9fF-
	P 2	



75	Nombre abreviado: Grimaldi-Bensouda 2014	Archivo: https://drive.google.com/open?id=1dSrBeFU_P-ZKrSaMwoaow6Pc9rst9isY
	P 9: LA-SER, an independent re	esearch organisation that owns and develops the PGRx.database.

P 3:

Human papillomavirus vaccination history was assessed using prescription records received from cases and referents, as well as directly from GPs and during the telephone interviews. In addition, the researchers obtained the vaccination status of subjects with whom a telephone connection wasn't made, which indicate they had another source for the information (see note to Fig 1, P 6)

Nombre abreviado:
Grimaldi-Bensouda 2014

Archivo:
https://drive.google.com/open?id=1dSrBeFU_P-ZKrSaMwoaow6Pc9rst9isY

P 3:
For each AD case, only referents with no history of that particular type of AD were selected as potential controls.

78	Nombre abreviado: Grimaldi-Bensouda 2014	Archivo: https://drive.google.com/open?id=1dSrBeFU_P-ZKrSaMwoaow6Pc9rst9isY
	P 4, Tabla 1	

79	Nombre del artículo:	PMID:
		15249303

Vaccination and Allergic Disease: A Birth Cohort Archivo: https://drive.google.com/open?id=13b5 http://ajph.aphapublications.org/doi/pdf/10.2105/ r3JluMRXKcXVsouZfPpCDPsnDqkqI AJPH.94.6.985 Autor principal/año: Revista:

Tricia M. McKeever, 2004

American Journal of Public Health

80 Nombre abreviado: Archivo: McKeever 2004 https://drive.google.com/open?id=13b5r3JluMRXKcXVsouZfP pCDPsnDqkqI

P 1.

Results. We found an association between vaccination and the development of allergic disease; however, this association was present only among children with the fewest physician visits and can be explained by this factor.

Conclusions. Our data suggest that currently recommended routine vaccinations are not a risk factor for asthma or eczema.

81-100

81 Nombre de la página: Archivo: School of Medicine - School staff listing http://archive.is/Hhsw2 Sitio web: University of Nottingham https://www.nottingham.ac.uk/medicine/people/tricia.mckeever

82 Nombre abreviado: Archivo: McKeever 2004 https://drive.google.com/open?id=13b5r3JluMRXKcXVsouZfP pCDPsnDqkqI

P 1:

An unexplained increase in the prevalence of allergic disease has occurred in the developed world in the past few decades. During the same period, there has been an increase in mass immunization, leading to the hypothesis that certain vaccines may increase the risk of allergic disease.

83 Nombre abreviado: Archivo: McKeever 2004 https://drive.google.com/open?id=13b5r3JluMRXKcXVsouZfP pCDPsnDqkqI

It is clearly important to gain a detailed understanding of the relationship between vaccination and allergic disease, because a perception that vaccination is harmful may have an adverse impact on the effectiveness of immunization programs.

	84	Nombre abreviado: McKeever 2004	Archivo: https://drive.google.com/open?id=13b5r3JluMRXKcXVsouZfP pcDPsnDqkqI
		P 2: Children who are not taken to the doctor are less likely to be vaccinated and also have less	

of an opportunity to have a diagnosis of allergic disease recorded.

85	Nombre abreviado: McKeever 2004	Archivo: https://drive.google.com/open?id=13b5r3JluMRXKcXVsouZfP
		nCDPsnDakaI

P 1:

We identified children who were registered with their general practitioner (GP) (their primary care physician) within 3 months of birth and whose medical history contained at least 1 physician visit at any time.

86	Nombre del artículo: Vaccination And Risk Of Allergic Disease https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1449840/		PMID: 15623850
Autor principal/año: Eric L. Hurwitz , 2005		Revista: American Journal of Public l	Health

Nombre abreviado:
McKeever 2004

Archivo:
https://drive.google.com/open?id=13b5r3JluMRXKcXVsouZfP

P 4:
These data, together with other published evidence, suggest that current vaccination practices do not have an adverse effect on the incidence of allergic disease.

88	Nombre del artículo: Pervasive Developmental Disorders in Montreal, Quebec, Canada: Prevalence and Links With		PMID: 16818529 Archivo:
	Immunizations http://pediatrics.aappublications.org/content/118/1/e139		https://drive.google.com/open?id=1lBvQzmoUd1U2XQk7vJR7fnwvS_XJPxMd
	Autor principal/año: Eric Fombonne, 2006	Revista: Pediatrics	

89 Some vaccies-autism Fombonne atricles:

No evidence for a new variant of measles-mumps-rubella-induced autism. http://www.ncbi.nlm.nih.gov/pubmed/11581466

MMR vaccination and pervasive developmental disorders: a case-control study. http://www.ncbi.nlm.nih.gov/pubmed/15364187

Is there an epidemic of autism?

https://www.ncbi.nlm.nih.gov/pubmed/11158478

Epidemiology of pervasive developmental disorders. https://www.ncbi.nlm.nih.gov/pubmed/19218885

Thimerosal disappears but autism remains.

https://www.ncbi.nlm.nih.gov/pubmed/18180423

90	Nombre abreviado:	Archivo:	
	Fombonne 2006	https://drive.google.com/open?id=11BvQzmoUd1U2XQk7vJR7	
		fnwvS XJPxMd	

P 1:

In the United Kingdom, Dr Fombonne has provided advice on the epidemiology and clinical aspects of autism to scientists advising parents, to vaccine manufacturers, and to several government committees between 1998 and 2001. Since June 2004, Dr Fombonne has been an expert witness for vaccine manufacturers in US thimerosal litigation. None of his research has ever been funded by the industry.

91 Nombre abreviado: Archivo: Fombonne 2006 https://drive.google.com/open?id=1lBvQzmoUd1U2XQk7vJR7 fnwvS XJPxMd

P 11:

Children with autism and their younger unaffected siblings should be vaccinated. Unvaccinated children are at much higher risk of contracting measles and suffering from its sometimes severe or lethal complications.

92 Nombre del artículo: Fecha: No Autism-Vaccine Link, Researchers Re-Confirm July 5, 2006 Sitio web: Archivo: MEDPAGE TODAY http://archive.is/NWRZ5 http://www.medpagetoday.com/infectiousdisease/vaccines/36 As the mercury-containing preservative thimerosal was removed from vaccines, and as fewer children received the mumps-measles-rubella vaccine, the rates of autism and related disorders rose among Canadian school children. In a study of nearly 28,000 children born between 1987 and 1998, the prevalence of pervasive developmental disorders was greater in those children vaccinated after the mercury-containing compound thimerosal was completely eliminated from vaccines in Canada, reported Eric Fombonne, M.D., of McGill University in Montreal, and colleagues. Nombre del artículo: Fecha: Vaccines And Autism July 6, 2006 Sitio web: Archivo: CBS http://archive.is/mPFH3 http://www.cbsnews.com/news/vaccines-and-autism/ New research from Canada may not end the debate about childhood vaccines and autism but it offers more evidence that vaccines are not to blame for the dramatic rise in reported cases of the developmental disorder. Nombre del artículo: Fecha: July 6, 2006 Study: Vaccines Don't Cause Autism Sitio web: Archivo: http://archive.is/4Dsbb WEBMD http://www.webmd.com/children/vaccines/news/20060706/stu dy-vaccines-dont-cause-autism New research from Canada may not end the debate about childhood vaccines and autism,

93	Nombre del artículo: Vaccines And Autism	Fecha: July 6, 2006
	Sitio web: CBS http://www.cbsnews.com/news/vaccines-and-autism/	Archivo: http://archive.is/mPFH3
	Our study once again rules out MMR as a cause for autism.	

but it offers more evidence that vaccines are not to blame for the dramatic rise in reported

The study examined outcomes among 28,000 children in Quebec, exposed to different

cases of the developmental disorder.

dosages of the measles, mumps, rubella (MMR) vaccine[...]

94	Nombre del artículo: No Autism-Vaccine Link, Researchers Re-Confirm	Fecha: July 5, 2006

Sitio web:

MEDPAGE TODAY

http://archive.is/NWRZ5

Archivo:

http://www.medpagetoday.com/infectiousdisease/vaccines/36

We hope this study will finally put to rest the pervasive belief linking vaccines with developmental diseases like autism.

95 As of July 2020

https://pediatrics.aappublications.org/content/118/1/e139/tab-article-info

96 Nombre del artículo:

Vaccines and Autism: Evidence Does Not Support a Causal Association

https://ascpt.onlinelibrary.wiley.com/doi/abs/10.1038/sj.clpt.6

Archivo:

PMID:

17928818

100407

https://drive.google.com/o pen?id=1UcEA2dqSucbfz vLnwCEzvP5F16QRzaSi

Autor principal/año: Revista:

Frank DeStefano, 2007 Clinical Pharmacology and Therapeutics

Similarly, a study conducted in Montreal found that the birth cohort prevalence of pervasive developmental disorders, which include autism, increased from 1987 to 1998, whereas during the same time MMR vaccination coverage showed a statistically significant decrease.

97 Nombre del documento:

The Childhood Immunization Schedule and Safety

Stakeholder Concerns, Scientific Evidence, and Future Studies

http://www.nap.edu/catalog/13563/the-childhood-immunization-schedule-and-safetystakeholder-concerns-scientific-evidence

Archivo: Autor/año:

https://drive.google.com/open?id=1no7T IOM, 2013 Zx03ToHXlEMGix9miyZMhiRIVtW

P 86 (103):

The initial literature search identified 32 papers on the relationship between immunizations or vaccines and pervasive developmental disorder... each of the other four papers might help with a study of the schedule.

This was an ecological study, but the data were interpreted carefully and the differences in appropriate trends were noted.

98 Nombre del documento:

Adverse Effects of Vaccines: Evidence and Causality

http://nationalacademies.org/hmd/reports/2011/adverse-effects-of-vaccines-evidence-andcausality.aspx

Archivo: Autor/año:

https://drive.google.com/open?id=1nl18cdV_y3Tt IOM, 2011 QBzoCq0tSiuYmHF1 yYQ

P 145 (174):

[it was] not considered in the weight of epidemiologic evidence because they provided... an ecological comparison study lacking individual-level data.

99 Nombre abreviado: Archivo: Fombonne 2006 https://drive.google.com/open?id=1lBvQzmoUd1U2XQk7vJR7 fnwvS XJPxMd P 5: For the 10 birth cohorts with available data, the average MMR uptake in Quebec was... And P7: Vaccination uptake of MMR was high in Quebec, averaging 93.2% over the study years.

Nombre abreviado: Fombonne 2006 Archivo: https://drive.google.com/open?id=11BvQzmoU		https://drive.google.com/open?id=11BvQzmoUd1U2XQk7vJR7
	1	the study period were available through the Direction de Sante' Jationale (N.Boulianne, BN, MSc, written communication, 2005).

101-114

101	Nombre del artículo: A Tale of Two Cities: Flawed Epidemiology	Fecha: Mar 7, 2007
	Author: F. Edward Yazbak	Archivo: http://archive.is/253mj

102	Nombre del artículo: A Tale of Two Cities: Flawed Epidemiology	Fecha: Mar 7, 2007
	Author: F. Edward Yazbak	Archivo: http://archive.is/253mj
	As a note, I believe the evidence of no link between MMR and worth publishing more on this subject. We will not be publishing correspondence	

103	Nombre abreviado: Fombonne 2006	Archivo: https://drive.google.com/open?id=11BvQzmoUd1U2XQk7vJR7fnwv8_XJPxMd
	P 3:	

the LBPSB has a special support team to monitor the progress of children with PDD in its schools. This team keeps a list of children with a PDD diagnosis, which is updated on a weekly basis. The children with PDD who are the focus of this study were identified via this list.

104	Nombre abreviado: Fombonne 2006	Archivo: https://drive.google.com/open?id=11BvQzmoUd1U2XQk7vJR7 fnwvS_XJPxMd
P 4: Individual immunization data were not available for study subjects.		data were not available for study subjects.

105 Nombre abreviado: Archivo: Fombonne 2006 https://drive.google.com/open?id=1lBvQzmoUd1U2XQk7vJR7 fnwvS XJPxMd P 10: ... data about regression in the course of the development of children with PDD were not available in this study ...

106 Nombre del artículo: PMID: Effects of Editorial Peer Review 12038911 A Systematic Review Archivo: http://jama.jamanetwork.com/article.aspx?arti https://drive.google.com/open?id=1RYb cleid=194989 FqONzxV07oMQMJSLJHZlkNHJCHz Autor principal/año: Revista: Tom Jefferson, 2002 **JAMA** P 1: CONCLUSIONS: Editorial peer review, although widely used, is largely untested and its effects are uncertain.

107 Nombre del artículo: PMID: Peer review: a flawed process at the heart of 16574968 science and journals Archivo: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1 https://drive.google.com/open?id=10 420798/pdf/0178.pdf al3x lv A7W xJKy12F0HsqhDA38 **RQJ** Autor principal/año: Revista: Richard Smith, 2006 Journal of the Royal Society of Medicine At the BMJ we did several studies where we inserted major errors into papers that we then sent to many reviewers. Nobody ever spotted all of the errors. Some reviewers did not spot any, and most reviewers spotted only about a quarter.

108 Nombre del artículo: Fecha: Should academics be paid for peer review? Mar 16, 2016 Sitio web: Archivo: THE http://archive.is/OUeBu https://www.timeshighereducation.com/news/shouldacademics-be-paid-for-peer-review As the number of papers needing review increases, journals are thinking of replacing a voluntary system with cash rewards

109 Nombre abreviado: Archivo: Smith 2006 https://drive.google.com/open?id=1Oal3x lv A7W xJKy12F0 HsqhDA38ROJ P 2: Peer review sometimes picks up fraud by chance, but generally it is not a reliable method for detecting fraud because it works on trust.

110	Nombre abreviado: Smith 2006	Archivo: https://drive.google.com/open?id=1Oal3x_lv_A7W_xJKy12F0
		HsqhDA38RQJ

P 5:

Some journals, including the BMJ, make it a condition of submission that the editors can ask for the raw data behind a study. We did so once or twice, only to discover that reviewing raw data is difficult, expensive, and time consuming.

111 Nombre abreviado:

Archivo:

Smith 2006

https://drive.google.com/open?id=1Oal3x lv A7W xJKy12F0

HsqhDA38RQJ

P 2:

So we have little evidence on the effectiveness of peer review, but we have considerable evidence on its defects. In addition to being poor at detecting gross defects and almost useless for detecting fraud it is slow, expensive, profligate of academic time, highly subjective, something of a lottery, prone to bias, and easily abused.

112 Nombre del artículo:

Fecha:

John Ioannidis has dedicated his life to quantifying how science is broken

Feb 16, 2015

Sitio web:

Archivo:

VOX

http://archive.is/4nIGf

http://www.vox.com/2015/2/16/8034143/john-ioannidisinterview

Recently there's increasing emphasis on trying to have post-publication review. Once a paper is published, you can comment on it, raise questions or concerns. But most of these efforts don't have an incentive structure in place that would help them take off. There's also no incentive for scientists or other stakeholders to make a very thorough and critical review of a study, to try to reproduce it, or to probe systematically and spend real effort on re-analysis. We need to find ways people would be rewarded for this type of reproducibility or bias checks.

113

Nombre del artículo:

PMID: 19478950

How Many Scientists Fabricate and Falsify Research? A Systematic Review and Meta-Analysis of Survey

Archivo:

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC268500 8/

https://drive.google.com/open?i d=1qOwUWd9WRgChSUNiNC8AJiaaT2vuEBR

Autor principal/año: Revista: Daniele Fanelli, 2009 PLOS One

A pooled weighted average of 1.97% [...] of scientists admitted to have fabricated, falsified or modified data or results at least once -a serious form of misconduct by any standard— and up to 33.7% admitted other questionable research practices. In surveys asking about the behaviour of colleagues, admission rates were 14.12% [...] for falsification, and up to 72% for other questionable research practices.

114

Nombre abreviado:

Archivo:

Smith 2006

https://drive.google.com/open?id=1Oal3x lv A7W xJKy12F0 HsqhDA38RQJ

P 2:

So we have little evidence on the effectiveness of peer review, but we have considerable evidence on its defects. In addition to being poor at detecting gross defects and almost useless for detecting fraud it is slow, expensive, profligate of academic time, highly subjective, something of a lottery, prone to bias, and easily abused.

Capítulo 6: Los estudios que nunca se harán

1-20

	1	Nombre de la página: The Journey of Your Child's Vaccine Archivo: https://archive.is/uuJeo			
		Sitio web: CDC website http://www.cdc.gov/vaccines/parents/infographics/journey-of-child-vaccine.html			

2 Nombre del documento:

The Childhood Immunization Schedule and Safety Stakeholder Concerns, Scientific Evidence, and Future Studies http://www.nap.edu/catalog/13563/the-childhood-immunization-schedule-and-safety-stakeholder-concerns-scientific-evidence

Autor/año:
IOM, 2013

Archivo:

https://drive.google.com/open?id=1no7T_Zx03To

HXIEMGix9mivZMhiRIVtW

P 40 (57):

...the sample sizes in prelicensing clinical trials may not have been adequate to detect rare adverse events, the prelicensing study population may not have been monitored for long-term adverse events, and populations may not have been heterogeneous.

3	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
	P 70 (87): The committee also acknowledges that the public health community has in place monitoring	

The committee also acknowledges that the public health community has in place monitoring systems that work very well for the detection of adverse events that occur in the short term after immunization.

Archivo: IOM 2013 Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 mivZMhiRIVtW

P 94 (111):

The committee's review confirmed that research on immunization safety has mostly developed around studies examining potential associations between individual vaccines and single outcomes. Few studies have attempted more global assessments of entire sequence of immunizations or variations in the overall immunization schedule and categories of health outcomes, and none has squarely examined the issue of health outcomes and stakeholder concerns in quite the way that the committee was asked to do in its statement of task. None has compared entirely unimmunized populations with those fully immunized for the health outcomes of concern to stakeholders.

IOM 2013 https://drive.google.com/open?id=1no7T_Zx03ToHXI mivZMhiRIVtW	EMGix9
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P 86-88 (103-105)

6 Nombre de la página:

Seeking The Truth About The Never-Vaccinated

Archivo:

http://archive.is/GDOXz

Sitio web:

Age of Autism

http://www.ageofautism.com/2007/12/seeking-the-tru.html

Nombre del documento:

Compulsory Vaccination Briefly Considered

Archivo: Autor/año:

https://drive.google.com/open?id=1 bol5t6Zyrnej John Gibbs, 1856

9goXH9P2fmoTOYrMI8X

P 10-11:

The main question for the consideration of science is not whether vaccination be a protection against one form of disease, but what is its general influence upon the constitution?

What is the percentage of deaths before a given age, from all epidemics, amongst the vaccinated, as compared with the unvaccinated? What is the percentage respectively of cases of disease of the respiratory organs, of skin diseases, of scrofula, and of convulsions? What is the average duration of life amongst the vaccinated and amongst the unvaccinated? Of a thousand children vaccinated within a given time after birth, and of a thousand unvaccinated, the whole two thousand being placed as nearly as possible in like circumstances, what percentage in each thousand attain the age of puberty? These are statistics with which the advocates of vaccination have never grappled.

7 Nombre de la página:

Congressional Record Volume 159

Archivo:

http://archive.is/f1WSi

Sitio web:

US Government Publishing Office

https://www.gpo.gov/fdsys/pkg/CREC-2013-04-26/html/CREC-2013-04-26-pt1-PgE576.htm

Before coming to Congress in 2009, I heard from some in the autism community who have advocated for a retrospective study to examine whether there are different health outcomes when comparing vaccinated children and unvaccinated children, including autism and chronic conditions. I have continued to hear these requests over the past four years.

8 Nombre de la página:

No MMR-Autism Link in Large Study of Vaccinated vs. Unvaccinated Kids

Archivo:

http://archive.is/5mWxz

Sitio web:

Autism Speaks

https://www.autismspeaks.org/science/science-news/no-mmr-autism-link-large-studvvaccinated-vs-unvaccinated-kids

Nombre del artículo: 9

Vaccination Status and Health in Children and

PMID: 21412506

Adolescents http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3057555/

Autor principal/año:

Roma Schmitz, 2011 Deutsches Ärzteblatt international

10 Nombre de la página: Archivo:

50 Anti-Vaccine Myths and https://web.archive.org/web/20150319024613/http:/ped Misinformation (item 37) iatrics.about.com/od/immunizations/tp/Anti-Vaccine-Myths-and-Misinformation.03.htm

Sitio web:

VeryWell Family

http://pediatrics.about.com/od/immunizations/tp/Anti-Vaccine-Myths-and-Misinformation.03.htm

In contrast, a real study in Germany, "Vaccination Status and Health in Children and Adolescents," looked at medical records from KiGGS to see "whether unvaccinated children and adolescents differ from those vaccinated in terms of health."

The diseases they looked at included allergies, eczema, obstructive bronchitis, pneumonia and otitis media, heart disease, anemia, epilepsy, and attention deficit hyperactivity disorder (ADHD).

Not surprisingly, this second study did find that unvaccinated children were more likely to get vaccine-preventable diseases. However, it also concluded that "the prevalence of allergic diseases and non-specific infections in children and adolescents was not found to depend on vaccination status."

So, since these unvaccinated and vaccinated children had the same incidence of allergies, pneumonia, and other conditions, etc., plus unvaccinated children were also more likely to have vaccine-preventable diseases, such as measles and mumps, that hardly sounds like unvaxed kids are healthier.

11	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
	P 86 (103)	

12	Nombre del artículo: Autism costs estimated to reach nearly \$500 billion, potentially \$1 trillion, by 2025	Fecha: July 28, 2015
	Sitio web: UC DAVIES https://www.ucdmc.ucdavis.edu/publish/news/newsroom/10214	Archivo: http://archive.is/XYc84

13	Nombre del artículo: Vaccination Usage Among An Old-O Amish Community In Illinois https://journals.lww.com/pidj/Fulltext	Vaccination Usage Among An Old-Order Amish Community In Illinois ttps://journals.lww.com/pidj/Fulltext/2006/12000/VAC CINATION_USAGE_AMONG_AN_OLD_ORDER_A MISH.16.aspx		
	Autor principal/año: Revista: Jonathan S. Yoder, 2006 The Pediatric		ectious Disease Journal	
	A survey of Amish vaccination rate and attitude in Ohio Nombre del artículo: Underimmunization in Ohio's Amish: Parental Fears Are a Greater Obstacle Than Access to Care		PMID: 21708796	
		Revista: Pediatrics		

14 Nombre del artículo: PMID: Underimmunization in Ohio's Amish: Parental Fears Are 21708796 a Greater Obstacle Than Access to Care Autor principal/año: Revista: Olivia K. Wenger, 2011 **Pediatrics** Similar to our study, a survey of an Arthur, Illinois, Amish population found that parents

15 Nombre del documento:

alignment with religious values.

Olmsted, who worked in news agency UPI, published the series on UPI's website. The series was later removed from the site. It can be read here:

were most concerned about vaccine safety rather than availability, cost, prioritization, or

https://drive.google.com/open?id=1BCJfmWLMrjSuZ8vRYa6LL4slSnhXdfk3

16 Nombre de la página: Archivo: Autism Spectrum Disorder (ASD) http://archive.is/NOyDo

Sitio web:

CDC

http://www.cdc.gov/ncbddd/autism/index.html

among the Amish of northeastern Ohio

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1403405

CDC is committed to continuing to provide essential data on ASD, search for factors that put children at risk for ASD and possible causes, and develop resources that help identify children with ASD as early as possible.

17 Nombre de la página: Archivo: Pertussis Outbreak in an Amish Community --http://archive.is/Kc2RD Kent County, Delaware, September 2004--February 2005 Sitio web: CDC http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5530a1.htm This report describes an outbreak of pertussis in an Amish community in Kent County, Delaware, during September 2004--February 2005, that resulted in 345 cases and affected primarily preschool-aged children. To maximize active surveillance and control measures, a door-to-door case finding and contact investigation program was instituted. Nombre del artículo: PMID: Haemophilus influenzae Type b disease among Amish 11581468 children in Pennsylvania: reasons for persistent disease Autor principal/año: Revista: AM Fry, 2001 Pediatrics We investigated recent cases, performed community surveys for Hib vaccination coverage and pharyngeal carriage, and administered a questionnaire assessing vaccination knowledge and attitudes to 298 members of 2 Amish communities (A and B) in Pennsylvania and, as a comparison group, 136 non-Amish family members who participated in state immunization clinics. Nombre del artículo: PMID: An epidemiologic investigation of a rubella outbreak 8341776

Archivo:

Autor principal/año: BM Jackson, 1993	Revista: Pediatrics	
Nombre del artículo: Measles among the Amish: a measles severity in primary ar households		PMID: 1984459 Archivo:
Autor principal/año: RW Sutter, 1991	Revista: Journal of Infectiou	s Diseases
An outbreak of measles among a predominantly unvaccinated and susceptible Amish population in Lebanon County, Pennsylvania, offered the opportunity to test the hypothesi that secondary cases in households are more severe than primary cases because the former have more intense exposure and receive a greater virus inoculum.		

18	Nombre del artículo: Study says cost of autism more than cancer, strokes and heart disease	Fecha: Jun 9, 2014
	Sitio web: The Guardian http://www.theguardian.com/society/2014/jun/09/autism-costs-more-cancer-strokes-heart-disease	Archivo: http://archive.is/b6uXH

19	Nombre del artículo: The Age of Autism: 'A pretty big secret'	Fecha: Dec 7, 2005
	Sitio web: UPI http://www.upi.com/Health_News/2005/12/07/The-Age-of-Autism-A-pretty-big-secret/68291133982531/	Archivo: http://archive.is/GEpma

"We have a fairly large practice. We have about 30,000 or 35,000 children that we've taken care of over the years, and I don't think we have a single case of autism in children delivered by us who never received vaccines," said Dr. Mayer Eisenstein, Homefirst's medical director who founded the practice in 1973. Homefirst doctors have delivered more than 15,000 babies at home, and thousands of them have never been vaccinated.

20	Nombre del artículo: A prevalence estimate of pervasive disorder among Immigrants to Isra https://www.researchgate.net/publevalence estimate of pervasive or among Immigrants to Israel a A file review_study	nel and Israeli natives ication/8649372_A_pr developmental_disorde	PMID: 15052396 Archivo: https://drive.google.com/open?i d=1jXh9kgpJS77gnPZXw0- HX1BqeDloNAS3
	Autor principal/año: Anat Kamer, 2004	Revista: Social Psychiatry and P	sychiatric Epidemiology

21-40

21 Nombre de la página: Why Is Autism Rate So High For Somalis In Minn. Sitio web: YouTube https://www.youtube.com/watch?v=xUf4L6UQhbk

22	Nombre de la página: Why Is Autism Rate So High For Somalis In Minn.	Archivo:
	Sitio web: YouTube	Minute 2:23
	https://youtu.be/xUf4L6UQhbk?t=143	

23	Nombre de la página: Why Is Autism Rate So High For Somalis In Minn.	Archivo:
	Sitio web:	Minute 3:17
	YouTube	
	https://youtu.be/xUf4L6UQhbk?t=197	

24 Nombre de la página: Archivo: Minneapolis Somali Autism Spectrum Disorder http://archive.is/VXvmu Prevalence Project Sitio web: University of Minnesota https://rtc.umn.edu/autism/ The Somali estimate of 1 in 32 compares to 1 in 36 White children, 1 in 62 Black children and 1 in 80 Hispanic children.

25 Nombre de la página: Fecha: June 25, 2007 Legislation Aims to Resolve Thimerosal Controversy Archivo: http://archive.is/pswYi

Sitio web:

Carolyn B. Maloney (member of Congress)

https://webcache.googleusercontent.com/search?q=cache:Pz1gbFVVuoUJ:https://maloney.h ouse.gov/media-center/press-releases/legislation-aims-resolve-thimerosalcontroversy+&cd=1&hl=en&ct=clnk&gl=il

26	Nombre de la página: H.R. 1757 (113th): Vaccine Safety Study Act (2013)	Archivo: http://archive.is/OwI6D	
	Sitio web: Govtrack https://www.govtrack.us/congress/bills/113/hr1757		
	Nombre de la página: H.R.3615 - Vaccine Safety Study Act (2017)	Archivo: http://archive.is/Q0V8j	
	Sitio web: Congress.gov https://www.congress.gov/bill/115th-congress/house-bill/3615		

27	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
	P 20 (37): On June 2, 2009, the National Vaccine Advisory Committee (NVAC) reviewed the nation's vaccine safety system and endorsed the recommendation of the NVAC Safety Working Group for an external expert committee, such as a committee convened by the Institute of	

Medicine (IOM), "with broad expertise in research methodologies, study design, and the

ethical conduct of research to consider the strengths and weaknesses, ethical issues and feasibility including timelines and cost of various study designs to examine outcomes in unvaccinated, vaccine-delayed and vaccinated children and report back to the NVAC"

The National Vaccine Program Office of HHS asked the IOM to convene a diverse committee of experts in pediatrics, neurology, medical ethics, immunology, statistics, epidemiology, and public health to identify study designs feasible to address questions about the safety of the United States' childhood immunization schedule.

28 Nombre abreviado: Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXlEMGix9 miyZMhiRIVtW

P 21 (38):

Identify potential research approaches, methodologies, and study designs that could inform this question, including an assessment of the potential strengths and limitations of each approach, methodology and design, as well as the financial and ethical feasibility of doing them.

29

Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 miyZMhiRIVtW

P 17 (34):

Vaccines have significantly contributed to worldwide reductions in morbidity and mortality by reducing the incidence of serious infectious diseases [...] However, as the incidence of vaccine- preventable disease has declined, many do not appreciate the potential of these diseases to reemerge, and the potential adverse effects of the vaccines themselves take on greater saliency among certain stakeholders. Indeed, vaccine safety concerns exist among a diverse range of individuals, institutions, and formal and informal networks worldwide.

30

Nombre de la página:

Archivo:

Vaccine Safety

http://archive.is/TJ196

Sitio web:

CDC

http://www.cdc.gov/Features/VaccineSafety/

The safety of vaccines is thoroughly studied before they are licensed for public use. Clinical trials are conducted to evaluate the safety and effectiveness of a vaccine before it can be brought to market. Vaccines are first tested in laboratory studies and animal studies. If the results indicate the vaccine is safe, additional testing in people must be done before the vaccine can be approved by the Food and Drug Administration (FDA).

31

Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 miyZMhiRIVtW

No studies have compared the differences in health outcomes that some stakeholders questioned between entirely unimmunized populations of children and fully immunized children.

32

Nombre abreviado:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9

miyZMhiRIVtW

P 11 (28):

Most vaccine-related research focuses on the outcomes of single immunizations or combinations of vaccines administered at a single visit.

33 Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9

miyZMhiRIVtW

P 11 (28):

Thus, key elements of the entire schedule—the number, frequency, timing, order, and age at administration of vaccines—have not been systematically examined in research studies.

34

Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9

miyZMhiRIVtW

P 130 (147):

Even though each new vaccine is evaluated in the context of the overall immunization schedule that existed at the time of review, individual elements of the schedule are not evaluated once it is adjusted to accommodate a new vaccine.

P 31 (48):

Although this process results in an evaluation of whether the observed benefits outweigh the observed risks for the new vaccine and, by extension, for the schedule, it does not include studies specifically designed to test variations in the schedule in an effort to identify the optimal schedule.

35

Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 mivZMhiRIVtW

P 11 (28):

The second major issue that the committee encountered was uncertainty over whether the scientific literature has addressed all health outcomes and safety concerns. The committee could not tell whether its list was complete or whether a more comprehensive system of surveillance might have been able to identify other outcomes of potential significance to vaccine safety. In addition, the conditions of concern to some stakeholders such as immunologic, neurologic, and developmental problems are illnesses and conditions for which etiologies, in general, are not well understood.

36

Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 miyZMhiRIVtW

P 11 (28):

Finally, the committee found that evidence assessing outcomes in subpopulations of children who may be potentially susceptible to adverse reactions to vaccines (such as children with a family history of autoimmune disease or allergies or children born prematurely) was limited and is characterized by uncertainty about the definition of populations of interest and definitions of exposures and outcomes.

37

Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHX1EMGix9 miyZMhiRIVtW

P 11 (28):

In summary, to consider whether and how to study the safety and health outcomes of the entire childhood immunization schedule, the field needs valid and accepted metrics of the entire schedule (the "exposure") and clearer definitions of health outcomes linked to stakeholder concerns (the "outcomes") in rigorous research that will ensure validity and generalizability.

38	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
	P 22 (39)	

39	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
	P 70-71 (87-88)	

40	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
	P 106 (123): Likewise, parents of intentionally unvaccinated children are unlikely to allow their children to be randomized to receive vaccines	

41-60

41	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 mivZMhiRIVtW
	IOM 2013	https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 mivZMhiRIVtW

P 106 (123):

...any child, even the child of a parent who staunchly rejects vaccination, who is randomized to a no-vaccination arm is essentially consigned to an elevated risk of severe illness and even possible death should the child contract a vaccine-preventable disease. P 107 (124)

The ethics of human experimentation always trump scientific and other considerations, and no study that needlessly endangers children is acceptable.

42 Nombre del documento: National, State, and Local Area Vaccination Coverage Among Children Aged 19-35 Months — United States, 2012 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6236a1.htm Archivo: Autor/año: http://archive.is/UtX6r CDC, 2013 Tabla 1, Vaccine coverage data 2008-2012: Children who received no vaccinations: 2011 - 0.8%, 2012 - 0.8%

43 Nombre del documento: National vaccine objection (conscientious objection) data 1999 to 2015 https://beta.health.gov.au/resources/publications/national-vaccine-objection-conscientiousobjection-data-1999-to-2015 Archivo: Autor/año: https://drive.google.com/open?id=1U7VlgPAzdcEE1SRg12T-AIR, 2018 00WlWRj27fo5

Data on conscientious objection for the period 2010-2015, P 2.

44 Nombre abreviado: Archivo: IOM 2013 https://drive.google.com/open?id=1no7T Zx03ToHXlEMGix9 miyZMhiRIVtW P 130 (147): In summary, to consider whether and how to study the safety and health outcomes of the entire childhood immunization schedule, the field needs... clearer definitions of health outcomes linked to stakeholder concerns...

45	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
	P 114 (131). Original study: Glanz 2013	

	46	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
		P 109 (126) for RCT, P 111 (128) for prospective study.	

47	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
	P 118 (135): In addition, the VSD system has a large enough proportion of unvaccinated children to investigate differences in health outcomes of unvaccinated and vaccinated children.	

48	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9
		miyZMhiRIVtW

On RCT for testing a different vaccination schedule, P 107 (124):

Although it is unobjectionable ethically, the committee considered the time and financial strains resulting from immunization on a dispersed schedule to be too prohibitively costly to recommend pursuing this line of research and, thus, does not endorse this method as a feasible option for studying the recommended immunization schedule.

On Prospective study, P 112 (129):

...the limits of studying distinct subgroups of naturally occurring unimmunized populations, and the high cost of pursuing prospective data collection, the committee does not consider the initiation of new prospective cohort studies to be the most feasible or fruitful approach to studying the recommended immunization schedule at this time.

49 Nombre abreviado: IOM 2013

Archivo:

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 miyZMhiRIVtW

P 108 (125):

Unless researchers somehow accounted for the occurrence of the more serious preventable diseases, it may appear that nonvaccination is "safer" in this respect. To further complicate matters, the rare unvaccinated child in an otherwise heavily vaccinated area will benefit from community immunity and may thus appear to have done better than his or her peers, some of whom will develop adverse effects, such as fever.

50 Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 miyZMhiRIVtW

P 111 (128):

However, such a study would have limited utility to accurately assess differences in health outcomes between unimmunized and fully immunized children... the study would need to account for the many confounding variables that distinguish distinct subgroups of naturally occurring unimmunized populations from the rest of the U.S. population, including lifestyle factors and known genetic variables that may play a role in the development of allergies, asthma, and other conditions.

51	Vaccine Refusal, Mandatory Immunization, and the Risks of Vaccine-Preventable Diseases https://www.nejm.org/doi/full/10.1056/NEJMsa0806477 https://www.nejm.org/doi/full/10.1056/NEJMsa0806477		PMID: 19420367 Archivo: https://drive.google.com/open?i d=1JVj1dDnlLTfLHDn6Z4e4M AeSDStdW89y		
	Autor principal/año: Saad B. Omer, 2009	Revista: NEJM			
	P 3: The reasons for the geographic clustering of exemptions from school vaccination requirements are not fully understood, but they may include characteristics of the local population (e.g., cultural issues, socioeconomic status, or educational level), the beliefs of local health care providers and opinion leaders (e.g., clergy and politicians), and local media coverage.				
	1		PMID: 21812176		
	Autor principal/año: Philip J. Smith, 2011	Revista: Public Health Reports			
	P 7, Tabla 3				
	In Canada they can't accurately vaccinating, also. Nombre del artículo: Anti-vaxxers among Canadians of finds: 'It could be your neighbour.	Fecha: Apr 9, 2012			
	Sitio web: USA TODAY http://news.nationalpost.com/news/canada/anti-vaxxers-among-canadians-of-all-demographics-poll-finds-it-could-be-your-neighbour-thats-the-scary-thing		Archivo: http://archive.is/IYVvI		

52	Nombre del artículo: After \$1 billion, experts see progress on autism's causes	Fecha: Apr 9, 2012
	Sitio web: USA TODAY http://usatoday30.usatoday.com/news/health/story/2012-04-09/researchers-autism-causes/54129282/1	Archivo: http://archive.is/ixi6Z
	More than \$1 billion has been spent over the past decade search	ing for the causes of autism

53 Nombre abreviado: Archivo: IOM 2013 https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 miyZMhiRIVtW

P 118 (135):

Secondary analyses with data from other existing databases similar to VSD would be feasible, ethical, and a lower-cost approach to investigating the research questions that the committee identified, including research on alternative immunization schedules.

In addition, the committee states that the VSD can be used for vaccinated-Unvaccinated studies., P 118 (135):

To date, the data obtained from VSD have already been used to study health outcomes of children with incomplete immunizations or who may follow alternative schedules, as described above. In addition, the VSD system has a large enough proportion of unvaccinated children to investigate differences in health outcomes of unvaccinated and vaccinated children.

54	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
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P 10 (27):

These concerns were not expressed by clinicians, public health personnel, or policy makers in the committee's review. Among the last three groups, the childhood immunization schedule is considered one of the most effective and safest public health interventions available to prevent serious disease and death.

55	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
		ndividuals and organizational representatives revealed a lack of roughness of vaccine safety research

56	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T Zx03ToHXlEMGix9 miyZMhiRIVtW
	P 18 (35):	

As the number of recommended vaccines has increased in recent years, some parents and advocacy groups have expressed the concern that the immunization schedule is too crowded and complex...

57	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
	P 62 (79): Two-thirds of these articles were categorized as studies of parental concerns about either safety $(n = 26)$ or communication between providers, public health authorities, and parents $(n = 31)$.	

58	Nombre del artículo: Effective messages in vaccine promotion: a randomized trial	PMID: 24590751
	Autor principal/año: B Nyhan, 2014	Revista: Pediatrics
	Nombre del artículo: Physician Communication Training and Parental Vaccine Hesitancy: A Randomized Trial	PMID: 26034240
	Autor principal/año: NB Henrikson, 2015	Revista: Pediatrics
	Nombre del artículo: The Influence of Provider Communication Behaviors on Parental Vaccine Acceptance and Visit Experience	PMID: 25790386
	Autor principal/año: DJ Opel, 2015	Revista: American Journal of Public health

59	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
	evidence (biological or epi	takeholder concerns may be used to drive a search for scientific demiological), although such concerns would not be sufficient ostly clinical research, such as new randomized controlled trials

60	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 miyZMhiRIVtW
	Recommendation 4-1, P 129 (146)	

61-73

61	Nombre abreviado: IOM 2013	Archivo: https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9 mivZMhiRIVtW
		IIIIyZIVIIIIKI V L VV

P 20 (37):

The NVAC report stated that "the strongest study design, a randomized clinical trial that includes a study arm receiving no vaccine or vaccine not given in accord with the current recommended schedule, is not ethical, would not pass Institutional Review Board (IRB) review, and cannot be done"... Furthermore, it may be impossible to draw unbiased results from an observational study of this issue because of potential differences in baseline health and social characteristics of populations and subgroups.

62 Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 miyZMhiRIVtW

P 127 (144):

The committee made a judgment based on the literature that failed to link adverse effects to schedule exposures or multiple immunizations, concluding that there is no evidence that the schedule is not safe.

63

Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9

mivZMhiRIVtW

P 127 (144):

The committee recognized that final decisions about research studies must await knowledge of further evidence, including biological plausibility and/or epidemiological evidence, feasibility, cost, and the exact circumstances of stakeholder concerns, before the planning and conduct of specific research projects.

64

Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 miyZMhiRIVtW

P 132 (149):

The committee recognizes that the establishment of priorities for research will be a challenge. Thus, the committee proposes a process for setting priorities that recognizes stakeholder concerns and establishes these priorities on the basis of epidemiological and other evidence (based on formal systematic reviews), biological plausibility, and feasibility.

65

Nombre abreviado:

Archivo: IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9

miyZMhiRIVtW

Recommendation 4-1, P 129 (146):

Recommendation 4-1: The committee recommends that the National Vaccine Program Office systematically collect and assess evidence regarding public confidence in and concerns about the entire childhood immunization schedule, with the goal to improve communication with health care professionals, and between health care professionals and the public regarding the safety of the schedule.

66

Nombre abreviado:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 miyZMhiRIVtW

Recommendation 6-3, P 118 (135):

Recommendation 6-3: The committee recommends that the Department of Health and Human Services (HHS) and its partners continue to fund and support the Vaccine Safety Datalink project to study the safety of the recommended immunization schedule.

Furthermore, HHS should consider expanding the collaboration with new health plan members and enhancing the data to improve its utility and generalizability.

67 Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T_Zx03ToHXIEMGix9

miyZMhiRIVtW

Recommendation 6-2, P 134 (151):

Recommendation 6-2: The Department of Health and Human Services should refrain from initiating randomized controlled trials of the childhood immunization schedule that compare safety outcomes in fully vaccinated children with those in unvaccinated children or those vaccinated by use of an alternative schedule.

68 Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 miyZMhiRIVtW

Recommendation 5-1, P 130 (147):

Recommendation 5-1: To improve the utility of studies of the entire childhood immunization schedule, the committee recommends that the National Vaccine Program Office develop a framework that clarifies and standardizes definitions of key elements of the schedule, relevant health outcomes, and populations that are potentially susceptible to adverse events.

69

Nombre abreviado:

Archivo:

IOM 2013

https://drive.google.com/open?id=1no7T Zx03ToHXIEMGix9 mivZMhiRIVtW

Recommendation 6-1, P 132 (149):

Recommendation 6-1: The committee recommends that the Department of Health and Human Services incorporate study of the safety of the overall childhood immunization schedule into its processes for setting priorities for research, recognizing stakeholder concerns, and establishing the priorities on the basis of epidemiological evidence, biological plausibility, and feasibility.

70

Nombre del artículo:

PMID: 23338829

A Population-Based Cohort Study of Undervaccination in 8 Managed Care

Archivo:

Organizations Across the United States

https://jamanetwork.com/journals/jamapediatrics/fullarti cle/1558057

https://drive.google.com/open?i d=1gS5reE25E9rQUicV8wsY3 4A-CPRXt5Vf

Autor principal/año: Revista: Jason M. Glanz, 2013 Jama Pediatrics

71

Nombre del artículo:

PMID: 29582071

Vaccination Patterns in Children After Autism Spectrum Disorder Diagnosis and in TheirYounger Siblings https://relaped.com/wp-content/uploads/2018/03/3-1.pdf

Archivo:

Autor principal/año: Revista: JAMA Pediatrics Ousseny Zerbo, 2018

72 Nombre abreviado: Archivo: $\underline{\text{https://drive.google.com/open?id=1no7T}}\underline{Zx03ToHXlEMGix9}\underline{miyZMhiRIVtW}$ IOM 2013 P 116 (133): Approximately 1.23 percent of children participating in VSD had no vaccinations recorded by age 1 year, and 1 percent of children had no vaccinations recorded by age 2 years.

73	Nombre del artículo: Vaccine-Preventable Diseases Requiring		PMID: 28768853
	Hospitalization http://pediatrics.aappublications.org/content/pediatrics/early/2017/07/31/peds.2017-0298.full.pdf		Archivo: https://drive.google.com/open?i d=1t9g5rGLUp- jUTu1xOedLHPmI0v7pHlNM
Autor principal/año: Gregory Williamson, 2017		Revista: Pediatrics	

Capítulo 7: Pautas de vacunación no fundamentadas

1-20

1	Nombre del documento: Recommended Child and Adolescent Immunization Schedule, for ages 18 years or younger https://drive.google.com/file/d/11tcxNEPzYibSrwe2RbnDnD2epCfnZlXo	Autor/año: CDC, 2020
	P 2, Tabla 1.	

2	Nombre del artículo: New Software and Genetic Analyses Aim to Reduce Problems with Multiple-Drug Combinations	Fecha: Oct 1, 2015
	Sitio web: Scientific American http://www.scientificamerican.com/article/new-software-and-genetic-analyses-aim-to-reduce-problems-with-multiple-drug-combinations/	Archivo: http://archive.is/gDYts

Certain combinations of medicines (prescription or otherwise) cause side effects that do not arise when the individual substances are taken alone. Studies published over the past two decades suggest that such "drug interactions" cause more than 30 percent of side effects from medications.

Sitio web: CDC

http://www.cdc.gov/vaccinesafety/concerns/multiple-vaccines-immunity.html

A number of studies have been done to look at the effects of giving various combinations of vaccines, and when every new vaccine is licensed, it has been tested along with the vaccines already recommended for a particular aged child.

4	Nombre del documento: Multiple Injections: Acceptability and Safety	Autor/año: WHO, 2014
	http://www.who.int/immunization/diseases/poliomy elitis/inactivated_polio_vaccine/multiple_injections _acceptability_safety.pdf	Archivo: https://drive.google.com/open?id=1u aF5IV5wSPs46nfRg_8hBEX6vziS3 K7i

P 1:

Vaccination schedules that involve multiple injections during the same visit are based on many years of pre-licensure and post-licensure safety and effectiveness data, including concomitant use studies.

are given at different times.

5 Nombre del artículo: PMID: Addressing Parents' Concerns: Do Multiple Vaccines 11773551 Overwhelm or Weaken the Infant's Immune System? Archivo: https://www.aap.org/enhttps://drive.google.com/open?i us/Documents/immunization overwhelm.pdf d=1N8EXqxq8RbTprBp0fZ1W egd8Qz BCn5r Autor principal/año: Revista: Paul A. Offit, 2002 **Pediatrics** P 4: If vaccines overwhelmed or weakened the immune system, then one would expect lesser immune responses when vaccines are given at the same time as compared with when they

Nombre del artículo:
Simultaneous administration of childhood vaccines: An important public health policy that is safe and efficacious

Autor principal/año:
King, 1994

Revista:
The Pediatric Infectious Disease Journal

Nombre del documento:
Recommended Child and Adolescent Immunization
Schedule, for ages 18 years or younger
https://drive.google.com/file/d/11tcxNEPzYibSrwe2RbnDnD2epCfnZlXo
P 2, Tabla 1.

Nombre del documento (hebreo):
Immunization Guide
https://drive.google.com/open?id=1db5nqObGNRg
8QwTaOUuTARsisHlPrf4U

Autor/año:
Israeli Ministry of Health, 2015

Por ejemplo, p 52 (traducido del hebreo):

Simultaneous administration of most vaccines, live-attenuated or killed, does not increase the extent of post-vaccination side effects and does not affect the efficacy of any of them.

Nombre de la página (traducido del hebreo):

Common Questions

Archivo:

http://archive.is/aiHZ0

Sitio web:

"Vaccines" website of Wolfson Hospital http://chisunim.co.il/Faq.aspx?cat=2&id=5

"Should I split the vaccines or spread it over a longer period in order to reduce the burden on the baby's immune system?

No! The part of the immune system that we use when giving the vaccines is negligible compared to the real and full capacity of the immune system, and therefore the concern of overloading is baseless."

9	Nombre del artículo: Reduced Rate of Side Effects Associated with Separate Administration of MMR and DT aP-Hib-IPV Vaccinations		PMID: 20166340
	Autor principal/año: Elena Shneyer, 2009	Revista: Israeli Medical Association Journal	

10 Nombre del artículo: PMID: Reduced Rate of Side Effects Associated with Separate 20166340 Administration of MMR and DT aP-Hib-IPV Vaccinations https://www.ncbi.nlm.nih.gov/pubmed/20166340

> Autor principal/año: Revista:

Elena Shneyer, 2009 Israeli Medical Association Journal

P 2:

Nurses at a primary care clinic in the Afula region observed that the mode of separate administration of these vaccines is associated with a lower rate of adverse effects.

11 Nombre del artículo: PMID: Reduced Rate of Side Effects Associated with Separate 20166340 Administration of MMR and DT aP-Hib-IPV Vaccinations https://www.ncbi.nlm.nih.gov/pubmed/20166340 Autor principal/año: Revista: Elena Shneyer, 2009 Israeli Medical Association Journal P 2.

12 Nombre del artículo: PMID: Reduced Rate of Side Effects Associated with Separate 20166340

> Administration of MMR and DT aP-Hib-IPV Vaccinations https://www.ncbi.nlm.nih.gov/pubmed/20166340

Autor principal/año: Revista:

Elena Shneyer, 2009 Israeli Medical Association Journal

The rate of adverse reaction among children who were vaccinated separately was significantly lower than in those who were vaccinated simultaneously: 28 of 74 (37.8%) versus 58 of 102 (56.9).

13 Nombre del artículo: PMID: Reduced Rate of Side Effects Associated with Separate 20166340

Administration of MMR and DT aP-Hib-IPV Vaccinations https://www.ncbi.nlm.nih.gov/pubmed/20166340

Autor principal/año: Revista:

Elena Shneyer, 2009 Israeli Medical Association Journal

P 4:

In this study it was demonstrated that the rate of adverse effects in the separately vaccinated group was significantly lower than in the simultaneously vaccinated group. The results of this study do not support the national recommendation of simultaneous vaccinations of MMR and DTaP-Hib-IPV. Rather, our data call for reconsideration of the current policy of simultaneous injections of MMR and DTaP-Hib-IPV – at least until a larger study is conducted.

14	Nombre del artículo (hebreo): Israeli study: Do not give 2 vaccines together at age one year	Fecha: Jan 6, 2010
	Sitio web:	Archivo:
	YNET	http://archive.is/a6hJ1
	http://www.ynet.co.il/articles/0,7340,L-3830484,00.html	

15 Nombre de la página:

Administering Vaccines

Archivo:

http://archive.is/MAslj

Sitio web:

Immunization Action Coalition

http://www.immunize.org/askexperts/administering-vaccines.asp

How many vaccines can be given during an office visit?

All vaccines can be administered at the same visit. There is no upper limit for the number of vaccines that can be administered during one visit.

16 Nombre del artículo:

Dr. Paul Offit: Debunking The Vaccine-Autism Link

Fecha:

Oct 24, 2008

Sitio web:

Newsweek

Archivo:

https://www.newsweek.com/dr-paul-offit-debunking-vaccine-

http://archive.is/kggwm

autism-link-91933

Recently, Offit set off a flurry of angry postings when he said that a baby's immune system could handle as many as 10,000 vaccines. Then he upped the ante, saying it was probably "closer to 100,000." Offit's assessment is based on data showing the vast capacity of a child's immunological response.

17

Nombre del artículo:

Addressing Parents' Concerns: Do Multiple Vaccines Overwhelm or Weaken the Infant's Immune System? https://www.aap.org/en-

us/Documents/immunization overwhelm.pdf

PMID:

11773551

Archivo:

https://drive.google.com/open?i d=1N8EXqxq8RbTprBp0fZ1W egd8Qz BCn5r

Autor principal/año: Paul A. Offit, 2002

Revista: Pediatrics

...each infant would have the theoretical capacity to respond to about 10,000 vaccines at any one time.

18

Nombre de la página:

Archivo:

Combination vaccines and multiple vaccinations

http://archive.is/1LpaD

University of Oxford - The Vaccine Knowledge Project

http://vk.ovg.ox.ac.uk/combination-vaccines-and-multiple-vaccinations

Each millilitre of blood contains ten million B cells, the white blood cells that are associated with the immune response. It is estimated that this would be enough to cope with thousands of vaccines at a time, meaning that a baby's immune system is not stretched at all by receiving several vaccines at once.

Nombre de la página (hebreo):

Archivo:

Common Questions

http://archive.is/t2klK

Sitio web:

"Vaccines" website of Wolfson Hospital

http://chisunim.co.il/Claim.aspx?cat=1&id=3&l=1

"Another common claim is that vaccines cause an unbearable burden on the immune system. The addition of new vaccines only increases this concern. In reality, a baby's immune system can respond to about 100,000 different organisms (bacteria, viruses, etc.). Therefore, vaccinating against 10 organisms will use 0.01% of the active immune capacity."

19 Nombre del documento:

Immunization Safety Review: Multiple Immunizations and Immune Dysfunction

https://www.nap.edu/catalog/10306/immunizationsafety-review-multiple-immunizations-and-immunedysfunction

Archivo:

https://drive.google.com/open?id= 1QuiT3DieBvlChf3vi4h18hjK1Q Qzx4Cp

Autor principal/año:

IOM, 2002

P 6 (21):

This is consistent with the theoretical estimates presented to the committee, which suggest that the capacity of the infant's immune system is at least 1000 times greater than that maximally required to respond to vaccines.

20

Nombre del documento:

INFANRIX-IPV-HIB Package Insert

https://drive.google.com/open?id=1L7FcWdJOT8-h8m4na4uSVtKuagBdK1gA

P 3.

21-31

21 Nombre del documento:

Vaccines When Your Child Is Sick

https://www.cdc.gov/vaccines/hcp/patient-ed/conversations/downloads/fs-child-sick.pdf

Autor/año:

Archivo:

CDC, 2014 https://drive.google.com/open?id=1rqg7CK6-

Y8kXI JWEQmKYEsLXNpKWr9z

P 1:

vaccines do not make a mild illness worse

Vaccines are safe and effective when given to children with mild illness

22 Nombre del documento:

Vaccines When Your Child Is Sick

https://www.cdc.gov/vaccines/hcp/patient-ed/conversations/downloads/fs-child-sick.pdf

Autor/año: Archivo:

CDC, 2014 https://drive.google.com/open?id=1rqg7CK6-

Y8kXI JWEQmKYEsLXNpKWr9z

P 1:

There is no health benefit to waiting to vaccinate your child if he or she has a mild illness. It's important that children get their vaccines on time—even if they don't feel well—so they're protected against serious diseases.

23 Nombre del artículo: PMID: Can children with minor illnesses be safely immunized 23024581 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC320238 Archivo: 2/pdf/pch16463.pdf https://drive.google.com/open?i d=1jeHfY_wUhqGi3HBqcc5gh M9K8RJtkjSI Autor principal/año: Revista: Keswadee Lapphra, 2011 Paediatric Child Health

24 PMID: Nombre del artículo: Can children with minor illnesses be safely immunized 23024581 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC320238 Archivo: 2/pdf/pch16463.pdf https://drive.google.com/open?i d=1jeHfY wUhqGi3HBqcc5gh M9K8RJtkjSI Autor principal/año: Revista: Keswadee Lapphra, 2011 Paediatric Child Health What is the evidence that minor illnesses are not a contraindication to most vaccinations?

25 PMID: Nombre del artículo: Can children with minor illnesses be safely immunized 23024581 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC320238 Archivo: 2/pdf/pch16463.pdf https://drive.google.com/open?i d=1jeHfY wUhqGi3HBqcc5gh M9K8RJtkiSI Autor principal/año: Revista: Keswadee Lapphra, 2011 Paediatric Child Health No publication in recent decades has assessed administering inactivated vaccines to mildly sick children.

26 Nombre del artículo: PMID: Antibody Response to Measles-Mumps-Rubella Vaccine 8594268 of Children With Mild Illness at the Time of Vaccination Autor principal/año: Revista: Gale E. King, 1996 **JAMA** P 1: 157 children had one of these mild illnesses and 229 were well

27 Nombre del artículo: PMID: Antibody response to measles-mumps-rubella 9481462 vaccine of children with mild illness at the time of Archivo: vaccination https://drive.google.com/open?id=191 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2 277572/pdf/canfamphys00047-0055.pdf dyoOKeqoCr8I3HTC25U mcLd493 Autor principal/año: Revista: Brian Watada, 1998 Canadian Family Physician P 2:

There is no confirmation in the study that any of the children were actually ill at the time of immunization, and no way of knowing whether these children had taken antipyretic medications to appear to have only mild illness.

P 3:

Finally, Canadian immunization guidelines indicate that children are to be vaccinated between 12 and 15 months of age. This study took patients between 15 and 23 months. Although 40% of the patients were 15 months old, most were older.

28 Nombre del artículo:

Can children with minor illnesses be safely immunized

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3 202382/pdf/pch16463.pdf

PMID: 23024581

Archivo:

https://drive.google.com/open?id=1jeH fY wUhqGi3HBqcc5ghM9K8RJtkjSI

Autor principal/año:

Revista:

Keswadee Lapphra, 2011

Paediatric Child Health

In summary, the health care provider should be reassured that mild illness is not a reason to delay routine vaccination. Many good-quality studies have provided strong support for the recommendation.

29 Nombre del artículo:

Addressing Parents' Concerns: Do Multiple Vaccines Overwhelm or Weaken the Infant's Immune System?

https://www.aap.org/en-

us/Documents/immunization_overwhelm.pdf

PMID:

11773551

Archivo:

https://drive.google.com/open?i d=1N8EXqxq8RbTprBp0fZ1W egd8Qz BCn5r

Autor principal/año: Paul A. Offit, 2002

Revista: **Pediatrics**

P 3:

However, vaccine-specific antibody responses and rates of vaccine-associated adverse reactions of children with mild or moderate illnesses are comparable to those of healthy children.

30

Nombre de la página:

Archivo:

Multiple Vaccines and the Immune System

http://archive.is/udrcT

Sitio web:

CDC

http://www.cdc.gov/vaccinesafety/concerns/multiple-vaccines-immunity.html

A number of studies have been done to look at the effects of giving various combinations of vaccines, and when every new vaccine is licensed, it has been tested along with the vaccines already recommended for a particular aged child.

31

Por ejemplo, clinical trial of rotavirus vaccine -Nombre de la página:

Archivo:

http://archive.is/SMTth

Safety and Immunogenicity of Rotavirus Vaccine (RotaTeq(R)) in Infants With Short Bowel Syndrome

Sitio web:

clinicaltrials.gov

https://clinicaltrials.gov/ct2/show/NCT00767364

Participants in the study will be monitored by telephone contacts on days 7, 14, and 42 after each dose and within 48 to 72 hours of each dose of the rotavirus vaccine regarding any serious adverse events.

Or, influenza vaccine trial Nombre de la página:
Immunogenicity and Safety of a Trivalent Inactivated
Influenza Vaccine, Formulation 2010-2011, in Healthy
Subjects Aged Over 6 Months Old to 18 Years Old

Sitio web:
clinicaltrials.gov
https://clinicaltrials.gov/ct2/show/NCT01356342

All participants will be followed, either by clinical visit or by telephone contact, for 6 months after the first vaccination for safety reasons.

Capítulo 8: La desaparición de la enfermedad

1-20

1 Nombre del artículo:

The Importance of Social Intervention in Britain's Mortality Decline c.1850-1914: a Re-interpretation of the Role of Public Health

https://pdfs.semanticscholar.org/a350/8f97eff18b8cffb5ccd 8c87feda108895c58.pdf

Archivo:

https://drive.google.com/open ?id=1c8AaRwdKf2O1On-VT0pI34G8xCEBWOIi

Autor principal/año: Revista:

Simon Szreter, 1988 Social History of Medicine

P 34

Thomas McKeown was born in 1912 and came to England from Canada as a postgraduate on a Rhodes scholarship, completing an Oxford D.Phil, in the Department of Human Anatomy in 1939. He then underwent formal medical training, acquiring an MB in the University of London in 1942. Apparently, he was offered the Chair in the new discipline of Social Medicine at Birmingham in 1944 because he had so impressed the interviewing panel when he unsuccessfully applied for the Chair of Anatomy the previous year (which went to Solly Zuckerman).

2 Nombre abreviado: Archivo:

Szreter 1988 <u>https://drive.google.com/open?id=1c8AaRwdKf2O1On-</u>

VT0pI34G8xCEBWOIj

P 2:

This work achieved something of a conceptual revolution in the disciplines of history and medicine, overturning a long-standing general orthodoxy regarding the importance of medical science and the medical profession in bringing about the decline in mortality which accompanied industrialization in Britain. It effectively demonstrated that those advances in the science of medicine which form the basis of today's conventional clinical and hospital teaching and practice, in particular the immuno- and chemo-therapies, played only a very minor role in accounting for the historic decline in mortality levels.

3 Nombre del artículo:

Reasons for the Decline of Mortality in England and Wales during the Nineteenth Century https://www.jstor.org/stable/2173119

Autor principal/año: Revista:

Thomas McKeown, 1962 Population Investigation Committee

P 7:

Since 1837 knowledge of the birth rate and the death rate of England and Wales has been available from national sources.

4 Nombre del artículo:

An Interpretation of the Modern Rise of Population in Europe https://www.jstor.org/stable/2173815

Autor principal/año: Revista:

Thomas McKeown, 1972 Population Investigation Committee

P 6

The nature of infectious disease was not understood before 1850; infectious organisms affecting man were not identified until the last quarter of the nineteenth century, and specific prevention or treatment is unlikely to have had much influence on the national death rate before the introduction of chemotherapy in the nineteen thirties.

5 Nombre abreviado: Link:

McKeown 1962 https://www.jstor.org/stable/2173119

P 12, table 3 shows the mortality decline in the 2nd half of the 19th century from tuberculosis and other major infectious diseases.

6 Nombre abreviado:

Link:

McKeown 1962

https://www.jstor.org/stable/2173119

P 29

The effect of therapy was restricted to smallpox and hence had only a trivial effect on the total reduction of the death rate.

And P 2:

...with the notable exception of vaccination against smallpox, specific preventive or curative measures could have had no significant influence on mortality before the twentieth century, and that we must look elsewhere for the explanation of the rise of population.

7 Nombre del artículo:

An Interpretation of the Decline of Mortality in England and Wales during the Twentieth Century

http://www.jstor.org/stable/2173935

Autor principal/año: Revista:

Thomas McKeown, 1975 Population Investigation Committee

P 3:

From the standardized rates it is clear that, with a short interruption in the fall of the male rate during the war years, mortality in both sexes has been declining since the beginning of the century.

8 Nombre abreviado: Link:

McKeown 1975 http://www.jstor.org/stable/2173935

P 11:

The last column of Table 4 summarizes the decline in mortality which occurred between 1901 and 1971. Approximately three-quarters (73 4 per cent) of the reduction was associated with the infections and one-quarter (26-6 per cent) with other conditions.

9 Nombre abreviado: Link:

McKeown 1975 http://www.jstor.org/stable/2173935

P 11

It is clear that the 1930s were a watershed in the history of treatment of infectious diseases, with the introduction of the sulphonamides followed, in the next decade, by the antibiotics. Since there were few effective therapeutic measures before 1935, it is interesting to consider the extent of the improvement in mortality from infections before and after this time. Table 5 shows the proportion of the total reduction which had occurred by 1931. Among the infections 56 per cent of the decline in mortality over the whole period (1901-71) occurred before 1931; among other conditions the proportion was 58 per cent. That is to say, in both cases more than half of the improvement took place in the first three of the seven decades, before the modern era of effective chemotherapy.

10 Nombre abreviado:

Link:

McKeown 1975

http://www.jstor.org/stable/2173935

P 23:

There was no effective treatment of scarlet fever before the use of prontosil in 1935. But, by the beginning of the century, mortality from the disease had fallen to a relatively low level (see Table 9), and between 1901 and 1971 the disease was associated with only 1 2 per cent of the total reduction from all causes. 89 per cent of this improvement occurred before the introduction of the sulphonamides.

11 Nombre abreviado:

Link:

McKeown 1975

http://www.jstor.org/stable/2173935

P 12, Tabla 4.

Dysentery and diarrhea went down 87% by 1931.

12 Nombre abreviado:

Link:

McKeown 1975

http://www.jstor.org/stable/2173935

P 22:

There is, therefore, little doubt that the death rate would have continued to fall even if effective therapeutic measures had not been applied. However, the decline was greatly accentuated by chemotherapy... We conclude that although therapy cannot be credited with the whole of the reduction since that time (3.6 per cent of the total) it was responsible for most of it.

Nombre abreviado:

Link:

McKeown 1975

http://www.jstor.org/stable/2173935

P 25

Whooping cough was associated with 2 7 per cent of the reduction in mortality from all causes. Treatment by sulphonamides and (later) antibiotics was not available before 1938, and even now its effect on the course of the disease is questionable. Immunization was used widely from 1952; the protective effect is variable, and has been estimated to lie between less than 20 and over 80 per cent. Mortality from whooping cough began to decline from the seventh decade of the nineteenth century, and 86 per cent of the reduction since 1901 occurred before the introduction of the sulphonamides.

14 Nombre abreviado: Link:

McKeown 1975 http://www.jstor.org/stable/2173935

P 25

Mortality fluctuated before 1915, but fell rapidly from that time. Between 1901 and 1971 the disease was responsible for 2 4 per cent of the total reduction. Effective specific measures against measles have only recently become available in the form of immunization and they can have had no significant effect on the trend of the death rate. However, mortality from the disease was attributable largely to invasion by secondary organisms, which have been treated by chemotherapy since 1935. 82 per cent of the decrease of deaths from measles had occurred before this date.

15 Nombre abreviado:

Link:

McKeown 1975

http://www.jstor.org/stable/2173935

P 25:

The disease was associated with 2 4 per cent of the fall of mortality from all causes between 1901 and 1971. It is not possible to assess with any precision the relative importance of the various influences which may have contributed. Antitoxin was first used in the late nineteenth century and has been the accepted form of treatment since that time. It is believed to have reduced the case fatality rate, which fell from 8 2 per 100 notifications in 1916-25 to 5 4 in 1933-42, while notifications remained at an average level of above 50,000 per year. The mortality rate increased at the beginning of the last war, but fell rapidly at about the time when national immunization was introduced.

16 Nombre abreviado:

Link:

McKeown 1975

http://www.jstor.org/stable/2173935

P 25:

It is tempting to attribute much of the decline of diphtheria mortality between 1901 and 1931 to treatment by antitoxin, and the rapid fall since 1941 to immunization. Nothing in British evidence is seriously inconsistent with this interpretation; however, experience in some other countries is not so consistent. Moreover, as already noted, other infections declined in the same period in the absence of effective prophylaxis or treatment.

17

Nombre abreviado: Lin

McKeown 1975 http

http://www.jstor.org/stable/2173935

P 20, Tabla 9.

The decrease in pertussis, diphtheria and measles is 7.5% of the overall decrease in deaths. In P 11 it is noted that the decline in infectious diseases was amounted to 75% of the overall decline in mortality. Thus, the decrease in pertussis, diphtheria and measles is about 10% of the the decline in mortality from infectious diseases.

18

Nombre abreviado:

Link:

McKeown 1972

http://www.jstor.org/stable/2173935

P 30:

There remains for consideration a miscellaneous group of conditions. Some of them are well-recognized infectious diseases which caused few deaths in this century, either because they were uncommon (as in the case of malaria, tetanus, poliomyelitis and encephalitis) or, because although common they were not often lethal (as in the case of mumps, chickenpox and German measles).

19 Nombre abreviado: Link:

McKeown 1972 https://www.jstor.org/stable/2173815

P 39

Although data for the nineteenth century are seriously deficient, analysis by cause of death for the four countries and England and Wales leaves little doubt that the decline of mortality was due to a reduction of deaths from infectious disease, almost wholly until 1900 and predominantly after that time. Vaccination against smallpox is the only medical measure likely to have been effective before the present century and it was not until 1935, with the introduction of the sulphonamides, that therapy became available which reduced mortality from infection to an extent that could be expected to lower the national death rate.

20

Colgrove 2002 (see reference 88 of this chapter) details the arguments made against McKeown's work, especially p 3. Szreter also (Szreter 1988 p 6 and 11) does not criticize the quality of McKeown's data.

21-40

21 Nombre abreviado: Archivo:

Szreter 1988 https://drive.google.com/open?id=1c8AaRwdKf2O1On-

VT0pI34G8xCEBWOIj

P 2-3:

It should be stressed at the outset that this achievement of McKeown's work, in deflating the historical claims of one particular section of the medical profession and its 'high tech' invasive and biochemical medicine, remains unaffected by the arguments set out below. McKeown's unanswerable point is precisely that this modern kind of applied medical science virtually did not exist during the period addressed here.

and P9:

The chapter then proceeded to demonstrate for each of the major diseases in turn that, with the exception of smallpox and diphtheria, the dates at which either effective immunization procedures or scientific medical treatments first became available were often far too late in time to be able to account for all but the last few percentage points of the overall decline of the disease. This was certainly true of respiratory tuberculosis, measles, and scarlet fever; and broadly true for whooping cough and the bronchitis, pneumonia, and influenza group. All had been declining very considerably in incidence long before effective chemotherapy or other scientific techniques had become available.

Nombre del artículo:

The Questionable Contribution of Medical Measures to the Decline of Mortality in the United States in the Twentieth Century

https://archive.org/details/McKinlayQuestionableContribution

Archivo:

https://drive.google.com/open?id=1N9Vt2A2iPPZW Hkwc_04IEMN1dIwEs65

ittps://aremve.org/details/ivieramay@destionable@ontributio

Autor principal/año: Revista:
John B. McKinlay, 1977 The Milbank M

The Milbank Memorial Fund Quarterly. Health and Society

P 11:

Between 1900 and 1973, there was a 69.2 percent decrease in overall mortality... Of the total fall in the standardized death rate between 1900 and 1973, 92.3 percent occurred prior to 1950... A major part of the decline in deaths from these causes since about 1900 may be attributed to the virtual disappearance of these infectious diseases.

Nombre abreviado: McKinlay 1977 Archivo: https://drive.google.com/open?id=1N9Vt2A2iPPZWHkwc_04I EMN1dIwEs65Q

P 15, Tabla 1

24 Nombre de la página: Archivo: Diphtheria, Tetanus, and Pertussis: Recommendations for http://archive.is/ETeaO Vaccine Use and Other Preventive Measures Recommendations of the Immunization Practices Advisory Committee (ACIP) Sitio web: CDC https://www.cdc.gov/mmwr/preview/mmwrhtml/00041645.htm The introduction and widespread use of standardized whole-cell pertussis vaccines combined with diphtheria and tetanus toxoids (DTP) in the late 1940s resulted in a substantial decline in pertussis disease, a decline which continued without interruption for nearly 30 years. Nombre de la página: Archivo: Pink Book - Diphtheria http://archive.is/4Tzlw Sitio web: CDC https://www.cdc.gov/vaccines/pubs/pinkbook/dip.html

Nombre abreviado: McKinlay 1977 Archivo: https://drive.google.com/open?id=1N9Vt2A2iPPZWHkwc_04I EMN1dIwEs65Q

P 15, Tabla1

A more rapid decrease began with the widespread use of diphtheria toxoid in the late 1940s.

Nombre abreviado: McKinlay 1977 Archivo: https://drive.google.com/open?id=1N9Vt2A2iPPZWHkwc_04I EMN1dIwEs65Q

P 22

In general, medical measures (both chemotherapeutic and prophylactic) appear to have contributed little to the overall decline in mortality in the United States since about 1900 - having in many instances been introduced several decades after a marked decline had already set in and having no detectable influence in most instances.

Nombre del artículo:
Trends in infectious disease mortality in the
United States during the 20th century
https://jamanetwork.com/journals/jama/fullarticle/768249
Archivo:
https://drive.google.com/open?id=1UuaAf
Ob3muFxfYgq-yGf3DsV1am1VjCM

Autor principal/año:
Gregory L. Armstrong, 1999
JAMA

 29 Nombre abreviado: Archivo: Armstrong 1999 https://drive.google.com/open?id=1UuaAfOb3muFxfYgqvGf3DsV1am1ViCM P 3, Figure 1

30 Nombre de la página:

Diphtheria, Tetanus, and Pertussis: Recommendations for Vaccine Use and Other Preventive Measures Recommendations of the Immunization Practices Advisory Committee (ACIP)

Archivo:

http://archive.is/ETeaO

Sitio web:

CDC

https://www.cdc.gov/mmwr/preview/mmwrhtml/00041645.htm

The introduction and widespread use of standardized whole-cell pertussis vaccines combined with diphtheria and tetanus toxoids (DTP) in the late 1940s resulted in a substantial decline in pertussis disease, a decline which continued without interruption for nearly 30 years.

31 Nombre abreviado: Archivo: Armstrong 1999 https://drive.google.com/open?id=1UuaAfOb3muFxfYgqvGf3DsV1am1ViCM Original Chart P 4, Figure 3

32 Nombre abreviado: Archivo: Armstrong 1999 https://drive.google.com/open?id=1UuaAfOb3muFxfYgqyGf3DsV1am1VjCM Original Chart P 5. Figure 4C. The original chart additionally includes polio.

33 Nombre abreviado: Archivo: https://drive.google.com/open?id=1UuaAfOb3muFxfYgq-Armstrong 1999 yGf3DsV1am1VjCM Original Chart P 5, Figure 4B

34 Nombre del artículo: PMID: Annual summary of vital statistics: trends in the 11099582 health of Americans during the 20th century

> Autor principal/año: Revista: Bernard Guyer, 2000 **Pediatrics**

P 8-9:

For children older than 1 year of age, the overall decline in mortality experienced during the 20th century has been spectacular. [...] Nearly 85% of this decline took place before World War II, a period when few antibiotics or modern vaccines and medications were available.[...] Once again, nearly 90% of the decline in infectious disease mortality among US children occurred before 1940, when few antibiotics or vaccines were available.

Vaccination, while first used in the 18th century, became more widely implemented in the middle part of the century. Vaccines against diphtheria, tetanus, and pertussis became available during the late 1920s but only widely used in routine pediatric practice after World War II. Thus vaccination does not account for the impressive declines in mortality seen in the first half of the century.

Public Health England

35 Pertussis mortality data -Archivo: https://drive.google.com/open Nombre del documento: ?id=1yxE1tZ--Pertussis notifications and deaths, England and Wales: 8Of74FPpCebxW-1940 - 2014mpRWqfvOkC https://www.gov.uk/government/publications/whoopingcough-pertussis-statistics Autor principal/año: **NHS** Measles mortality data -Archivo: http://archive.is/8YVzg Nombre de la página: Measles notifications and deaths in England and Wales: 1940 to 2016 https://www.gov.uk/government/publications/measlesdeaths-by-age-group-from-1980-to-2013-onsdata/measles-notifications-and-deaths-in-england-andwales-1940-to-2013 Sitio web:

36 Nombre del artículo: PMID: A Century of Changes in the Mortality and 21032289 Incidence of the Principal Infections of Archivo: Childhood https://www.ncbi.nlm.nih.gov/pmc/articles/PM https://drive.google.com/open?id=1c291 gAXasOhKEMg3Nxu7Z8i1sJ1w7DDk C1987926/ Autor principal/año: Revista: Archives Of Disease In Childhood AH Gale, 1945 P 1: ...the information about mortality is so much more complete and goes back so much further than does that about incidence.

Nombre del documento:
Annual Summary 1979
Reported Morbidity and Mortality in the United states

Autor principal/año:
CDC, 1980

P.5
Archivo:
https://drive.google.com/open?id=1NgxD
UuXCDNgNzFwBovBkn7186ThcIrUQ

P.5-

In 1893, an act provided for collection of information on a weekly basis... It was not until 1925, however, that that all states began to report regularly.

Nombre del documento:
Annual Summary 1979
Reported Morbidity and Mortality in the United states

Archivo:
https://drive.google.com/open?id=1NgxDUuXCDNgNzFwBovBkn7

Autor principal/año:
CDC, 1980

P 6:
These data should be interpreted with caution[...]. Despite these limitations the data in this report have proven to be useful in the analysis of trends.

Nombre del documento:

Annual Summary 1979 Reported Morbidity and Mortality in the United states

Archivo:

https://drive.google.com/open?id=1NgxDUuXCDNgNzFwBovBkn7186ThcIrUQ

Autor principal/año:

CDC, 1980

U.S. official morbidity data for the years 1930-1979 appear on pages 19-23. Except in the 1970s, the data are presented as a total number of cases, rather than as a percentage of the population.

40 Nombre de la página:

Diphtheria

Archivo:

http://archive.is/I9Uwf

Sitio web:

NHS

http://www.nhs.uk/conditions/diphtheria/pages/introduction.aspx

Before a vaccination programme was introduced in 1940, diphtheria was a very common condition and one of the leading causes of death in children.

41-60

41 Nombre de la página:

Notifiable diseases: historic annual totals

Cases of infectious diseases: annual total figures from 1912 to

2017

 $\underline{https://www.gov.uk/government/publications/notifiable-diseases-\underline{historic-annual-totals}}$

Sitio web:

GOV.UK

Archivo:

http://archive.is/2zzwJ

See official morbidity data - US (note 39) and UK (note 41). Typhoid fever also appears in the table under the names Paratyphoid fevers and Enteric fever.

43 Título del libro:

Vaccines (6th edition)

Published by Elsevier Saunders

https://www.elsevier.com/books/vaccines/plotkin/978-1-4557-

0090-5

Autor principal/año:

Stanley Plotkin, 2013

P 789:

There probably is no other widely used vaccine that is as controversial as BCG. Its effects in extremely large, randomized, controlled, and case-control studies have been widely disparate, in some cases demonstrating a great degree of protection and in others offering no benefit.

44 See official morbidity data - US (note 39) and UK (note 41).

45 Nombre de la página:

Childhood Vaccination and the NHS

https://peopleshistorynhs.org/encyclopaedia/childhood-vaccination-and-the-nhs/

Archivo:

http://archive.is/Ezq6V

Sitio web:

People's History of the NHS

Indeed, by the end of 1950 BCG vaccination programmes were operating in earnest throughout Scotland and had spread nationwide by early 1953.

46

Título del libro:

Vaccines (6th edition)

Published by Elsevier Saunders

https://www.elsevier.com/books/vaccines/plotkin/978-1-4557-0090-5

Autor principal/año:

Stanley Plotkin, 2013

P 780

The bacille Calmette-Gurin (BCG) vaccines [...] have been used routinely since the 1960s in almost all countries of the world except the United States and the Netherlands.

47

Measles mortality data -

Nombre de la página:

Measles notifications and deaths in England and Wales: 1940 to 2016

https://www.gov.uk/government/publications/measles-deaths-by-age-group-from-1980-to-2013-ons-data/measles-notifications-and-deaths-in-england-and-wales-1940-to-2013

Archivo:

http://archive.is/8YVzg

Sitio web:

Public Health England

48

See official morbidity data - US (note 39).

49

Nombre de la página:

Elimination of Malaria in the United States (1947 — 1951)

Archivo:

http://archive.is/7B0E

Sitio web:

CDC

https://www.cdc.gov/malaria/about/history/elimination_us.html

The National Malaria Eradication Program was a cooperative undertaking by state and local health agencies of 13 southeastern states and the Communicable Disease Center of the U. S. Public Health Service, originally proposed by Dr. L. L. Williams. The program commenced operations on July 1, 1947. It consisted primarily of DDT application to the interior surfaces of rural homes or entire premises in counties where malaria was reported to have been prevalent in recent years... Total elimination of transmission was slowly achieved. In 1949, the country was declared free of malaria as a significant public health problem.

Nombre del artículo:

Penicillin Treatment of Syphilis

http://jamanetwork.com/journals/jama/fullarticle/183391

PMID: 19224755

Archivo:

http://archive.is/8Uckh

Autor principal/año: Revista: John M. Douglas, 2009 JAMA

Within years, widespread use of penicillin for treatment of all stages of syphilis (primary, secondary, tertiary, latent) resulted in dramatic decreases in the incidence of syphilis and associated mortality.

From 1944 to 1954, rates of reported cases of syphilis of any stage decreased by more than 75% (from 368/100 000 to 83/100 000) with even greater declines in primary and secondary syphilis (from 62/100 000 to 4.5/100 000), which reflect more recent acquisition.

51 Título del libro:

Corn and Capitalism: How a Botanical Bastard Grew to Global Dominance https://books.google.co.il/books?id=cRnjAQAAQBAJ&pg=PA172#v=onepage&q&f=false

Autor principal/año:

Arturo Warman, 2003

P 171-172:

In 1915 the number of the stricken was estimated at between 75,000 and 160,000.

The tendency for the number of those affected by pellagra to climb turned the corner during the same period. In 1940 pellagra sufferers were estimated at fewer than 50,000 and their numbers fell by half over the next five years. In the 1950s pellagra became a clinical curiosity, a disease of the past.

52 | Título del libro:

Vaccines (6th edition)

Published by Elsevier Saunders

https://www.elsevier.com/books/vaccines/plotkin/978-1-4557-0090-5

Autor principal/año:

Stanley Plotkin, 2013

P 1407:

There is little doubt that the introduction of routine tetanus toxoid vaccination in the 1940s had an impact on trends and patterns of the disease. However, because the incidence of tetanus was declining prior to widespread vaccination, as a result of decreasing exposure (fewer people in contact with soil and animal feces, which are the main reservoirs of the tetanus bacillus), and because of the widespread use of tetanus toxoid in wound management, it is difficult to assess the extent to which routine prophylactic vaccination contributed to the decline in tetanus morbidity.

See official morbidity data - US (note 39) and UK (note 41).

54 Nombre abreviado: Link: McKeown 1972 https://www.jstor.org/stable/2173815 From the nineteenth century the contribution of improved food supplies to the reduction of mortality was supported by that of other influences: a general increase in the standard of living; better hygiene; and specific preventive and therapeutic measures introduced progressively during the twentieth century. Nombre abreviado: Archivo: Armstrong 1999 https://drive.google.com/open?id=1UuaAfOb3muFxfYgqyGf3DsV1am1VjCM P 4: From the nineteenth century the contribution of improved food supplies to the reduction of mortality was supported by that of other influences: a general increase in the standard of living; better hygiene; and specific preventive and therapeutic measures introduced progressively during the twentieth century.

Nombre del artículo: Annual summary of vital statistics: trends in the health of Americans during the 20th century PMID: 11099582

Autor principal/año: Revista: Bernard Guyer, 2000 Pediatrics

P 10:

The major declines in child mortality that occurred in the first third of the 20th century have been attributable to a combination of improved socioeconomic conditions in this country and the public health strategies to protect the health of Americans. These public health measures included the establishment of local health departments in nearly all of the states. State and local health departments implemented these public health measures including water treatment, food safety, organized solid waste disposal, and public education about hygienic practices. These improvements in water and food safety and purity are linked to the major decline in diarrheal diseases seen in the early years of the century. Similarly, improvements in housing and decreased crowding in US cities are linked to the reductions in mortality from tuberculosis and other diseases attributable to person-to-person airborne transmission..

55	Nombre del artículo:	Archivo:
-	TT 1 TT 1 1 TT 1 1	1 1 1/1 // 1/1 *

Urban Wastewater Management in the United States: Past, Present, and Future http://wvwv.sewerhistory.org/articles/whregion/ur ban wwm mgmt/urban wwm mgmt.pdf

https://drive.google.com/open?id=1VP eNmgPhp0L2lxxWa33zYdLHx3Mx8fY

Autor principal/año: Revista:

Steven J.Burian, 2000 Journal of Urban Technology

P 4:

There were fewer public sewers than private in the early nineteenth century, and most were constructed primarily for the purpose of removing storm water... Dry sewage systems and public and private sewers were commonly used in Europe and the United States, but the predominant wastewater management technology in the first half of the nineteenth century was the privy vault-cesspool system operated in a decentralized manner. Privy vaults and cesspools were basically holes in the ground, occasionally lined, constructed in cellars, beneath residences, or within close proximity to residences.

Nombre abreviado: Burian 2000 Archivo: https://drive.google.com/open?id=1VPeNmgPhp0L2lxxWa33z

YdLHx3Mx8-fY

P 4-5:

The unplanned and uncontrolled drainage of wastewater from privy vaults and cesspools contaminated soils and groundwater, and that occasionally led to contaminated drinking water and disease outbreaks.

[...]

Wastes accumulated till privies and cesspools overflowed and produced nuisance conditions and potential public health problems. In most cases, both lined and unlined privy vaults and cesspools proved unable to manage urban wastewater effectively during the mid-nineteenth century because the lined ones required too frequent cleaning to be cost effective over a long term, and the unlined ones contaminated groundwater and the surrounding soil.

None of the centralized or decentralized management technologies implemented during the early nineteenth century consistently prevented contamination of nearby surface water or

[...]

groundwater.

From 1820 to 1880, most major cities in the United States experienced considerable growth. For example, during this time Boston's population increased eightfold, New York City's tenfold, Philadelphia's thirteen fold, and Washington, D.C.'s fivefold. As a result of this increased population density in urban areas, the decentralized privy vault-cesspool wastewater management systems became overtaxed.

57	Nombre abreviado: Szreter 1988	Archivo: https://drive.google.com/open?id=1c8AaRwdKf2O1On-
		VT0pI34G8xCEBWOIj

P 20-21:

This followed a long period of extremely harmful, highly localized initiatives by the property-owning classes. They were the first to install their own water-flushing closets in large numbers from the 1770s onwards; but in the absence of a mains sewage system, these were simply allowed to empty into the nearest culvert or river, from which much of the town's population in turn took their drinking water. Unfortunately, this development was to be repeated in other cities and towns around the country in the course of the nineteenth century. The lethal lesson was only slowly learned that selective sanitation for the upper classes alone was not a sufficient panacea in the prevention of water-borne disease.

Nombre abreviado:	Archivo:
Burian 2000	https://drive.google.com/open?id=1VPeNmgPhp0L2lxxWa33z
	YdLHx3Mx8-fY

P 6:

The water closet probably had the most significant effect on wastewater management compared to the other plumbing fixtures because it increased not only wastewater quantity, but also the quantity of fecal matter in discharges. The high level of fecal matter being discharged with the wastewater heightened the risk of disease transfer and outbreak, but this was not understood at the time.

58	Nombre abreviado:	Archivo:
	Burian 2000	https://drive.google.com/open?id=1VPeNmgPhp0L2lxxWa33z
		YdLHx3Mx8-fY

P 8

Dr. Snow recorded the location of outbreaks during the [1854] epidemic and charted the drinking water source of infected individuals. He was able to show statistically that cholera victims drew their drinking water from a sewage-contaminated part of the River Thames, while those who remained healthy drew their water from an uncontaminated part.

Nombre abreviado: Archivo: https://drive.google.com/open?id=1c8AaRwdKf2O1On-

VT0pI34G8xCEBWOIj

P 21:

Sewering alone, without commensurate attention to the purity of the water supply, could prove a downright liability, as was tragically demonstrated by London's final cholera epidemic of 1866-7, immediately following the completion of London's sewers system. This was the last such epidemic and it was the famous occasion on which William Farr was able, using a method pioneered at the previous outbreak of 1853/4, to trace precisely the culprit. By dividing London into districts according to the different companies supplying water, the problem was narrowed down to the East London Waterworks Co., who were illegally supplying water from the Old Ford reservoir in Bethnal Green, which was contaminated by the recently completed West Ham sewage system.

60	Nombre abreviado: Burian 2000	Archivo: https://drive.google.com/open?id=1VPeNmgPhp0L2lxxWa33z
----	----------------------------------	--

P 8:

Prodded by public outcry... that linked sewage-polluted water with disease, Parliament passed an act in 1855 to improve the waste management of the metropolis. This act provided the foundation for the development of London's comprehensive water-carriage sewer system eventually designed by Joseph W. Bazalgette.

61-80

Archivo: Burian 2000 Archivo: https://drive.google.com/open?id=1VPeNmgPhp0L2lxxWa33z YdLHx3Mx8-fY

P 8

In the United States, repeated cholera epidemics and other disease outbreaks gradually influenced municipalities to improve sanitation practices. Between 1832 and 1873, numerous American cities were afflicted with major outbreaks of disease, including cholera in 1832, 1849, and 1866 and typhoid in 1848. The causes of the outbreaks were attributed to a variety of reasons including unsanitary conditions and punishment from God. The experience gained from the epidemics improved the understanding of cholera and other diseases and their corresponding etiology.

P 14:

At the end of the nineteenth century, the basic techniques of urban wastewater collection were established, the sewer technologies were mostly developed, and the necessary construction materials and equipment were available. By that time, most major U.S. cities had also constructed some form of a sewer system.

Nombre del artículo: The role of public health improvements in health advances: The twentieth-century United States

https://link.springer.com/article/10.1353/dem.2005.0002

Autor principal/año: Revista:
David Cutler, 2005 Demography

P 5, chapter "Clean Water Technologies: Filtration and Chlorination."

63 Nombre del artículo:

The role of public health improvements in health advances: The twentieth-century United

https://link.springer.com/article/10.1353/dem.2005.0002

Autor principal/año: Revista: Demography David Cutler, 2005

P 15-16:

A striking finding is that clean water technologies appear to have reduced typhoid fever by 26% initially and by another 65% after five years, leading to its near-eradication by 1936.

64 Nombre abreviado:

I ink. McKeown 1962 https://www.jstor.org/stable/2173119

P 25-26:

But with this reservation there is little doubt about the main reasons for the rapid reduction of mortality from the bowel infections in the late nineteen century... We therefore conclude that the reduction of mortality attributable to the decline of bowel infection resulted from the specific measures introduced under the sanitary revolution.

Nombre abreviado: Link:

McKeown 1975 http://www.jstor.org/stable/2173935

P 27:

WATER- AND FOOD-BORNE DISEASES Together, these infections accounted for about one-sixth (16-4 per cent) of the reduction in mortality from all causes (Table 4). The same diseases were responsible for about one-third of the total decline in the nineteenth century.

65 Nombre abreviado:

Archivo:

https://drive.google.com/open?id=1c8AaRwdKf2O1On-Szreter 1988

VT0pI34G8xCEBWOIi

P 18:

There can be little doubt that the first two-thirds of the nineteenth century witnessed an increasing incidence of such diseases, which was directly attributable to the unplanned proliferation of overcrowded cities and towns lacking even the most basic sanitary facilities such as proper water supply and waste disposal systems. Conversely, the ensuing disappearance of water-borne diseases in the last third of the century was due to the eventual provision of adequate sanitary facilities, long delayed but finally implemented.

66 Nombre del artículo:

Archivo:

The Horse & the Urban Environment https://enviroliteracy.org/environmentsociety/transportation/the-horse-the-urbanenvironment/

https://drive.google.com/open?id=1Kfk 5osa-wcmHc0f9R5nfynqmavChV5ug

Autor principal/año:

Joel Tarr, 1997

The most severe problem was that caused by horses defecating and urinating in the streets, but dead animals and noise pollution also produced serious annoyances and even health problems. The normal city horse produced between fifteen and thirty-five pounds of manure a day and about a quart of urine, usually distributed along the course of its route or deposited in the stable. While cities made sporadic attempts to keep the streets clean, the manure was everywhere, along the roadway, heaped in piles or next to stables, or ground up by the traffic and blown about by the wind.

Nombre de la página:

Tetanus

Archivo:

http://archive.is/mFSuM

Sitio web:

NHS Wales

http://www.nhsdirect.wales.nhs.uk/encyclopaedia/t/article/tetanus/

Tetanus is caused by bacteria called Clostridium tetani. These bacteria can survive for a long time outside the body, and are commonly found in soil and the manure of animals such as horses and cows.

Nombre de la página:

Tetanus

Archivo:

http://archive.is/pNRwR

Sitio web:

Victoria State Government – Better Health

https://www.betterhealth.vic.gov.au/health/healthyliving/tetanus

Tetanus bacteria live in soil, dust and manure, particularly horse manure.

Nombre abreviado:

Tarr 1997

Archivo:

https://drive.google.com/open?id=1Kfk5osa-wcmHc0f9R5nfynqmavChV5ug

P 1:

Manure piles also produced huge numbers of flies, in reality a much more serious vector for infectious diseases such as typhoid fever than odors. By the turn of the century public health officials had largely accepted the bacterial theory of disease and had identified the "queen of the dung-heap" or fly, as a major source. Inventors and city officials devised improved methods of street cleaning and street sweeping became a major urban expense.

69 Nombre abreviado:

Tarr 1997

Archivo:

https://drive.google.com/open?id=1Kfk5osa-

wcmHc0f9R5nfynqmavChV5ug

P 2:

If the horse created many problems for the city, it was also true that urban life was extremely hard on the horse. The average streetcar horse had a life expectancy of about four years... In 1880, New York City removed 15,000 dead horses from its streets, and late as 1916 Chicago carted away 9,202 horse carcasses. Special trucks were devised to remove dead horses.

70

Nombre abreviado:

Archivo:

Tarr 1997

https://drive.google.com/open?id=1Kfk5osa-

wcmHc0f9R5nfynqmavChV5ug

P 2-3:

It has already been noted that, while horse-powered machines persisted in manufacturing until about 1850, they were largely replaced by other energy sources in the following decade.

[...]

The next use of urban horses to disappear was pulling streetcars. Their demise was very rapid, as between 1888 and 1892 almost every street railway in the U.S. was electrified.

[...]

The coming of the automobile dealt another large blow to the horse...

71 Nombre del artículo:

Charles-Jules-Henri Nicolle

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2819868/

PMID: PMC2819868

Archivo:

https://drive.google.com/open?id=18kd BvjD2UKLU8rEZNmYKPM3ahYvcq 47z

Autor principal/año: Revista:

Emerging Infectious Diseases | Myron G. Schultz, 2009

P 1:

Throughout history, typhus had been a highly communicable and frequently fatal disease... It devastated armies during wars ("war typhus") and prisoners living under unsanitary conditions ("jail typhus" or "jail fever"); it affected displaced populations suffering from famine, floods, and other natural disasters; and in general, it was a disease of poverty.

72 Nombre del artículo:

Charles-Jules-Henri Nicolle https://www.ncbi.nlm.nih.gov/p mc/articles/PMC2819868/

PMID:

PMC2819868

Archivo:

https://drive.google.com/open?id=18kdBvjD2UKLU8rEZNmYKPM3ahYvcq47z

Autor principal/año:

Emerging Infectious Diseases

Revista:

Myron G. Schultz, 2009

P 2:

Nicolle observed that typhus patients who were admitted spread their infections to others up to the point at which they entered the hospital waiting room. Included among these secondary cases were persons who took charge of their clothing. However, patients became completely noninfectious as soon as they were bathed and dressed in a hospital uniform. They could then enter the general wards without posing a risk to others. Once Nicolle realized this, he reasoned that lice on patients' clothes were most likely the vectors.

73

Nombre abreviado:

Archivo:

Szreter 1988

https://drive.google.com/open?id=1c8AaRwdKf2O1On-

VT0pI34G8xCEBWOIj

P 13:

Droplet-transmitted airborne diseases will spread most effectively where humans are in close and unventilated proximity with the exhalations of victims or carriers. It is most probable that overcrowded conditions of living, sleeping, and working became more prevalent as industrialization and urbanization intensified.

74

Nombre abreviado:

Archivo:

Szreter 1988

https://drive.google.com/open?id=1c8AaRwdKf2O1On-VT0pI34G8xCEBWOIj

Szreter mentions this in the context of infant diseases

P 31

... the root of the general problem of infants' vulnerability lay in the fundamentally unhygienic conditions and associated practices of the urban working-class home, virtually inevitable in small overcrowded households lacking their own water supply and water closet. Until it began to be improved from the 1890s onwards, such an environment was continuously introducing infants to bacterial organisms (in particular some strains of Escherichia coli) which, although not harmful to the more developed digestive system of elder children and adults, could produce fatal diarrhea attacks in infants

75 Nombre del artículo:

Food in 19th-Century American Cities

http://americanhistory.oxfordre.com/view/10.1093/acrefore/9780199329175.001.0001/acrefore-9780199329175-e-281

Autor principal/año: Revista:

Cindy R. Lobel, 2016 Oxford Research Encyclopedia of American History

P 1:

Food provisioning was very local. Farmers, hunters, fishermen, and dairymen from a few miles away brought food by rowboats and ferryboats and by horse carts to centralized public markets within established cities. Dietary options were seasonal as well as regional.

76 Nombre abreviado: Archivo:

Lobel 2016 http://americanhistory.oxfordre.com/view/10.1093/acrefore/978

0199329175.001.0001/acrefore-9780199329175-e-281

P 11:

Before refrigeration and reliable transportation, perishable foods were scant in the diet of most urbanites. Even the wealthiest were accustomed to eating spoiled or rancid food or forgoing fresh produce in the colder months.

P 6:

The summer months were most abundant and diverse, with stone fruits, berries, apples, tomatoes, watermelons, lettuces, and other warm-weather produce crowding the tables under the market-house roofs. Food also spoiled quickest in these months, and observers noted the rapidity with which meat spoiled and vegetables wilted.

P 12:

As for fresh vegetables, they were not commonly consumed in the 1800s, though the diet expanded to incorporate them by the second half of the century... Fruits also were more commonly eaten in stewed and dessert forms rather than fresh.

77 Nombre abreviado: Link:

McKeown 1975 <u>http://www.jstor.org/stable/2173935</u>

P 25:

Epidemiological evidence suggests that nutrition plays an important part in the individual's reaction to measles. In this country, until recently, infection rates were high and approximately the same in all social classes; but mortality rates were much greater among the poor than among the well-to-do. Similarly, in developing countries to-day, there is little doubt that the devastating effects of measles are associated with low living standards. The explanation accepted by most epidemiologists with extensive experience of measles is that although infection rates are largely independent of social circumstances, the mortality which results from the infection is determined mainly by nutritional state.

78 Nombre abreviado: Archivo: http://americanhistory.oxfordre.com/view/10.1093/acrefore/978 0199329175.001.0001/acrefore-9780199329175-e-281

P 2:

A host of technological developments—from canal and railroad building to the manufacturing of ice and the creation of refrigerated railcars—indelibly altered urban American foodways during the 19th century. The most crucial of these developments involved new forms of transportation that eased and cheapened the carriage of foodstuffs from rural to urban areas.

P 3

The new transportation networks also improved the quality of food entering American cities... Foods that previously had perished during travel along rudimentary roads now endured long distances without spoiling. Railroads carried milk from rural areas to far-off cities, oysters from New York City to Buffalo, wild game from Iowa to Baltimore, salmon from Maine to Philadelphia, even lobster from the East Coast to Chicago.

	79	Nombre abreviado: Lobel 2016	Archivo: http://americanhistory.oxfordre.com/view/10.1093/acrefore/978 0199329175.001.0001/acrefore-9780199329175-e-281
to the tra		Technologies related direct	tly to food storage, preservation, and processing also contributed oan food habits. Among the most important were those involved on and storage of ice.

80	Nombre abreviado:	Archivo:
	Lobel 2016	http://americanhistory.oxfordre.com/view/10.1093/acrefore/978
		<u>0199329175.001.0001/acrefore-9780199329175-e-281</u>

P 4:

Food-safety issues arose periodically over the course of the 19th century because of the absence of any regulation of large conglomerates or small, food-related businesses. The milk supply was of particular concern, as distilleries in places like New York, Chicago, and Cincinnati paired with dairies within the city limits.

81-100

81	Nombre de la página: About FDA - Part I: The 1906 Food and Drugs Act and Its Enforcement	Archivo: http://archive.is/A0SeF
	Sitio web:	
	https://www.fda.gov/AboutFDA/History/FOrgsHistory/EvolvingPo	wers/ucm054819.htm

82 Nombre abreviado: Archivo:

Szreter 1988 <u>https://drive.google.com/open?id=1c8AaRwdKf2O1On-</u>

VT0pI34G8xCEBWOIi

P 24-25:

Another example is that of the increasingly close regulation of the quality of the urban food supply, which duly resulted from the attention which Medical Officers in the 1860s had begun to pay to adulterated and defective foodstuffs, particularly meat and milk, as a source of disease. The Adulteration of Foods Acts followed in the 1870s, leading to the appointment of professional inspectors and public analysts by most local authorities in the 1880s; also Weights and Measures Acts in 1878 and 1889 and a final consolidating Sale of Food & Drugs Act 1899.

83 Nombre de la página:

Archivo:

A history of medicine – Modern Medicine

http://archive.is/7ONEG

Sitio web:

Medical News Today

http://www.medicalnewstoday.com/info/medicine/modern-medicine.php

Nombre abreviado:

Link:

McKeown 1972

https://www.jstor.org/stable/2173815

P 7:

Virtually nothing was known about the aetiology and natural history of disease before the late nineteenth century. Effective measures were few and their use was largely misunderstood. Surgery was limited without anaesthesia and dangerous without knowledge of antisepsis. In the absence of understanding of the nature of infectious disease and the mechanisms by which it spreads, there were inevitable risks associated with hospital care, when patients, some of whom were infected, were brought in to close contact with one another.

Nombre de la página:

Archivo:

Medicine In The 20th Century

http://archive.is/DCGLC

Sitio web:

Encyclopedia Britannica

https://www.britannica.com/topic/history-of-medicine/Medicine-in-the-20th-century

[In early 1900s] There was still little to be done for the victims of most infectious organisms beyond drainage, poultices, and ointments, in the case of local infections, and rest and nourishment for severe diseases.

86

Nombre abreviado:

Archivo:

Szreter 1988

https://drive.google.com/open?id=1c8AaRwdKf2O1On-VT0pI34G8xCEBWOIj

P 2:

This work achieved something of a conceptual revolution in the disciplines of history and medicine, overturning a long-standing general orthodoxy regarding the importance of medical science and the medical profession in bringing about the decline in mortality which accompanied industrialization in Britain. It effectively demonstrated that those advances in the science of medicine which form the basis of today's conventional clinical and hospital teaching and practice, in particular the immuno- and chemo-therapies, played only a very minor role in accounting for the historic decline in mortality levels.

Nombre abreviado: Link:

McKeown 1962 https://www.jstor.org/stable/2173119

P 6

The practice of grouping as "medical advances" both therapy and environmental measures is undesirable not only because the latter were by no means exclusively the work of medical men. These two classes of influence differ grossly in their nature and effectiveness, and for interpretation of trends in the nineteenth century it is essential that they should be considered separately.

88 Nombre del artículo:

The McKeown Thesis: A Historical Controversy and Its Enduring Influence

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1

447153/

PMID: 11988435

Archivo:

https://drive.google.com/open?id=1k4u ypinpP1qhajclU-Uc Q5o8qwphlJt

Autor principal/año: Revista: James Colgrove, 2002 Americar

American Journal of Public Health

P 4:

The consensus among most historians about the McKeown thesis a quarter century after it first stirred controversy is that one narrow aspect of it was correct—that curative medical measures played little role in mortality decline prior to the mid-20th century...

89 Nombre de la página:

Ten Great Public Health Achievements in the 20th Century

Archivo:

http://archive.is/Lo3I

Sitio web:

CDC

https://www.cdc.gov/about/history/tengpha.htm

90 Nombre de la página:

Achievements in Public Health, 1900-1999: Control of Infectious Diseases

Archivo:

http://archive.is/Zj4lp

Sitio web:

CDC

https://www.cdc.gov/mmwr/preview/mmwrhtml/mm4829a1.htm

By 1900, however, the incidence of many of these diseases had begun to decline because of public health improvements, implementation of which continued into the 20th century. Local, state, and federal efforts to improve sanitation and hygiene reinforced the concept of collective "public health" action (e.g., to prevent infection by providing clean drinking water).

91 Nombre del documento:

Immunization Safety Review: Multiple Immunizations and Immune Dysfunction

https://www.nap.edu/catalog/10306/immunizationsafety-review-multiple-immunizations-and-immunedysfunction

Archivo:

https://drive.google.com/open?id= 1QujT3DieBvlChf3vi4h18hjK1O Qzx4Cp

Autor principal/año:

IOM, 2002

P 7 (22):

In any case, the number of infections prevented by immunization is actually quite small compared with the total number of infections prevented by other hygienic interventions such as clean water, food, and living conditions.

92 Nombre de la página:

Archivo: Five Important Reasons to Vaccinate Your Child http://archive.is/AF6HN

Sitio web:

Vaccines.gov

https://www.vaccines.gov/more info/features/five-important-reasons-to-vaccinate-yourchild.html

Because of advances in medical science, your child can be protected against more diseases than ever before. Some diseases that once injured or killed thousands of children, have been eliminated completely and others are close to extinction – primarily due to safe and effective vaccines.

93 A typical example:

Nombre del artículo:

Historical Comparisons of Morbidity and Mortality for Vaccine-Preventable Diseases in the United States

https://jamanetwork.com/journals/jama/ful larticle/209448

Autor principal/año: Sandra W. Roush, 2007 PMID. 18000199

Archivo:

https://drive.google.com/open?id=1nSuvGi5SAWi39wJ00oGlx0EWWiCb9v

94 Nombre de la página:

Medical Definition of Chronic disease

Archivo:

http://archive.is/q3URx

Sitio web:

MedicineNet.com

http://www.medicinenet.com/script/main/art.asp?articlekey=33490

Revista:

JAMA

Chronic disease: A disease that persists for a long time. A chronic disease is one lasting 3 months or more, by the definition of the U.S. National Center for Health Statistics. Chronic diseases generally cannot be prevented by vaccines or cured by medication, nor do they just disappear.

95 Nombre del artículo:

Trends in Childhood Disability

https://www.ncbi.nlm.nih.gov/pmc/articles /PMC1651471/pdf/amjph00626-0040.pdf

PMID: 6230017

Archivo:

https://drive.google.com/open?id=10cA6x A9 xIhBojRWvqPn8ru0YNa6manG

Autor principal/año: Revista:

Paul W. Newacheck, 1984 American Journal of Public Health

P 2, Tabla 1

96 Nombre del artículo:

Childhood Chronic Illness: Prevalence, Severity, and Impact

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1 694379/pdf/amjph00540-0038.pdf

PMID: 1536351

Archivo:

https://drive.google.com/open?id=1-24wBSNubDTj7cBDBRqX8sEqLeiqA xWG

Autor principal/año: Revista:

Paul W. Newacheck, 1992 American Journal of Public Health

The figure of the number of children with a chronic condition that limits them in routine activities does not appear, for some reason, in the article. However, it can be calculated according to the data of 31% of the children with some chronic problem (p. 4, Table 2), of which 13.3% with some limitation in routine activity (p. 5, Table 5). The rate of 4.1% is an underestimation (compared to the 1981 survey) because the 1988 survey did not include mental problems (p. 2).

97 Nombre del artículo:

Prevalence and Impact of Disabling Chronic Conditions in Childhood

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1 508436/pdf/amjph00016-0074.pdf

PMID: 9551003

Archivo:

https://drive.google.com/open?id=1OH f6M1Ufbx71JtHf7mPyDxHuWPhX0f wv

Autor principal/año: Revista:

Paul W. Newacheck, 1998 American Journal of Public Health

P 2:

On average, approximately 446 000 (0.7%) children younger than age 18 were estimated to be unable to conduct their major activity each year during 1992 through 1994, approximately 2726000 (4.0%) were limited in the kind or amount of their major activity, and about 1 224000 (1.8%) were limited in other activities. Thus, an annual average of 4 396000 (6.5%) children experienced some degree of disability.

98 Nombre del artículo:

The Rise In Chronic Conditions Among Infants, Children, And Youth Can Be Met With

Continued

Health System Innovations

https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.2014.0832

PMID: 25489027

Archivo:

https://drive.google.com/open?id=199b LfWqYYf0JFd2QRXSMhBU9nQFUH 2C2

Autor principal/año: Revista: James M. Perrin, 2014 Health Affairs

P 3:

In 1960, 1.8 percent of children were reported to have a health condition severe enough to interfere with usual daily activities. In 2010, more than 8 percent of children had a health condition that interfered with daily activities—an increase of more than 400 percent in fifty years.

99 Nombre del artículo:

A National and State Profile of Leading Health Problems and Health Care Quality for US Children: Key Insurance Disparities and Across-State Variations PMID: 21570014

Autor principal/año: Revista:

Christina D. Bethell, 2011 Academic Pediatrics

100	Nombre del artículo: Poverty and Trends in Three Common Chronic Disorders http://pediatrics.aappublications.org/content/early/2017/02/09/peds.2016-2539		PMID: 28193790 Archivo: https://drive.google.com/open?id=1cY EgX8RyrC_WqcVI3QHnr- JYPvHB98TY
	Autor principal/año: Christian D. Pulcini, 2016 P 3	Revista: Pediatrics	

101-120

101	Nombre del artículo: Dynamics of Obesity and Chronic Health Conditions Among Children and Youth https://jamanetwork.com/journals/jama/fullarticle/ e/185391		PMID: 20159870 Archivo: https://drive.google.com/open?id=1aO ddhiCdNzVF9PStJPMYU- 8lmuyhLDRY
	Autor principal/año: Jeanne Van Cleave, 2010 P 4	Revista: JAMA	

102	Nombre del artículo: So Young and So Many Pills	Fecha: Dec 28, 2010
	Sitio web: Wall Street Journal https://www.wsj.com/articles/SB10001424052970203731004 576046073896475588	Archivo: http://archive.is/IGY7m
	Nombre del artículo: More than 25% of Kids and Teens in the U.S. Take Prescriptions on a Regular Basis	Fecha: May 19, 2011
	Sitio web: IWB http://investmentwatchblog.com/more-than-25-of-kids-and-teens-in-the-u-s-take-prescriptions-on-a-regular-basis/	Archivo: http://archive.is/t9r1N
	Nombre del artículo: Prescription drug use by US children on the rise	Fecha: May 19, 2010
	Sitio web: Reuters http://www.reuters.com/article/medco-children-idUSN1924289520100519	Archivo: http://archive.is/I3rfR

103

Nombre del artículo:

Increasing Prevalence of Medically Complex Children in US Hospitals

https://pdfs.semanticscholar.org/0c08/f41f3061c

c21f7e9a39202d1c7934c1762a6.pdf

PMID: 20855383

Archivo:

https://drive.google.com/open?id=1GO anye2s01-

bEmNfkpRPcxRx4voVLNKE

Autor principal/año: Katherine H. Burns, 2010 Revista: Pediatrics

P 3-4:

The hospitalization rates of children with diagnoses in a single CCC category increased by an average of 5.59% each year-group from 763.7 per 100 000 to 943.2 per 100 000 (P < .022). The hospitalization rates of children with diagnoses in more than 1 CCC category increased by an average of 17.6% each year-group and doubled from 83.7 per 100 000 in 1991–1993 to 166.3 per 100 000 in 2003–2005 (P < .001).

104

Nombre del artículo:

Children With Complex Chronic Conditions in Inpatient Hospital Settings in the United States https://www.ncbi.nlm.nih.gov/pmc/articles/PM C2962571/pdf/nihms-238735.pdf

PMID: 20855394

Archivo:

https://drive.google.com/open?id=1Kys bgd3eBzzF-BiPo-DJbaGvi3NsK9Sr

Autor principal/año: Tamara D. Simon, 2010

Revista: **Pediatrics**

P 5:

CCCs composed 10% of admissions, 25% of hospital days, 40% of hospital charges, 75% to 92% of technology-assistance procedures, and 43% of inpatient deaths among US children in 2006.

105

Nombre de la página:

Asthma facts and statistics

Archivo:

http://archive.is/RhF80

Sitio web:

Asthma.org

https://www.asthma.org.uk/about/media/facts-and-statistics/

One in 11 children in the UK has asthma.

106

Nombre del documento:

Diabetes: Facts and Stats

https://www.mrc.ac.uk/documents/pdf/diabetes-ukfacts-and-stats-june-2015/

Archivo:

https://drive.google.com/open?id= 1r7gv9E1GKXhyq4Vnqu Z6kjV

MThtfvBH

Autor principal/año:

MRC, 2015

107

Nombre del artículo:

The rise of childhood type 1 diabetes in the 20th century

PMID: 12453886

Autor principal/año: Revista: Edwin A.M. Gale, 2002 Diabetes

The best evidence available suggests that childhood diabetes showed a stable and relatively low incidence over the first half of the 20th century, followed by a clear increase that began at some time around or soon after the middle of the century. This increase occurred around the same time in Scandinavia, the U.K., the U.S., and Sardinia but may have occurred later in other parts of the world.

108 Nombre de la página:

Food allergy

Archivo:

http://archive.is/7Ciz4

Sitio web:

NHS

http://www.nhs.uk/conditions/food-allergy/Pages/Intro1.aspx

Most food allergies affect younger children under the age of three. It's estimated around 1 in every 14 children of this age has at least one food allergy. [...]

For reasons that are unclear, rates of food allergies have risen sharply in the last 20 years.

109 ∣ N

Nombre del artículo:

Trends in the incidence of type 1 diabetes among Jews and Arabs in Israel

PMID: 24283719

Autor principal/año:

Revista:

Orit Blumenfeld, 2014

Pediatric Diabetes

P 2:

The mean age-adjusted incidence increased by 52.6%, from 8.0 per 100,000 in 1997 to 13.2 per 100,000 in 2010.

110

Nombre del documento:

Health Status in Israel 2010 Report (hebreo)
https://www.health.gov.il/PublicationsFiles/Health_S
tatus in Israel2010.pdf

Archivo:

https://drive.google.com/open?id= 1RRmkP_eUQJKC2XEGZ2ck4f GGHb71rsTu

Autor principal/año:

Israeli Department of Health, 2011

P 236 (Traducido del hebreo):

"In a 2008 survey, 7.9 percent of eighth-graders reported having asthma or spastic bronchitis at present, and 13.9 percent of Jewish and Arab students reported ever having asthma or spastic bronchitis."

111

Nombre del artículo (traducido del hebreo):
Research: A surge in the number of children

Research: A surge in the number of children diagnosed with ADHD

Fecha:

Jan 13, 2016

Archivo:

http://archive.is/vsmuc

Sitio web:

YNET

https://www.ynet.co.il/articles/0,7340,L-4752240,00.html

The researchers, led by Dr. Davidovich - Director of Child Development at Maccabi Health Services and a member of the Faculty of Medicine at Bar-Ilan University, found that if in 2005 6.8% of children were diagnosed with ADHD, then in 2014 there was a jump and the rate of diagnoses rose to 14.4% - that is, 1 in 7 children.

112

Nombre del documento (traducido del hebreo):

The use of the drug Ritalin among students in the education system

Archivo:

https://drive.google.com/open?id=1 uCb1q406FDebqWqzof8aFnU0qa2 -Fu-f

Autor principal/año:

Knesset [Israeli Parliamnet] Research Center, 2013

P 2 (hebreo):

"Our examination revealed that the education system does not have data on the number of students diagnosed with ADHD or patients taking Ritalin or its alternatives. The Ministry of Education publishes general guidelines regarding Ritalin treatment among students in schools, but emphasizes that this issue is the responsibility of the Ministry of Health. The Ministry of Health does not have accurate information on the number of students diagnosed with ADHD or on the number of students treated with Ritalin."

113

Nombre del artículo (traducido del hebreo):

A lesson in sensitivity: Schools will work for allergic children

Fecha:

Dec 2, 2016

Archivo:

http://archive.is/WH2zR

Sitio web:

Israel Today

http://www.israelhayom.co.il/article/432489

A step forward in integrating children with food allergies into the education system: A circular issued by the director general of the Ministry of Education this week defines that any class in which an allergic student studies will be declared a 'safe environment', to which the allergenic food component will be banned. In other classrooms, safety precautions will be taken, such as cleaning tables with wipes, to protect allergic students. The circular also defines that schools will also have alternative areas where it will be possible to eat food products that contain allergens, for the benefit of other students.

[...]

It is estimated that in Israel there are about 15,000 children in the education system who suffer from allergies of various severity levels. About 2,600 children in first and second grades are assisted by personal assistants, but after this age the assistance is ceased.

114

Nombre del documento (hebreo):

Presentation by the Ministry of Health and Education - Food Allergy

http://cms.education.gov.il/NR/rdonlyres/03E94519-E25D-4E0E-97B0-A19B086415F0/121418/RgishutMazon.ppt

Archivo:

https://drive.google.com/open?id=1TAxnWNl1mMncNnjGK_DCUk2-rosgFoW9

Autor principal/año:

Israeli Ministry of Health, 2010

Slide 7

1,044 children up to the age of 18 were hospitalized for a food allergic reaction in 2008

Nombre del artículo:
Direct and Indirect Costs of Asthma in Schoolage Children
https://www.cdc.gov/pcd/issues/2005/jan/pdf/04
Archivo:
https://www.cdc.gov/pcd/issues/2005/jan/pdf/04
Archivo:
https://archive.is/nkY0y

Autor principal/año:

Li Yan Wang, 2005
Preventing Chronic Disease

Costs of Asthma in US School Children in 1996:
Total economic impact of asthma in school-age children was \$1993.6 million (\$791 per

116 Nombre del documento: Archivo: https://driv

Reported Morbidity and Mortality in the United states

https://drive.google.com/open?id=1NgxD UuXCDNgNzFwBovBkn7186ThcIrUQ

Autor principal/año:

child with asthma).

CDC, 1980

P 18. Summary of infectious diseases in 1979, excluding gonorrhea, syphilis and rabies (in animals).

117 Nombre del artículo: PMID: Trends in Childhood Disability 6230017

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1651471/pdf/amjph00626-0040.pdf

Archivo:

https://drive.google.com/open?id=10cA6x A9xIhBojRWvqPn8ru0YNa6manG

Autor principal/año: Revista:

Paul W. Newacheck, 1984 | American Journal of Public Health

Page 2, Table 1 shows the morbidity rate in 1979. The number 2 million appears on page 2, referring to 1981, which had a similar proportion of sick children to that of 1979:

Data from the NHIS for 1981 show that over two million children suffer some degree of limitation of their activities because of their health or disability...

118 Nombre del artículo:

More than 25% of Kids and Teens in the U.S. Take Prescriptions on a Regular Basis

Fecha: May 19, 2011

Archivo:

http://archive.is/t9r1N

Sitio web:

IWB

 $\underline{http://investmentwatchblog.com/more-than-25-of-kids-and-teens-in-the-u-s-take-prescriptions-on-a-regular-basis/}$

119 Nombre del artículo: PMID: Infectious Disease Hospitalizations in the 19708796 Archivo: https://academic.oup.com/cid/article/49/7/1025/ https://drive.google.com/open?id=1iba 314998 OMusV86pnftihJHFcynefRmRL70eY Autor principal/año: Revista: Krista L. Yorita Christensen, Clinical Infectious Diseases 2009 P 3, Tabla 2: A weighted average calculation of the hospitalization rate for ages 0-19 (assuming cohorts of similar size) gives a result of 1,027 hospitalizations per 100,000 or 1.02%.

120 Nombre de la página: Archivo: The 2009 H1N1 Pandemic: Summary Highlights, April 2009http://archive.is/aBxT April 2010 Sitio web: CDC https://www.cdc.gov/h1n1flu/cdcresponse.htm CDC activated its Emergency Operations Center (EOC) on April 22, 2009, to coordinate the response to this emerging public health threat. Nombre de la página: Archivo: Swine influenza http://archive.is/kX13O Sitio web: WHO http://www.who.int/mediacentre/news/statements/2009/h1n1 20090425/en/ In response to cases of swine influenza A(H1N1), reported in Mexico and the United States of America, the Director-General convened a meeting of the Emergency Committee to assess the situation and advise her on appropriate responses... The Committee nevertheless agreed that the current situation constitutes a public health emergency of international concern. Based on this advice, the Director-General has determined that the current events constitute a public health emergency of international concern, under the Regulations.

121-125

121	Nombre del artículo: CDC: Measles Outbreak a 'Wake-Up Call'	Fecha: Jan 29, 2015	
		Archivo: http://archive.is/5sLoj	
	Sitio web:		
	Medpagetoday		
	http://www.medpagetoday.com/primarycare/vaccines/49786		
	Anne Schuchat, MD, director of the CDC's National Center for Immunization and Respiratory Diseases, told reporters on a conference call that 84 people in 14 states have been diagnosed with measles so far in 2015 and, of them, 67 are linked to the Disneylan outbreak []		
	The Disneyland-centered outbreak is "a wake-that future imported cases don't spread.	up call" for Americans to be vaccinated so	

122

Nombre del artículo:

The Rise In Chronic Conditions Among Infants, Children, And Youth Can Be Met With Continued

Health System Innovations

https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.2014.0832

PMID: 25489027

Archivo:

https://drive.google.com/open?id=199b LfWqYYf0JFd2QRXSMhBU9nQFUH 2C2

Autor principal/año: Revista:
James M. Perrin, 2014 Health Affairs

P 4:

What has caused such substantial growth in common conditions in recent decades? Increasingly, evidence points to genetic bases for these conditions, but genetic drift—changes in the gene pool of reproductive-age adolescents and young adults—alone cannot explain this rapid growth.

123

Nombre del artículo:

The rise of childhood type 1 diabetes in the 20th century

PMID:

12453886

Autor principal/año: Revista: Edwin A.M. Gale, 2002 Diabetes

P 1

A rapid change in incidence within a genetically stable population implies that nongenetic factors are active and that the influence of genes is relative to population, time, and place. It suggests that something has changed in the environment our children encounter or in the way they are treated.

124

Nombre abreviado:

Archivo:

Perrin 2014

https://drive.google.com/open?id=199bLfWqYYf0JFd2QRXSMhBU9nQFUH2C2

P 4:

Additionally, growing public awareness of these conditions coupled with advances in screening in health care and school settings may identify mildly affected children who in previous years may have gone undiagnosed, accounting for some of the rapid increase in overall prevalence.

125

Nombre abreviado:

reviado: Archivo:

Perrin 2014

https://drive.google.com/open?id=199bLfWqYYf0JFd2QRXS

MhBU9nQFUH2C2

P 3

However, premature infants of higher birthweight experience much less longterm morbidity than in years past, and the absolute numbers of extremely low-birthweight infants are small (less than 1 percent of all births). Advances in prenatal and newborn screening for genetic and infectious conditions have also prevented a significant proportion of intellectual disabilities.

Capítulo 9: Inmunidad de rebaño

1-20

1 Título del libro:

Vaccines (6th edition)

Published by Elsevier Saunders

https://www.elsevier.com/books/vaccines/plotkin/978-1-4557-0090-5

Autor principal/año:

Stanley Plotkin, 2013

P 1395:

...the concept of herd immunity... refers to the prevalence or proportion of immune persons in a population... which, if achieved, should lead to the elimination of an infection from a population.

2 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

Autor principal/año:

Stanley Plotkin, 2013

P 1395

herd immunity, a term that refers to... indirect protection of nonimmune persons, attributable to the presence and proximity of immune persons.

3 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

Autor principal/año:

Stanley Plotkin, 2013

P 1396:

if an infection or vaccine induces some degree of immunity against infection, then some nonimmune people will be protected indirectly, by the presence and proximity of immune persons, and transmission should stop in a population prior to the infection of all susceptible individuals.

4 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

For example, exposure to the measles virus results in lifelong immunity.

P 1403

One of the remarkable observations about measles is that immunity induced by natural infection appears to remain strong for life: thus, Panum observed that individuals exposed to measles in 1781 in the Faroe Islands were still immune when the virus was next introduced, 65 years later, in 1846.

5 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

For example, immunity to the Hib bacterium, P 1406:

The absence of disease in the neonatal period is a result of maternal antibody, passed to the infant either transplacentally or via breast milk. As infant antibody levels fall, susceptibility rises...

6 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1397-1398.

7 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1406.

If a vaccine were to protect only against disease, and not at all against infection, then it would have no influence on infection transmission in the community and there would be no indirect protection (vaccination of one person would have no influence on any others in the community). It would be possible to reduce disease with such a vaccine but not to eradicate the infection.

8 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 748:

The most common source of environmental exposure to *C. tetani* bacilli and spores is soil, where the organism is widely but variably distributed.

9 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 756:

Immunization histories were reported for 986 (49%) of the tetanus cases reported from 1972 to 2009 (Centers for Disease Control and Prevention, unpublished data). Of those 986 cases, 163 (16%) had received at least a three-dose primary series of tetanus toxoid before onset of tetanus; 62 (6%) reported that the last dose of tetanus toxoid was received less than 10 years before the illness.

10 Nombre de la página:

Notifiable diseases: historic annual totals

Sitio web:

GOV.UK

https://www.gov.uk/government/publications/notifiable-diseases-historic-annual-totals

For example, in the UK, an average of 5 cases of tetanus were recorded each year in 2001-2015. Official UK (England-Wales) morbidity data on the UK Ministry of Health website.

Nombre del documento:

Infectious diseases requiring notification in Israel

Archivo:

https://drive.google.com/open?id=1QEXa9 ZV_xDKvAdsUhN4ByWAfc7FbMjsH

Autor/año:

Israeli Ministry of Health, 2012

P 56.

In Israel, less than one case per year was recorded between 1990-2010.

11 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1396

The focal point of much of the theoretical work on community immunity has been the recognition that, if an infection or vaccine induces some degree of immunity against infection, then some nonimmune people will be protected indirectly, by the presence and proximity of immune persons, and transmission should stop in a population prior to the infection of all susceptible individuals.

12 Nombre del artículo:

Immunity for the People: The Challenge of Achieving High Vaccine Coverage in

American History

 $\frac{https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1}{820430/pdf/phr122000248.pdf}$

PMID: 17357368

Archivo:

https://drive.google.com/open?id=1jQ B7kYQeKFlBJCukM7Cv8ekpOELQJ wiT

Autor principal/año:

Revista:

James Colgrove, 2007

Public Health Reports

P 1

[vaccination], unlike other health interventions that benefit the individual, also carries a societal benefit through the herd immunity it creates. Thus, some observers have analogized immunization to public health responsibilities such as providing clean water or sewage disposal that are not left to the free market.

13 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1395

The social benefits of such indirect protection have important policy implications, including provision of a rationale for mandating immunization.

14 Nombre del artículo:

Immunity for the People: The Challenge of Achieving High Vaccine Coverage in

American History

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1820430/pdf/phr122000248.pdf

PMID: 17357368

Archivo:

https://drive.google.com/open?id=1jQ B7kYQeKFlBJCukM7Cv8ekpOELQJ wiT

Autor principal/año:

Revista:

James Colgrove, 2007 Public Health Reports

P 1

It is a widely accepted tenet of public health practice that persuasive approaches are preferable to coercive ones whenever possible. But because the failure to immunize oneself or one's children can contribute to the spread of infectious diseases, the United States has invoked compulsory measures, primarily laws requiring immunization before children may enter school.

Nombre de la página: State Vaccination Requirements Sitio web: CDC https://www.cdc.gov/vaccines/imz-managers/laws/state-reqs.html Nombre de la página: Italy approves hotly contested mandatory vaccine program Archivo: http://archive.is/XPOoo

Sitio web:

Daily Mail

https://www.dailymail.co.uk/wires/ap/article-4739388/Italy-approves-hotly-contested-vaccine-program.html

Under Italy's new requirements, parents must present proof of vaccinations to gain admission into preschools, while parents of children of mandatory school age face fines of up to 500 euros (\$588) for noncompliance. The requirements cover 10 vaccinations, including diphtheria, tetanus, measles, mumps, rubella and chicken pox.

Nombre de la página:

Archivo:

The 11 vaccines set to become compulsory in France and why French doctors are firmly in favour

http://archive.is/XRzRu

Sitio web:

TheLocal.fr

https://www.thelocal.fr/20170705/these-are-the-eleven-vaccines-that-will-be-compulsory-in-france-from-2018

Three vaccines: diptheria, tetanus and polio are already obligatory but from 2018 these will be joined by eight more: whooping cough, measles, mumps, rubella, hepatitus B, influenza, pneumonia and meningitis C.

16 Nombre de la página:

Archivo:

MMR jab should be compulsory for all children starting school, expert says

http://archive.is/EeFQh

Sitio web:

The Guardian

https://www.theguardian.com/society/2009/jun/03/mmr-jab-compulsory-schoolchildren

Welsh health minister revealed she is exploring whether to make the vaccination compulsory for school and nursery entry. Edwina Hart said she was prepared to "explore further the options" for a compulsory childhood vaccination policy as Wales experiences its largest outbreak of measles since the MMR vaccine was introduced 20 years ago, with 253 cases so far.

Nombre de la página (traducido del hebreo):

Archivo:

Compulsory Vaccinations?

http://archive.is/VZGva

Sitio web:

Vaccines

http://chisunim.co.il/Article.aspx?id=28

In the State of Israel, there is no legal obligation to vaccinate. Until a few years ago, it seemed that there was no need for such legislation due to the high rate of immunization of children in Israel, which was among the highest in the world.

However, due to an increase in the rate of those who oppose vaccines, this issue is expected to come up.

17 Nombre del documento:

PREVNAR Package Insert

https://drive.google.com/open?id=1VLR6NluMGK0E4yXUZM18IpUpi MI7-MP

Number of participants in the clinical trial - p. 3. Number of cases avoided (of all strains) - Table 1, p. 4 (per protocol).

Nombre del artículo:

PMID:

Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children

10749457

Autor principal/año: Revista:
Steven Black, 2000 PEDIATRIC INFECTIOUS DISEASE JOURNAL

P 5

Overall 513 pneumococcal vaccine recipients and 579 controls were hospitalized within 60 days of receipt of a dose of vaccine.

[...:

Review of emergency room visits within 30 days of vaccination revealed 1188 visits in pneumococcal vaccine recipients and 1169 visits in controls.

18 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1396:

The focal point of much of the theoretical work on community immunity has been the recognition that, if an infection or vaccine induces some degree of immunity against infection, then some nonimmune people will be protected indirectly, by the presence and proximity of immune persons, and transmission should stop in a population prior to the infection of all susceptible individuals. This insight encourages the estimation of threshold numbers or proportions of immune persons necessary for this cessation to occur.

19 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 400:

The elegant theory just summarized is built on extreme assumptions: that all individuals mix at random, that individuals are either fully susceptible or fully immune, and that the population is uniform (ie, that all individuals behave the same way and all infected individuals are equally infectious). These assumptions are unlikely to hold for any infection in any human population.

20 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1401.

21-40

21 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1403:

Published estimates of herd immunity thresholds required to eradicate measles have ranged from 55% to 96%, depending on the modeling approach and the assumptions employed (eg, whether age or seasonality of transmission was included). The logic and the flaws underlying the various estimates have been discussed elsewhere.

22 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1405:

Published estimates of a crude herd immunity threshold for diphtheria have ranged from 50% to 90%.

23

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1404

Several investigations have concluded that, for the incidence of CRS to decrease in the long term, the minimal vaccination coverage that must be achieved and maintained in young children of both sexes is in the region of 50% to 80%.

24

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1411:

The herd immunity threshold concept provides an epidemiologic attribute with which to characterize particular infections. Although precision may not be possible because of population heterogeneities or because of variability in the immune status of individuals—the crude thresholds are naively optimistic in practice—even crude estimates can be of use in giving a rough guideline for predicting the impact of a vaccination program and at least a hint as to the potential for eradication.

25

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1402:

If a vaccine were to protect only against disease, and not at all against infection, then it would have no influence on infection transmission in the community and there would be no indirect protection (vaccination of one person would have no influence on any others in the community). It would be possible to reduce disease with such a vaccine but not to eradicate the infection.

26

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 746:

Tetanus is unique among vaccine-preventable diseases in that it is not communicable. Clostridium tetani, the causative agent of tetanus, is widespread in the environment; many animals in addition to humans can harbor and excrete the organism and its spores. When spores of C. tetani are introduced into the anaerobic conditions found in devitalized tissue or punctures, they germinate to vegetative bacilli that elaborate toxin. The clinical presentation results from the actions of this toxin on the central nervous system (CNS). Many animal species besides humans are susceptible to the disease.

27

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 752-754:

A decline in tetanus incidence in industrialized countries began in the early 1900s. By the mid-1930s, many European countries had tetanus mortality rates of less than 1 per 100,000 Factors that contributed to the decline included urbanization, mechanization of agriculture, adoption of aseptic surgical and medical techniques, hygienic childbirth and wound care practices, use of prophylactic tetanus antitoxin, and, ultimately, use of antibiotics.

[...]

Historically, tetanus was a dreaded consequence of war, with incidence rates on the order of two cases per 1,000 injured troops;

 $[\dots]$

In 1947, when national reporting began, the incidence of reported cases was 0.39 per 100,000.

28

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1407

Clostridium tetani is not communicable between human hosts, and thus vaccination cannot lead to indirect protection in the sense implied in many definitions of herd immunity. Certainly there is no threshold proportion of immune persons, below 100%, that can ensure total absence of tetanus from a community.

29

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1407

It appears that wild-type polioviruses ceased to circulate in most of the United States by 1970, at which time only some 65% of children were receiving a complete course of OPV. However, given the complex history of previous IPV and then OPV programs in the country, and the propensity of OPV—let alone wild—viruses to circulate in the community, the actual level of immunity in the population at that time is unknown.

It is also possible that the disappearance of wild-type polioviruses from the United States and other countries employing OPV has resulted not only from the achievement of some herd immunity threshold, but also from the competition for ecologic space between the wild-type viruses and the constantly introduced vaccine strains.

30

Nombre del artículo:

Epidemiology Of Poliomyelitis And Allied Diseases--1963

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2604573/pdf/yjbm00599-0011.pdf

PMID: 14064722

Archivo:

https://drive.google.com/open?id=1fV_w0 3BSOROKex-hR7DkGZH44EXUwpTv

Autor principal/año:

Revista:

Dorothy M. Horstmann, 1963

Yale Journal of Biology and Medicine

P 9:

The inactivated vaccine, since its introduction in 1955, has greatly reduced the incidence of paralytic poliomyelitis in countries in which its use has been extensive. This has been accomplished by inducing serologic immunity in vaccinees, which prevents CNS invasion. However the extent to which the inactivated vaccine has suppressed the circulation of wild polioviruses and the incidence of inapparent intestinal infection is not well documented... This is not surprising, for although the vaccine induces antibody formation, it does not provide a significant barrier to intestinal infection with either wild or vaccine strains.

31

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1407

...there is good epidemiologic evidence for indirect protection by IPVs. Countries that have used only IPV (eg, Sweden, Finland, and the Netherlands) experienced elimination of circulating wild-type polioviruses for long periods of time.

32 Nombre del documento:

Polio - The Beginning Of The End

Autor/año: Archivo:

WHO, 1997

https://drive.google.com/open?id=1r0R4dlS
UiB6jOtNta-FvrKDD-gFlzW9h

P 20:

Inactivated polio vaccine (IPV) works by producing protective antibodies in the blood—thus preventing the spread of poliovirus to the central nervous system. However, it induces only very low- level immunity to poliovirus inside the gut. As a result, it provides individual protection against polio paralysis but only marginally reduces the spread of wild poliovirus. In a person immunized with IPV, wild virus can still multiply inside the intestines and be shed in stools. Because of this, IPV could not be used to eradicate polio.

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 631

Continued use of OPV will induce effective intestinal immunity, thereby enhancing community resistance to transmission of imported wild poliovirus.

34 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1407:

...live poliovirus vaccine virus is excreted in the feces and by the oropharynx in sufficient quantities for it to be transmitted to contacts. This unique attribute of OPV provides a special mechanism for indirect protection of non-vaccinees—in effect by vaccinating them surreptitiously.

Nombre de la página:

Archivo:

WHO vaccine-preventable diseases: monitoring system. 2018 global summary

http://archive.is/AVUQN

Sitio web:

WHO

http://apps.who.int/immunization_monitoring/globalsummary/schedules?sc%5Br%5D%5B %5D=AMRO&sc%5Br%5D%5B%5D=EURO&sc%5Bd%5D=&sc%5Bv%5D%5B%5D= OPV&sc%5BOK%5D=OK

Nombre del artículo:

Acellular pertussis vaccines protect against disease but fail to prevent infection and transmission in a nonhuman primate model http://www.pnas.org/content/pnas/111/2/787.full.pdf

PMID: 24277828

Archivo:

https://drive.google.com/open?id=1XS P3srbYjgMOiC1TtGMRMQpl2SQDH RDr

Autor principal/año: Revista: Jason M. Warfel, 2014 PNAS

P 3:

Therefore, no experimental data exist on whether vaccination prevents B. pertussis colonization or transmission in humans.

Nombre del artículo: PMID: 28928960

The relationship between mucosal immunity, nasopharyngeal carriage, asymptomatic transmission and the resurgence of Bordetella pertussis

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5 580413/pdf/f1000research-6-12588.pdf Archivo:

https://drive.google.com/open?id=1bCr u-8-TfSy2uwMt01noQ yY3B-6laEB

Autor principal/año: Revista: Christopher Gill, 2017 F1000 Research

principle, then, pertussis can be eradicated.

P 3

A significant, but surprisingly under-examined, unknown is whether an asymptomatic infection state exists for *B. pertussis*, as is the case for many other bacterial respiratory pathogens, notably *Streptococcus pneumoniae*, *Haemophilus influenzae* type B (HiB), and *Neisseria meningitidis*... But does B. pertussis exist in an asymptomatic infection state also? Can pertussis transmit from asymptomatic individuals? Do pertussis vaccines interfere with these processes? And, if so, how? These are fundamental unresolved questions.

37 PMID: Nombre del artículo: The relationship between mucosal immunity, 28928960 nasopharyngeal carriage, asymptomatic transmission Archivo: and the resurgence of Bordetella pertussis https://drive.google.com/open?id= https://www.ncbi.nlm.nih.gov/pmc/articles/PMC55804 1bCru-8-13/pdf/f1000research-6-12588.pdf TfSy2uwMt01noQ yY3B-6laEB Autor principal/año: Revista: Christopher Gill, 2017 F1000 Research P 3: There is increasing consensus that earlier whole cell pertussis (wP) vaccines impeded infections (not just clinical disease), generating herd immunity. Nombre abreviado: Plotkin 2013 - Vaccines (6th edition)

38	Nombre abreviado:	Archivo:
	Warfel 2014	https://drive.google.com/open?id=1XSP3srb
		VigMOiC1TtGMRMOnl2SODHRDr

Humans are the only reservoir for pertussis, and chronic carriage is not known to occur. In

39	Nombre del artículo: Comparison of Three Whole-Cell Pertussis Vaccines in the Baboon Model of Pertussis		PMID: 26561389
	Autor principal/año: Jason M. Warfel, 2015	Revista: Clinical and Vaccine Immunology	
	P 4: Infection of baboons (<i>Papio anubis</i>) with <i>B. pertussis</i> results in a disease that is very similar to severe clinical pertussis. Upon challenge with a recent clinical isolate of <i>B. pertussis</i> , baboons experience respiratory colonization for about 4 to 6 weeks, paroxysmal coughing, and leukocytosis. In addition, infected baboons can transmit <i>B. pertussis</i> to unchallenged baboons by airborne transmission.		
	Warfel 2014 http		chivo: tps://drive.google.com/open?id=1XSP3srb gMOiC1TtGMRMQpl2SQDHRDr
	P 1.		

40	Nombre abreviado: Warfel 2014	Archivo: https://drive.google.com/open?id=1XSP3srb YjgMOiC1TtGMRMQpl2SQDHRDr
	P 2.	

41-60

41	Nombre abreviado: Warfel 2014	Archivo: https://drive.google.com/open?id=1XSP3srb YjgMOiC1TtGMRMQpl2SQDHRDr	
	P 2: To assess the ability of vaccination to prevent pertussis infection by transmission, two aP-vaccinated animals and one unvaccinated animal were cohoused with a directly challenged, unvaccinated animal. Similar to our previous findings (18), all animals became colonized 7–10 d after cohousing with the infected animal.		

42	Nombre abreviado: Warfel 2014	Archivo: https://drive.google.com/open?id=1XSP3srb YjgMOiC1TtGMRMQpl2SQDHRDr
	P 3:the key finding of this study: aP vaccines do not prevent infection or transmission of Bordetella pertussis even 1 mo after completing the primary vaccination series.	

43	Nombre del artículo: Comparison of Three Whole-Cell Pertussis Vaccines in the Baboon Model of Pertussis		PMID: 26561389
	Autor principal/año: Jason M. Warfel, 2015	Revista: Clinical and Vaccine Immunology	
	P 2: Similar to our previous data, there was no difference in the duration of colonization between unvaccinated and DTaP-vaccinated animals, while previously infected animals were not colonized following reinfection.		

44	Nombre abreviado: Warfel 2014	Archivo: https://drive.google.com/open?id=1XSP3srb YjgMOiC1TtGMRMQpl2SQDHRDr
	P 3:aP-vaccinated individuals can act as asymptomatic or mildly symptomatic carriers and contribute significantly to transmission in the population.	

45	Nombre abreviado: Warfel 2014	Archivo: https://drive.google.com/open?id=1XSP3srb YjgMOiC1TtGMRMQpl2SQDHRDr	
	P 5: However, to protect the most vulnerable members of the population and achieve optimal herd immunity, it will be necessary to develop a vaccination strategy that effectively blocks pertussis infection and transmission.		

Archivo: Warfel 2014 Archivo: https://drive.google.com/open?id=1XSP3srb YjgMOiC1TtGMRMQpl2SQDHRDr P 1: ...optimal control of pertussis will require the development of improved vaccines

47 Nombre del artículo: PMID: What to do about pertussis vaccines? Linking 26253079 what we know about pertussis vaccine Archivo: effectiveness, immunology and disease https://drive.google.com/open?id=12W transmission to create a better vaccine **UI26**https://academic.oup.com/femspd/article/73/8/ftv PfhUcgXCbLoxuAs4yLClEwa8V 057/2467538 Autor principal/año: Revista:

P 2:

Shelly Bolotin, 2015

Close examination of outbreak patterns revealed that, although the interepidemic period remained the same, the amplitude of disease cycles increased following periods of low vaccine uptake (Fine and Clarkson 1982, 1987), an epidemiological signal that the vaccine may not be controlling infection and disease transmission, but rather clinical disease severity.

FEMS Pathogens and Disease

48	Nombre del artículo: Widespread Silent Transmission of Pertussis in Families: Antibody Correlates of Infection and Symptomatology		PMID: 2313126	
	Autor principal/año: Sarah S. Long, 1990	Revista: Journal of Infectious Diseases		
	P 7: In summary, this family study showed that extensive transmission of pertussis occurred during heavy exposure in immunized contacts. Subclinical infection was common; vaccination and probably natural disease provided more protection against disease than against infection.			
	Nombre del artículo: Pertussis Infection in Fully Vaccinated Children in Day-Care Centers, Israel https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2 627963/pdf/10998384.pdf		PMID: 10998384	
			Archivo: https://drive.google.com/open?id=1SrN d8ZYYkZAFj0E81M4djqhlLRI62uNk	
	Autor principal/año: Isaac Srugo, 2000	Revista: Emerging Infectious Diseases		
	P 3: Vaccinated adolescents and adults may serve as reservoirs for silent infection and become			

Vaccinated adolescents and adults may serve as reservoirs for silent infection and become potential transmitters to unprotected infants. The whole-cell vaccine for pertussis is protective only against clinical disease, not against infection. Therefore, even young, recently vaccinated children may serve as reservoirs and potential transmitters of infection.

Nombre del artículo: Determination of Serum Antibody to Bordetella pertussis Adenylate Cyclase Toxin in Vaccinated and Unvaccinated Children and in Children and Adults with Pertussis https://academic.oup.com/cid/article/38/4/502/351 Archivo: https://drive.google.com/open?id=1vN O704stsFQ0r0b-wYtiyVsGQidc9UGv

Autor principal/año: James D. Cherry, 2004	Revista: Clinical Infectious Diseases
James D. Cherry, 2004	Cillical Illectious Diseases

Nombre del artículo:

Different Effects of Whole-Cell and Acellular Vaccines on Bordetella Transmission

24443545 Archivo:

PMID:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4 038146/pdf/jiu030.pdf

https://drive.google.com/open?id=1gws -394ES_r0XRf9ihpMFQ6uc67SwM5R

Autor principal/año:

William E. Smallridge, 2014

Revista: Journal of Infectious Diseases

P 7

We were surprised to determine that an acellular vaccine previously found to affect pathology and colonization of the lungs was ineffective at inhibiting shedding and transmission.

Nombre abreviado:

Smallridge 2014

Archivo:

https://drive.google.com/open?id=1gws-394ES r0XRf9ihpMFO6uc67SwM5R

P 2:

Together these results suggest that the resurgence of B. pertussis could be due to 2 deficiencies of the acellular vaccines: failure to protect the vaccinated individual from infection, only blunting the severity of disease, and failure to prevent the transmission of B. pertussis.

52 Nombre abreviado:

Smallridge 2014

Archivo:

https://drive.google.com/open?id=1gws-394ES r0XRf9ihpMFQ6uc67SwM5R

P 7:

...current vaccines do not effectively prevent transmission of Bordetella and thus fail to confer the full benefits of herd immunity in reducing clinical cases.

Nombre del artículo:

The relationship between mucosal immunity, nasopharyngeal carriage, asymptomatic transmission and the resurgence of Bordetella pertussis

PMID: 28928960

Archivo:

https://drive.google.com/open?id=1bCr u-8-TfSy2uwMt01noQ yY3B-6laEB

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5 580413/pdf/f1000research-6-12588.pdf

Autor principal/año: Revista: Christopher Gill, 2017 F1000 Research

P 11

Fundamental aspects of pertussis epidemiology and immunology were left unexplained following the introduction of wP vaccines in the 1950s. The wP vaccines worked: disease rates plummeted, mortality fell, and the pertussis problem appeared largely solved. The fact that we did not know then, and still do not know now, how wP vaccines did this was inconvenient and has remained problematic in the aP vaccine era, since it created no clear immunologic surrogate by which to bridge these vaccine classes. Had carriage studies been conducted in parallel with wP introductions, then this might have provided supportive evidence that infections were being blocked. But carriage studies were not done. Rather, it was assumed that because wP vaccines appeared to confer herd immunity, they therefore blocked carriage.

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 471-472.

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1405:

It is hoped thereby to prevent infection transmission to young infants, in whom the disease is most severe. This has been extended to selective vaccination of parents and others in contact with young infants, a strategy known as cocooning, yet another approach to manipulating the community distribution of immunity.

Nombre abreviado:

Warfel 2014

Archivo:

https://drive.google.com/open?id=1XSP3srb YigMOiC1TtGMRMOpl2SODHRDr

P 5

One recommendation to reduce transmission of pertussis to infants is by "cocooning," or vaccinating people who have contact with infants. Our data... suggest that cocooning is unlikely to be an effective strategy to reduce the burden of pertussis in infants.

Nombre del artículo:

The relationship between mucosal immunity, nasopharyngeal carriage, asymptomatic transmission and the resurgence of Bordetella pertussis

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5 580413/pdf/f1000research-6-12588.pdf 28928960 Archivo:

PMID:

https://drive.google.com/open?id=1bCr u-8-TfSy2uwMt01noQ yY3B-6laEB

Autor principal/año: Christopher Gill, 2017 Revista: F1000 Research

P 11

In conclusion, the preponderance of available evidence now suggests that the list of plausible explanations for the resurgence of pertussis in the aP vaccination era goes beyond the "poor persistence" and "waning efficacy" of these vaccines to include an additional and likely pivotal factor: "lack of sterilizing mucosal immunity".

58

Nombre de la página:

Pertussis Frequently Asked Questions

Archivo:

http://archive.is/xBSyn

Sitio web:

CDC

https://www.cdc.gov/pertussis/about/faqs.html#immunity

Second, make sure everyone around the baby is up-to-date with their pertussis vaccines. This includes parents, siblings, grandparents (including those 65 years and older), other family members, babysitters, etc. They should be up-to-date with the age-appropriate vaccine (DTaP or Tdap) at least two weeks before coming into close contact with the baby.

Г 1

Q: Doesn't herd immunity protect most people?

A: [...] Since pertussis spreads so easily, vaccine protection decreases over time, and acellular pertussis vaccines may not prevent colonization (carrying the bacteria in your body without getting sick) or spread of the bacteria, we can't rely on herd immunity to protect people from pertussis.

59 Nombre del artículo:

The relationship between mucosal immunity, nasopharyngeal carriage, asymptomatic transmission and the resurgence of Bordetella pertussis

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5 580413/pdf/f1000research-6-12588.pdf

PMID: 28928960

Archivo:

https://drive.google.com/open?id=1bCr u-8-TfSy2uwMt01noQ yY3B-6laEB

Autor principal/año: Revista: F1000 Research Christopher Gill, 2017

These models also offer a possible explanation for the surprising failure of "cocooning" to protect infants from pertussis... Unfortunately, several controlled trials of cocooning in the US found no efficacy. These counterintuitive results conflict with expectations if aP vaccines block carriage and transmission but fit well if aP vaccines only prevent disease but have more limited ability to block infections.

60 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

The entire operon is under the control of a repressor gene, dtxR, which in the presence of iron binds to and inhibits the tox gene; toxin is produced only under low-iron conditions.

61-80

61 Nombre del documento:

CDC Pink Book - Diphtheria

Autor/año: CDC, 2011

https://drive.google.com/file/d/1RHDvOU2YvPDflcvqiEC9LPBMM22GEwo/view?usp=sharing

Only toxigenic strains can cause severe disease.

62 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

...the frequency of these various complications appears to vary considerably between epidemics, for which no clear explanation is available.

63 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

The precise microbial events responsible for the transmission of diphtheria remain unclear.

64 Nombre del documento:

CDC Pink Book - Diphtheria

Autor/año: CDC, 2011

https://drive.google.com/file/d/1RHDvOU2YvPDfIcvqiEC9LPBMM22GEwo/view?usp=sharing

P 81.

65 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1405

The protection against disease imparted by diphtheria toxoid vaccines has never been evaluated in formal trials, although observational studies provide estimates ranging from 55% to 90%.

Nombre del artículo: Diphtheria Immunisation Campaign Revista: British Journal of Nursing Revista: British Journal of Nursing Archivo: https://drive.google.com/open?id=1INU0IsPgiT4WVNMXUMKj7cT9ZmPtzcnM

P 1

Immunisation affords a good degree of protection, though not complete protection, against an attack of diphtheria. It affords a very high degree of protection indeed against the risk of death from diphtheria. Immunised people, if they get diphtheria, nearly always get it very lightly.

[...]

A child who has been immunised is about four times less likely to catch diphtheria, and about 25 times less likely to die from it than one who has not.

67	Nombre del documento: CDC Pink Book - Diphtheria https://drive.google.com/file/d/1RHDvQU2YyPDflcv- qiEC9LPBMM22GEwo/view?usp=sharing	Autor/año: CDC, 2011
	P 78.	

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 156:

Although diphtheria antitoxin is the mainstay of diphtheria therapy, penicillin or, alternatively, erythromycin should be given to hasten clearance of the organism, prevent transmission, and cease further production of diphtheria toxin... Before the development of antibiotic therapy, convalescent carriage of toxigenic organisms was a major problem. Up to 50% and 25% of patients continued to harbor the organism 2 and 4 weeks after onset, respectively. As late as 2 months after onset, reported carriage rates varied between 1% and 8%.

69	Nombre del documento: CDC Pink Book - Diphtheria https://drive.google.com/file/d/1RHDvQU2YyPDfIcv- qiEC9LPBMM22GEwo/view?usp=sharing	Autor/año: CDC, 2011
	P 70 84	

70	Nombre del artículo: Diphtheria Immunization	PMID: 5026197
	Effect Upon Carriers and the Control of Outbreaks	

Autor principal/año: Revista:

Louis W. Miller, 1972 The American Journal Of Diseases Of Children

P 3:

When diphtheria toxoid became available, it was generally believed that it induced immunity that protected individuals from symptomatic illness but not from asymptomatic

646466/pdf/amjph00288-0037.pdf

infection. This was based on the observation that immunity is related to the neutralization of toxin elaborated by C diphtheriae and not interference with diphtheria infection.

Nombre del artículo:

Diphtheria in the United States, 1971-81 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1

PMID: 4061710

Archivo:

https://drive.google.com/open?id=1Xx x6iNJSFo6djykLNV7QV7pQDM521P

Autor principal/año:

Revista:

Robert T. Chen, 1985

American Journal of Public Health

P 4:

However, immunization with diphtheria toxoid is protective only against the phage-mediated toxin, and not against infection by the C. diphtheriae organism. Thus immunized persons have less severe disease when infected, but may remain important as asymptomatic carriers in the transmission of disease.

71

Nombre abreviado:

Miller 1972

P 3:

In 1936, Frost et al alluded to a paucity of observations on record concerning antitoxic immunity and the carrier state. Nonetheless, he stated that the limited data suggested that there is little, if any, difference between those individuals with and those without antitoxic immunity in their risk of becoming infected. [...] The findings in Elgin corroborate the assumptions of Frost et al and show that there is no difference in the risk of diphtheria acquisition among those with full, lapsed, inadequate, and no immunizations.

72

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1406

Given that diphtheria toxin is not a constituent of Corynebacterium diphtheriae per se, but exists as a consequence of bacteriophage infection, the immunity induced by toxoid vaccination may not provide protection against infection at all. However, toxoid vaccines do protect against toxin mediated disease, and transmission of the diphtheria bacillus is more efficient from clinical patients than from subclinical carriers - thus the toxoid vaccines may protect against infectiousness and infection transmission, but not (or more than) against infection receipt... This may have been an important contributor to the disappearance of diphtheria in vaccinated populations.

73

Nombre del artículo:

The Epidemiological Importance Of Diphtheria Carriers https://academic.oup.com/aje/article-abstract/5/4/508/149362?redirectedFrom=fulltext

Autor principal/año: Revista:

James A. Doull, 1925 American Journal of Epidemiology

P 20

After making necessary allowance for differences in age-distribution of the two groups of contacts, it is a conservative estimate to state that the risk of attack is ten times as great for family contacts of cases as for those in similar association with known bacillus carriers.

Nombre abreviado:

Doull 1925

P 1:

...and as carriers are much more numerous than clinically recognizable cases, and are for the most part subject to no restriction of their intercourse with the general public, it is reasonable to infer that they may be, in the aggregate, the most frequent sources of clinical infection.

75

Nombre abreviado:

Doull 1925

P 2:

A similar conclusion is indicated by the results of attempts to trace the sources of infection of recognized cases. For example, in a study of some 500 cases reported in a limited section of Baltimore, investigators from this school have been able to find evidence of prior association with recognized or even suspected cases of clinical diphtheria in only about 20 per cent, of the cases investigated. Making all due allowance for the imperfections of such an investigation, it still appears that a large proportion of the cases investigated must have contracted their infections from unrecognized clinical cases or from carriers.

76

Nombre abreviado:

Doull 1925

P 20:

It seems impossible to explain the general distribution of diphtheria and the usual absence of traceable lines of contact from clinical cases on any other hypothesis except that infection is spread largely by carriers.

77

Nombre abreviado:

Miller 1972

P 2:

Throat cultures were done on 306 children and staff; toxigenic C diphtheriae, gravis type, was isolated from 104 (34%). Fifteen of these (14%) were cases, and 89 (86%) were carriers. There was no statistical difference in the risk of diphtheria infection among those with full, lapsed, inadequate, or no previous diphtheria immunization.

78

Nombre abreviado:

Miller 1972

P 3

Recent epidemics in Austin and Elgin Texas, provided ample evidence that carriers continue to play a very important role in the transmission of diphtheria.

79

Nombre abreviado:

Miller 1972

P 3:

However, diphtheria outbreaks have been described in populations with as much as 94% of the people being previously immunized. These outbreaks, the known importance of carriers in the spread of diphtheria, and the demonstrated failure of toxoid to prevent the carrier state lead us to conclude that the concept of herd immunity is not applicable in the prevention of diphtheria

Nombre del artículo:

The Austin, Texas, Diphtheria Outbreak Clinical and Epidemiological Aspects

PMID:

4984784

Autor principal/año: Revista: Victor M. Zalma, 1970 JAMA

A similar conclusion was reached by Zalma and his colleagues, also from the CDC, who investigated the outbreak in Austin Texas.

P 5

Although toxoid reduces the severity of disease caused by toxigenic organisms, it does not eradicate such organisms and, hence, as long as there are susceptibles in an area where C diphtheriae exists, cases can continue to occur.

80 Nombre del artículo:

Diphtheria in the Russian Federation in the 1990s

PMID: 10657187

Autor principal/año: Revista:

Svetlana S. Markina, 2000 Journal of Infectious Diseases

P 7:

The Soviet and Russian experience has been that of persistent circulation of toxigenic strains of C. diphtheriae and at least two resurgences of diphtheria despite fairly high levels of vaccine coverage among most childhood age groups. Studies in 1969–1970 documented that reintroduction of toxigenic strains into schools with 100% coverage of children produced widespread transmission of the organism for months despite an absence of cases. A study in several oblasts in 1980–1981 found low-level circulation of toxigenic strains despite immunity in >97% of 20,000 children who were 4–14 years of age, as measured by Schick testing. While inadequate implementation of immunization played a role in permitting circulation of diphtheria organisms to continue, the experience in Russia and elsewhere suggests that circulation is likely to persist in areas of lesser economic development even with good overall immunization levels.

81-100

81 Nombre abreviado:

Chen 1985

P 3:

The decline in diphtheria incidence in the United States during 1971-81 occurred despite serologic studies during the 1970s showing subprotective serum diphtheria antitoxin levels in approximately 25 per cent of the children and 75 per cent of the adults tested in three US cities.

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 165:

Despite the relatively low levels of immunity among adults in many countries, diphtheria has remained well controlled in most countries with effective childhood immunization programs... Serologic studies in Europe and the United States have demonstrated that many adults in these countries remain susceptible to diphtheria.

82 Nombre abreviado:

Chen 1985

P 3:

The frequency of diphtheria carriage in the United States is not known accurately.

83 | Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1405

Estimates aside, the proportion of the population actually immune to diphtheria today is elusive. Vaccine coverage is difficult to define because it has varied over time, and because at least three doses are recommended, although one or two provide some protection.

Nombre del artículo:

PMID:

Penicillin In Treatment Of Diphtheria And Diphtheria Carriers

20280343

Autor principal/año:

Revista:

Samuel Karelitz, 1947

The Journal Of Pediatrics

P 10

Penicillin was ineffective in preventing toxic complications of diphtheria, but seemed to hasten the clearing and further the development of complications due to pyogenic organisms. Penicillin should not be used as a substitute for diphtheria antitoxin.

85

Nombre abreviado:

Karelitz 1947

P 10.

Patients with faucial diphtheria treated with antitoxin and penicillin... were rendered diphtheria negative more rapidly than were the patients who received antitoxin and no penicillin. Carriers of virulent C. diphtheria were likewise rendered free of the bacteria by treatment with penicillin.

86

Nombre abreviado:

Zalma 1970

P 4:

Fourteen of 142 treated carriers (9.9%) were not cleared of C diphtheriae after treatment with procaine penicillin, administered intramuscularly, 600,000 to 2,000,000 units a day for seven to ten days, and most were given a course of erythromycin, which eradicated the organism in every patient.

Nombre abreviado:

Miller 1972

P 3

At the first appearance of a diphtheria case, control activities should be directed toward identifying, isolating, and treating carriers, as well as toward immunizing persons with less than full immunization status. This dual approach will reduce or eliminate the spread of infection by reducing the number of carriers, and it will reduce the number of cases by improving the immunization status of exposed individuals.

87

Nombre del documento:

Autor/año: CDC, 2011

CDC Pink Book - Diphtheria

https://drive.google.com/file/d/1RHDvQU2YyPDfIcv-qiEC9LPBMM22GEwo/view?usp=sharing

P 78-79.

Persons with suspected diphtheria should be given antibiotics and antitoxin in adequate dosage and placed in isolation after the provisional clinical diagnosis is made and appropriate cultures are obtained.

[...]

The disease is usually not contagious 48 hours after antibiotics are instituted. Elimination of the organism should be documented by two consecutive negative cultures after therapy is completed.

88 Nombre abreviado:

Chen 1985

P 4:

The Rumanian experience lends support for this hypothesis; improved immunization led to a sharp decline in diphtheria morbidity disproportionate to the actual number of persons with Schick-proven immunity, and surveillance cultures in epidemic and nonepidemic communities showed a concomitant drop in the percentage of toxigenic strains from 86 per cent in 1955-66 to 5 per cent in 1977.

89 Nombre del artículo:

Corynebacterium diphtheriae: Microbiological Methods Used in Clinical and Epidemiological Investigations

https://www.sciencedirect.com/science/article/pii/S058095170870374X

Autor principal/año:

Alice Saragea, 1979

P 165 (also in the chart on p 166):

1. Epidemiological methods

[...]

(g) Diagnosis, isolation and treatment of contacts (treatment by antibiotics).

90 Nombre del artículo:

nion: 9866730

PMID:

Diphtheria in the Former Soviet Union: Reemergence of a Pandemic Disease

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2640235/pdf/9866730.pdf

Autor principal/año: Revista:

Charles R. Vitek, 1998 Emerging Infectious Diseases

P 9:

Russia was never totally free of reported cases of diphtheria....

91 Nombre abreviado:

Markina 2000

P 2.

92 Nombre abreviado:

Markina 2000

P 7:

The Soviet and Russian experience has been that of persistent circulation of toxigenic strains of C. diphtheriae and at least two resurgences of diphtheria despite fairly high levels of vaccine coverage among most childhood age groups.

Nombre del artículo: Diphtheria Surveillance and Control in the Former Soviet Union and the Newly Independent States PMID: 10657186

Autor principal/año: Revista:

Charles R. Vitek, 2000 Journal of Infectious Diseases

P 2:

Soviet epidemiologists did not recommend prophylactic treatment with antibiotics for contacts of diphtheria cases. There was a strongly held conviction that antibiotics had an adverse effect on the normal bacterial flora.

94

Nombre abreviado:

Vitek 2000

P 2:

Soviet public health officials believed that this tightly controlled system of laboratory and clinical surveillance would identify individuals needing treatment sufficiently early to avoid the need for prophylactic antibiotic treatment.

95

Nombre abreviado:

Vitek 2000

P 4.

Prophylactic antibiotics were not given to close contacts of cases or carriers of diphtheria in a school or work place.

96

Nombre abreviado:

Markina 2000

P 7

Toxigenic C. diphtheriae continues to circulate throughout the Russian Federation, and interruption of circulation in most areas is unlikely in the near future.

97

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 260.

98

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 274-279

99

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 292

However, although it might be assumed that high vaccine coverage in communities would lead to reduced community transmission and to reductions in severe influenza-related outcomes, no large prospective study has yet convincingly demonstrated that vaccinating entire populations, or epidemiologically important subpopulations such as school-age children, will provide significant protection against influenza-related complications (eg, death or hospitalization) for other groups.

100

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 284:

Although studies have not consistently demonstrated community benefits, the variability by season, vaccine coverage, and circulating strains, as well as difficulty in monitoring outpatient illness among adult contacts, have presented formidable challenges to the conducting of this type of study.

P 292:

Demonstrating significant reductions in influenza-related complications has been difficult because of the yearly variability of influenza epidemiology, the infrequent use of specific laboratory testing that could serve as the source of reliable surveillance data, the need to study a large population to capture enough severe outcomes, and the relatively low coverage achieved in areas where universal vaccination has been recommended.

101-120

101 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 183-188.

102 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 188-191.

103 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 193

Young children have the highest rates of infection and are often the source of infection for others, primarily because infections in this age group are usually asymptomatic and standards of hygiene are generally lower among young children than among adults.

Archivo:

https://drive.google.com/ope

n?id=1jWjwQsaeXHiqagzxr

2SZXJq6KuBeu78U

104 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 189-190.

105 Nombre del documento (hebreo):

National Hepatitis Prevention Programs

00155d010977 11 7600.pdf

Autor/año:

Flora Koch Davidovich, Knesset Research Center, 2014

106 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 202:

Vaccine coverage data and examination of age-specific incidence trends indicate that incidence declines have occurred with modest levels of coverage and in unvaccinated age groups, suggesting a strong herd immunity effect.

107 | Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 183:

Children are less likely to have symptomatic infection compared with adults; 50% to 90% of infections acquired before the age of 5 years are asymptomatic, but 70% to 95% of infected adults will have symptoms. Jaundice is rare among young children but will occur in the majority of adults with hepatitis A.

P 184:

The case-fatality rate among cases reported through national surveillance in the United States for the 2001-2005 period ranged from 0% among children younger than 5 years to 1.4% of people older than 60 years, with an overall mortality rate of 0.5%.

108 Nombre del documento:

CDC Pink Book – Hepatitis B

https://drive.google.com/file/d/1PeVszIcp5GNIES278_QQX Y8tDo-Vnf3t/view?usp=sharing

P 116-117.

109

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 215:

HBV is not transmitted by air, food, or water.

110

Nombre del documento:

CDC Pink Book - Hepatitis B

https://drive.google.com/file/d/1PeVszIcp5GNIES278_QQXY8tDo-Vnf3t/view?usp=sharing

Autor/año: CDC, 2011

Autor/año: CDC, 2011

P 119:

The virus is transmitted by parenteral or mucosal exposure to HBsAg-positive body fluids from persons who have acute or chronic HBV infection. The highest concentrations of virus are in blood and serous fluids; lower titers are found in other fluids, such as saliva and semen. Saliva can be a vehicle of transmission through bites; however, other types of exposure to saliva, including kissing, are unlikely modes of transmission. There appears to be no transmission of HBV via tears, sweat, urine, stool, or droplet nuclei.

111

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 215-216.

112

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 217, Figure 1.

113

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

Assuming a million carriers in a population of 324 million. Plotkin 2013, p. 215, estimates between 800,000 and 1,400,000 U.S. carriers.

114

Nombre de la página:

Recommendations of the Immunization Practices Advisory Committee Prevention of Perinatal Transmission of Hepatitis B Virus: Prenatal Screening of all Pregnant Women for Hepatitis B Surface Antigen

Archivo:

http://archive.is/XZzZs

Sitio web:

CDC website

https://www.cdc.gov/Mmwr/preview/mmwrhtml/00000036.htm?fref=gc

The estimate is based on pre-vaccine CDC data - below. (Plotkin 2013 mentions an estimate of 0.6 percent).

Screening the approximately 3.5 million pregnant women per year for HBsAg would identify 16,500 positive women and allow treatment that would prevent about 3,500 infants from becoming HBV carriers.

115 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

In the United States, the race-adjusted prevalence of HBsAg among pregnant women is about 0.6%

[...]

In 2007, a total of 1,815 HBV-associated deaths (0.56 deaths per 100,000 population) were recorded in the United States.

116 Nombre de la página:

Hepatitis B virus

Archivo:

http://archive.is/oOPwj

Sitio web:

HSE website

http://www.hse.gov.uk/biosafety/blood-borne-viruses/hepatitis-b.htm

The UK is a low prevalence area, with a carriage rate of 0.1-0.5%, although rates may vary between individual communities.

117 Nombre del documento (hebreo):

National Hepatitis Prevention Programs

http://fs.knesset.gov.il/globaldocs/MMM/40c28d55-f7f7e411-80c8-00155d010977/2 40c28d55-f7f7-e411-80c8-00155d010977 11 7600.pdf

Archivo:

https://drive.google.com/ope n?id=1jWjwQsaeXHiqagzxr 2SZXJq6KuBeu78U

Autor/año:

Flora Koch Davidovich, Knesset Research Center, 2014

P 2.

118 Nombre del artículo:

Prevalence of HBsAg Carriers in Native and

PMID: 1834799

Immigrant PregnancFemale Populations in Israel and

PassivelActive Vaccination Against HBV of Newborns at Risk

Autor principal/año: Revista:

Journal of Medical Virology V. Bogomolski-Yahalom, 1991

Nombre del artículo:

Vertical HBV transmission in Jerusalem in the vaccine era

PMID: 23330257

Autor principal/año: Revista: R Michaiel, 2012 Harefuah.

Nombre del artículo:

HBV and HCV Epidemiology In Israel

Autor principal/año:

Archivo:

https://drive.google.com/open?id=11JcqsIZCPFZYu6q2 Eli Zuckerman, 2014 9YXVGmrRdeg7K9i7

Nombre del documento:

CDC Pink Book - Hepatitis B

https://drive.google.com/file/d/1PeVszIcp5GNIES278 QQX Y8tDo-Vnf3t/view?usp=sharing

Autor/año:

CDC, 2011

The first recorded cases of "serum hepatitis," or hepatitis B, are thought to be those that followed the administration of smallpox vaccine containing human lymph to shipyard workers in Germany in 1883.

120

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 205:

The largest outbreak of what is now recognized as hepatitis B was recorded in 1942, when 28,585 American soldiers inoculated with yellow fever vaccine developed jaundice and 62 died. This outbreak was traced to a specific lot of vaccine that contained human serum; a follow-up study in the 1980s confirmed the hepatitis B viral cause.

121-140

121

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

Infants born to mothers with chronic HBV infection can acquire perinatal HBV infection, which usually occurs at the time of birth; in utero transmission of HBV is relatively rare (accounting for $\leq 2\%$ of infections transmitted from mother to infant), and the virus is not transmitted through breastfeeding.

122

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

Person-to-person transmission probably occurs from inadvertent percutaneous or mucosal contact with blood or infectious body fluids during certain activities, such as sharing toothbrushes or razors, contact with exudates from dermatologic lesions, contact with saliva through bites or other breaks in the skin, premastication of food, sharing of gum and other food items, and contact with HBsAg-contaminated surfaces.

123

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 206:

The risk for developing chronic HBV infection varies inversely with age: approximately 90% of infants infected during the first year of life develop chronic infection, compared with 30% of children infected between ages 1 and 4 years and less than 5% of persons infected as adults.

124

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

In [...] areas of high endemicity [...] most infections are acquired during the perinatal period and early childhood, when the risk for developing chronic infection is greatest; acute hepatitis B is rarely detected because most infections in early childhood are asymptomatic.

125 | Nombre del artículo:

'Self-Destructing' Syringes Force Safer Injection Practices

Fecha: Nov 2, 2011

Sitio web:

PBS

Archivo:

http://www.pbs.org/newshour/rundown/self-destructing-syringes-force-safer-injection-practices/

http://archive.is/Z26jo

About 40 percent of all injections are given with unsterilized, reused syringes and needles, reports the World Health Organization. An estimated 1.3 million deaths — and 21.7 million new Hepatitis B infections — occur each year as a result of the unsafe practice.

126

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 217-218.

127

Nombre de la página:

Archivo:

http://archive.is/kccin

Hepatitis B Virus: A Comprehensive Strategy for Eliminating Transmission in the United States Through Universal Childhood Vaccination: Recommendations of the Immunization Practices Advisory Committee (ACIP)

Sitio web:

CDC website

https://www.cdc.gov/mmwr/preview/mmwrhtml/00033405.htm?fref=gc

Section: EPIDEMIOLOGY AND PREVENTION OF HEPATITIS B

VIRUS INFECTION

Infections among Infants and Children

128

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 215

Other settings where person-to-person transmission typically occurs include child-care centers and schools.

129

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 218:

No increased risk for HBV infection resulting from occupational exposures has been documented in persons infrequently exposed to blood or body fluids, such as ward clerks, dietary workers, maintenance workers, housekeeping personnel, lifeguards, teachers, and persons employed in child day-care settings.

130

Nombre del documento:

Archivo:

Unusual Cases of Hepatitis B Virus Transmission in the Community

1tNQw80K3IY-

FNOoaAcxrDe2oVmt0bb5p

https://drive.google.com/open?id=

http://www.immunize.org/catg.d/p2100.pdf

Autor/año:

Immunize.org

131 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

n79hEokf30r1Rtr4-PT/view?usp=sharing

Breast-feeding clearly protects against rotavirus disease.

132 Nombre del documento:

CDC Pink Book - Rotavirus

https://drive.google.com/file/d/17oSPucPglFR3-

P 244-246.

133 Nombre del documento:

CDC Pink Book – Rotavirus

https://drive.google.com/file/d/17oSPucPglFR3n79hEokf30r1Rtr4-PT/view?usp=sharing

P 265.

134 Nombre del documento:

CDC Pink Book - Rotavirus

https://drive.google.com/file/d/17oSPucPglFR3n79hEokf30r1Rtr4-PT/view?usp=sharing

Autor/año: CDC, 2011

Autor/año:

CDC, 2011

Autor/año: CDC, 2011

After a single natural infection, 38% of children are protected against any subsequent rotavirus infection, 77% are protected against rotavirus diarrhea, and 87% are protected against severe diarrhea. Reinfection can occur at any age.

The first infection after 3 months of age is generally the most severe.

In addition, infants may experience multiple episodes of rotavirus diarrhea because the initial infection may provide only partial immunity.

135 Nombre del documento:

CDC Pink Book - Rotavirus

https://drive.google.com/file/d/17oSPucPglFR3n79hEokf30r1Rtr4-PT/view?usp=sharing

Autor/año: CDC, 2011

Rotavirus infection is not nationally notifiable in the United States. Estimates of incidence and disease burden are based on special surveys, cohort studies, and hospital discharge data. In the prevaccine era an estimated 3 million rotavirus infections occurred every year in the United States and 95% of children experienced at least one rotavirus infection by age 5 years. The incidence of rotavirus is similar in developed and developing countries, suggesting that improved sanitation alone is not sufficient to prevent the infection.

136	Nombre del documento: CDC Pink Book – Rotavirus https://drive.google.com/file/d/17oSPucPglFR3- n79hEokf30r1Rtr4-PT/view?usp=sharing	Autor/año: CDC, 2011
	P 266.	
	Nombre abreviado: Plotkin 2013 - Vaccines (6th edition)	

P 674:

These estimates, prior to the use of rotavirus vaccines, indicated that by the end of the second or third year of life, 60% to 80% of all children developed a rotaviral diarrheal illness (approximately 2.7 million episodes per year), 1 in 6.5 sought medical attention, 1 in 70 (55,000 to 70,000 patients) were hospitalized, and 1 in 66,000 to 1 in 200,000 (20 to 60 children) died as a result of the rotavirus.

137

Nombre del artículo:

Estimating the Number of Deaths with Rotavirus as a Cause in England and Wales

https://www.tandfonline.com/doi/pdf/10.4161/hv.3.1.3748

PMID: 17264682

Archivo:

https://drive.google.com/open?i d=1Dk7uJeWAlb4ftsoUHL7mq 4IYEjuQIhaX

Autor principal/año: Mark Jit, 2007 Revista: Human Vaccines

P 5:

The two methods we used gave similarly low figures of 3.3 and 3.2 deaths a year. Hence, our analysis predicts that the annual mortality burden for rotavirus in England and Wales is extremely low. Also, these estimates do not accurately capture the mortality attributable to rotavirus alone as in almost all cases of death due to rotavirus there are other contributing causes. This suggests that universal rotavirus vaccination will have a limited impact on childhood mortality in the United Kingdom.

138

Nombre de la página (hebreo):

Rotavirus

Archivo:

http://archive.is/lpSxT

Sitio web:

Israeli Ministry of Health

 $\underline{https://www.health.gov.il/Subjects/pregnancy/Childbirth/Vaccination_of_infants/Pages/Ro_ta_Virus.aspx}$

The history of the disease in Israel

Before the vaccine existed, the virus caused 4,400 hospitalizations of children a year in Israel. Death from this virus is common in developing countries and very rare in developed countries and in Israel.

139

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 686

Several countries that have introduced rotavirus vaccines in their national childhood immunization programs have already seen remarkable declines in severe rotavirus gastroenteritis after vaccine introduction.

140

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 687:

In 2010, results of phase III trials of both RotaTeq and Rotarix conducted in developing countries of Africa and Asia were reported... Although the exact reasons for the somewhat diminished performance of rotavirus vaccines in developing countries are unclear, other live oral vaccines such as those against polio, cholera, and typhoid have also not worked equally well in populations in developed and developing country settings.

141-160

141

Nombre del artículo:

Rotavirus vaccination and herd immunity: an evidence-based review https://www.dovepress.com/rotavirus-vaccination-and-herd-immunity-an-evidence-basedreview-peer-reviewed-article-PHMT

Autor principal/año: Revista:

Lorna M Seybolt, 2012 Pediatric Health, Medicine and Therapeutics

A peculiarity of rotavirus natural infection, however, is that while it protects against subsequent clinical infection it does not prevent subclinical reinfection and virus circulation – a phenomenon consistently shown in cohorts of neonates, young children, and adults. A vaccine would not be expected to perform better than natural infection.

As this was only an isolated finding, the authoritative conclusion remained that rotavirus vaccines, despite being efficacious, would not be expected to significantly decrease the circulation of rotaviruses.

Nombre del artículo:

Correlates of protection for rotavirus vaccines: Possible alternative trial endpoints, opportunities, and challenges

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC45140 48/pdf/khvi-10-12-977728.pdf

PMID: 25483685

Archivo:

https://drive.google.com/open?i d=13USFrSUT1 LA2Fd5SYjaS i8n6PmT9sSH

Autor principal/año: Revista:

Juana Angel, 2014 Human Vaccines & Immunotherapeutics

Natural RV infection does not generate sterilizing immunity, thus, reasonable goals of vaccination are to decrease or eliminate severe disease in children, but not to prevent infection.

142

Nombre abreviado:

Seybolt 2012

Herd immunity – the indirect protection of unimmunized individuals as a result of others being immunized – was not expected to be a benefit of rotavirus vaccination programs since the vaccines were thought to reduce severe disease but not to decrease virus transmission significantly. Postlicensure studies, however, have suggested that this assumption may need reassessment. Studies in a variety of settings have shown evidence of greater than expected declines in rotavirus disease.

143

Nombre abreviado:

Seybolt 2012

P 11:

Yet, it seems highly compelling that many studies in different countries, under different conditions, and using different surveillance systems have consistently found some evidence of herd immunity with similar results for both vaccines. If a real phenomenon, it may be explained by decreased circulation of rotavirus, a fact that was suggested by one prelicensure study but has not been evaluated postlicensure. An alternative explanation is transmission of the vaccine virus from immunized infants to those unimmunized resulting in secondary immunization, as in the case of oral poliovirus vaccine.

Nombre abreviado:

Seybolt 2012

P 11

The evidence regarding herd immunity associated with rotavirus vaccines is of poor quality because this effect was not anticipated and studies were not specifically designed to detect it. [...] Studies used time series with short before and/or after observation periods, a situation vulnerable to temporal changes in rotavirus activity. Also, vaccine coverage was either unknown or inferred from external sources, which may or may not have been applicable to the study group.

P 5

For all these reasons, every study reviewed has significant potential flaws in relation to herd immunity and thus should be interpreted with caution and in conjunction with other available data.

145

Nombre abreviado:

Seybolt 2012

P 10.

146

Nombre del artículo:

PMID:

Estimating the herd immunity effect of rotavirus vaccine

<u>26116</u>250

Autor principal/año: Suzanne L. Pollard, 2015 Revista: Vaccine

P 2

Thus, in this paper we present a systematic review and meta-analysis to estimate the herd effects of rotavirus vaccines... [p. 4] To our knowledge, this is the first study to estimate the herd effect of rotavirus vaccine.

147

Nombre abreviado:

Pollard 2015

P 3, paragraphs 2.6-2.8.

148

Nombre abreviado:

Pollard 2015

P 5:

There are several explanations that may explain this inconsistency [...]

149

Nombre abreviado:

Pollard 2015

P 5:

In 13 of the 16 outcome years in Latin America, the observed reductions in all cause diarrhea hospitalizations or mortality were higher than the theoretical maximum (23.4%) reduction based on the estimated regional proportion of diarrhea mortality among children under 5 years of age.

150

Nombre abreviado:

Pollard 2015

P 5

We were unable to determine the functional relationship between coverage and the magnitude of herd immunity effects... If studies had reported measured coverage values at

additional time points between introduction and attainment of universal coverage, we would have been better able to understand the relationship between coverage and the degree of herd immunity observed.

151

Nombre abreviado:

Pollard 2015

P 5:

There is evidence that rotavirus vaccination confers a herd immunity effect among children under one year of age in the United States and Latin American countries. Given the high variability in vaccine efficacy across regions, more studies are needed to better examine herd immunity effects in high mortality regions.

152

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1406

There are at least 93 immunologically distinct pneumococcal serotypes that cause disease in humans... Pathogenicity varies with serotype, and different serotypes are more or less likely to affect different age groups, although all can cause disease in all age groups. To further complicate issues, the duration of carriage and the ability of a carriage episode to immunize an individual is also variable and dependent on age and serotype.

153

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 529:

Pneumococci are constantly on the move in the population, being transmitted and acquired at high rates, especially in young children.

154

Nombre del documento:

Autor/año:

CDC Pink Book – Pneumococcal Disease

https://drive.google.com/file/d/17nHF95iC1QlRcMYqUTj5b6ThstrdL2d/view?usp=sharing CDC, 2011

P 233, 237.

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 506-507.

155

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 504-505.

156

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 505.

157

Nombre del documento:

Archivo:

Infectious diseases requiring notification in Israel

https://www.health.gov.il/PublicationsFiles/Disease1951_2010.pdf

https://drive.google.com/open?id=1QEXa9 ZV xDKvAdsUhN4ByWAfc7FbMjsH

Autor/año: Israeli Ministry of Health	2012		
P 103, 131.	P 103, 131.		
Nombre del documento Estimating the herd immu vaccine		PMID: 26116250	
Autor principal/año: Suzanne L. Pollard, 2012	Revista: Vaccine		
	es [p. 4] To our knowled	nd meta-analysis to estimate the herd lge, this is the first study to estimate	

158	Nombre del documento: CDC Pink Book – Pneumococcal Disease https://drive.google.com/file/d/17nHF95iC1QlRcMYqUT- j5b6ThstrdL2d/view?usp=sharing	Autor/año: CDC, 2011
	P 238-240.	

159 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1406:

The introduction of a 7-valent pneumococcal conjugate vaccine in the United States in 2000 had a dramatic impact. Although the substantial fall in infant invasive pneumococcal disease rates was as expected, it was associated with significant falls in pneumococcal disease among adults, more than doubling the overall benefits to the community.

160 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

Despite these powerful effects, wherever carriage has been studied, vaccination has not affected pneumococcal carriage rates overall, but has led to a reduction in the carriage of vaccine serotypes, with a compensatory rise in carriage of nonvaccine serotypes.

[...]

The substantial herd effect in adults in the general population indicates that either the replacement nonvaccine serotypes are less likely to cause disease in adults, or there are qualitative differences in carriage in vaccinated children, rendering them less likely to transmit the organism.

161-180

161 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

Thus, as for direct effect of PCV7s on carriage, an overall reduction of carriage of VT serotypes can be attributed to PCVs, with a parallel increase in non-VT serotypes (termed replacement). This phenomenon is expected to be of great magnitude, resulting in herd immunity against vaccine serotype disease on the one hand, but a potential for replacement disease on the other hand.

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1406

To a variable extent, there has also been an increase in disease associated with the replacement nonvaccine serotypes, and this has reduced the initial impact of the disease reduction by the vaccine in both children and adults.

PMID: 26647277

Archivo:

XYfe6iE5cONm

Autor/año:

CDC, 2011

https://drive.google.com/open?i

<u>d=1kkntOBsCi3ayGCud0Q</u>dM

Nombre del artículo:

Pneumococcal serotype distribution in adults with invasive disease and in carrier children in Italy: Should we expect herd protection of adults through infants' vaccination?

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5049737/pdf/khvi-12-02-1102811.pdf

Autor principal/año: Revista:

Chiara Azzari, 2016 Human Vaccines & Immunotherapeutics

P 2:

The same effect was present, even though less evident, in Europe where the decrease in adult IPD associated to PCV7 serotypes was counterbalanced by a rapid increase in IPD due to non-PCV7 serotypes.

163

Nombre del documento:

CDC Pink Book – Pneumococcal Disease https://drive.google.com/file/d/17nHF95iC1QIRcMYqUT-j5b6ThstrdL2d/view?usp=sharing

P 239:

In 2010 a 13-valent pneumococcal conjugate vaccine (PCV13) was licensed in the United States. It contains the 7 serotypes of S pneumonia as PCV7 plus serotypes 1, 3, 5, 6A, 7F and 19A... ABCs data indicate that in 2008, a total of 61% of invasive pneumococcal disease cases among children younger than 5 years were attributable to the serotypes included in PCV13...

164

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1407:

In the United Kingdom, the story has been more complicated, as after only 3 years of use of the 7-valent vaccine, serotype replacement has forced authorities to move to a higher-valency preparation.

165

Nombre del documento (hebreo):

Immunization Guide

https://drive.google.com/open?id=1db5nqObGNRg8QwTaOUuTARsisHlPrf4U

Autor/año:

Israeli Ministry of Health, 2015

P 10.

166

Nombre del artículo:

Effect of use of 13-valent pneumococcal conjugate vaccine in children on invasive pneumococcal disease in children and adults in the USA: analysis of multisite, population-based surveillance

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC48768 55/pdf/nihms787116.pdf

PMID:

25656600

Archivo:

https://drive.google.com/open?id=1t24aage5OhA0oNKvLuO8iUTca0D-tSEe

Autor principal/año: Revista:

Matthew R Moore, 2015 European Respiratory Journal

P 7

Our analysis shows there were substantial and rapid reductions in IPD within 3 years of the introduction of PCV13 in the USA. The serotypes most affected were those most common before introduction of PCV13, particularly serotypes 19A and 7F. Also, the age groups that experienced the earliest reductions in PCV13 minus PCV7 type IPD were those targeted for vaccination: children younger than 5 years.

[...]

We found a reduction in IPD in adults associated with introduction of PCV13 in children. In all adult age groups, PCV13 minus PCV7 type IPD (especially serotypes 19A and 7F) declined by 58–72%, which is comparable with that reported early after the introduction of PCV7, leading to overall reductions in IPD of 12–32%. These findings are consistent with the hypothesis that PCV13 prevents nasopharyngeal colonisation with serotypes 19A and 7F among children and, therefore, prevents trans mission of these types between children and adults.

167

Sweden -

Nombre del artículo:

Effects of PCV7 and PCV13 on invasive pneumococcal disease and carriage in Stockholm. Sweden

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4819883/pdf/ERJ-01451-2015.pdf

Autor principal/año: Revista:

Ilias Galanis, 2016 European Respiratory Journal

P 9:

However, due to expansion of non-PCV13 strains, no large beneficial effect on the IPD incidence was observed by replacing PCV7 with PCV13 for the youngest children or for the elderly.

Italy -

Nombre del artículo:

Pneumococcal pneumonia prevention among adults: is the herd effect of pneumococcal conjugate vaccination in children as good a way as the active immunization of elderly?

https://www.tandfonline.com/doi/full/10.1185/03007995.2015.1131150

PMID:

PMID:

26797033

Archivo:

bvQIoBj5tcL8

26652736

Archivo:

https://drive.google.com/open?i d=1m8hAno7UOJZoJuN2T5um XUUh2U5tH s-

https://drive.google.com/open?i

d=1YMmi3eLP2J6vkPKhQG35

Autor principal/año: Revista:

Rosa Prato, 2015 Current Medical Research and Opinion

P 4:

In 2011, PCV13 coverage reached nearly 90% on a national basis... The hospitalization rates for pneumococcal pneumonia and the incidence rates of invasive disease in the elderly population have remained stable or increased over the past decade, suggesting that the indirect benefit of routine infant vaccination did not occur in this age group Not yet published preliminary analyses by Martinelli et al. seem to indicate that in Italy more than 65% of pneumococcal pneumonia cases in older adults were caused by the serotypes targeted by PCV13.

Denmark and UK -

Nombre del artículo:

Indirect Effects of Pneumococcal Conjugate Vaccines in National Immunization Programs for Children on Adult Pneumococcal Disease

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5204004/pdf/ic-48-257.pdf

PMID:

28032483

Archivo:

https://drive.google.com/open?i d=1UmSJwz1som0iOzgCG0xX UVBJ_WipDBsH

Autor principal/año: Young Keun Kim , 2016	Revista: Infection & Chemotherapy
P 4.	

168	Nombre del artículo: Pneumococcal carriage in children and adults two years after introduction of the thirteen valent pneumococcal conjugate vaccine in England		PMID: <u>24657717</u>
	Autor principal/año: Albert Jan van Hoek , 2014	Revista: Vaccine	
	P 3.		
	Nombre abreviado: Azzari 2016		
	P 4: NP swabs were found positive for Streptococcus pneumoniae in over 50% or healthy children included in the study, confirming our previous results.		
	Nombre abreviado: Galanis 2016		
	P 10: We observed that PCV introduction resulted in an almost complete replacement of vaccine types to NVTs in the nasopharynx of healthy children, without affecting carriage rates substantially.		

169 Nombre abreviado: Azzari 2016 P 5: Herd protection of adults through PCV13 might be therefore more limited than what previously described for PCV7. Nombre abreviado: Galanis 2016 The herd protection effects post-PCV13 were less pronounced as compared with the effects post-PCV7. In addition, in the elderly, the incidence of IPD caused by the six extra serotypes in PCV13 remained high post-PCV13. Nombre abreviado: Prato 2015 P 4: The hospitalization rates for pneumococcal pneumonia and the incidence rates of invasive disease in the elderly population have remained stable or increased over the past decade, suggesting that the indirect benefit of routine infant vaccination did not occur in this age group. [...] In Italy, even after pediatric vaccination with PCVs, vaccine serotypes are still responsible for most pneumonia and invasive diseases in the elderly population.

170	Denmark and UK - Nombre del artículo:	PMID: 28032483
	Indirect Effects of Pneumococcal Conjugate Vaccines in National Immunization Programs for Children on	Archivo:
	Adult Pneumococcal Disease	

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC52040 https://drive.google.com/open?i 04/pdf/ic-48-257.pdf d=1UmSJwz1som0iOzgCG0xX UVBJ WipDBsH Autor principal/año: Revista: Young Keun Kim, 2016 Infection & Chemotherapy While serotype replacement has certainly occurred and must be monitored over time, the reduction in overall IPD suggests a net-beneficial effect of PCV. Nombre del artículo: PMID: Indirect (herd) protection, following pneumococcal 28449971 conjugated vaccines Archivo:

introduction: A systematic review of the literature

Autor principal/año: Revista: Gal Tsaban, 2017 Vaccine

P 8:

Nevertheless, pneumococcal diseases burden among adult population remains a major concern in terms of morbidity, mortality, and health-economy burden.

171 Nombre abreviado:

Azzari 2016

P 4:

Moreover recent studies have demonstrated that PCV is not able to eliminate carriage state forever probably because of the physiological decrease in antibody titers, which remain high enough to prevent invasive infections but not enough to prevent carriage state.

172 | Nombre abreviado:

Galanis 2016

P 10:

The elimination of vaccine type strains in healthy carriage will create profound changes in the entire pneumococcal population structure within a community since different pneumococcal strains most likely coevolve as a result of reciprocal adaptation and counter-adaptation between interacting strains.

173 Nombre abreviado:

Galanis 2016

P 10:

Our findings here demonstrate that serotype diversity during carriage increases significantly as a result of PCV vaccination. The increased serotype diversity in IPD post-PCV is most likely a reflection of the increased number of serotypes prevailing in vaccinated carriers, which will influence the success of current vaccine strategies and must be taken into account when future strategies are developed.

174 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 507:

Although it would be preferable to include a larger number of different polysaccharides in a conjugate vaccine, doing so is technically challenging. Moreover, the total amount of carrier protein in the final vaccine may need to be limited because too much carrier protein can impair the antibody response to the polysaccharide antigen.

175 Nombre del artículo:

Conjugate Vaccines and the Carriage of Haemophilus influenzae Type b

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC26268 02/pdf/8903227.pdf PMID: 8903227

Archivo:

https://drive.google.com/open?id=1VP5OvAZPxbSZzJesAzsaP-k7NqskaMGK

Autor principal/año:

Revista:

Marina L. Barbour, 1996 Emerging Infectious Diseases

P 2:

It seems that close contact and generous exchange of respiratory secretions is required for the transmission of Hib between hosts. Even when the contact between a known carrier and a susceptible child is intimate, spread of Hib occurs slowly over weeks or months.

176 Nombre del documento:

CDC Pink Book – Haemophilus influenzae type b https://drive.google.com/file/d/1WJ4IgC2gyzbnSvpmr6I5p OZMPGnuFj-V/view?usp=sharing

P 88-91.

177 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 168:

Only a minority of people with Hib colonization become ill.

178 Nombre del documento:

CDC Pink Book – Haemophilus influenzae type b https://drive.google.com/file/d/1WJ4IgC2gyzbnSvpmr6I5p OZMPGnuFj-V/view?usp=sharing

P 88-90.

Autor/año: CDC, 2011

Autor/año: CDC, 2011

179 Nombre del documento:

CDC Pink Book – Haemophilus influenzae type b https://drive.google.com/file/d/1WJ4IgC2gyzbnSvpmr6I5p OZMPGnuFj-V/view?usp=sharing

P 91.

Autor/año: CDC, 2011

180 Nombre del documento:

Infectious diseases requiring notification in Israel

https://www.health.gov.il/PublicationsFiles/ Disease1951_2010.pdf Archivo:

https://drive.google.com/open?id=1QEXa9 ZV xDKvAdsUhN4ByWAfc7FbMjsH

Autor/año:

Israeli Ministry of Health, 2012

P 99, 101, 127, 129.

181-200

181	Nombre del documento: CDC Pink Book – Haemophilus influenzae type b https://drive.google.com/file/d/1WJ4IgC2gyzbnSvpmr6I5p OZMPGnuFj-V/view?usp=sharing	Autor/año: CDC, 2011
	P 91, 93.	

182	Nombre del documento: Infectious diseases requiring notification in Israel https://www.health.gov.il/PublicationsFiles/ Disease1951_2010.pdf	Archivo: https://drive.google.com/open?id=1QEXa9 ZV_xDKvAdsUhN4ByWAfc7FbMjsH
	Autor/año: Israeli Ministry of Health, 2012	
	P 103, 131	

183	Nombre abreviado: Plotkin 2013 - Vaccines (6th edition)
	P 180.

184	Nombre abreviado: Plotkin 2013 - Vaccines (6th edition)
	P 179.

185	Nombre del artículo: Decreased Haemophilus colonization in children vaccinated with Haemophilus influenzae type b conjugate vaccine		PMID: 8463894
	Autor principal/año: Revista: Journal of Pediatrics		
	Nombre del artículo: The Impact of Conjugate Vaccine on Carriage of Haemophilus influenzae Type b Autor principal/año: Marina L. Barbour , 1995 Revista: Journal of Infectious Diseases		PMID: 7798687

186	Nombre del artículo: Anti-Capsular Polysaccharide Antibodies Reduce Nasopharyngeal Colonization by Haemophilus influenzae Type b in Infant Rats		PMID: 8421170
	Autor principal/año: Revista: Maija Kauppi, 1993 Journal of Infectious Diseases		
	Nombre del artículo: Anti-capsular polysaccharide antibody concentrations in saliva after immunization with Haemophilus influenzae type b conjugate vaccines		PMID: 7603810

Autor principal/año: Maija Kauppi, 1995		
	Nombre del artículo: Antibodies to <i>Haemophilus influenzae</i> Type b Polysaccharide Affect Bacterial Adherence and Multiplication	
Autor principal/año: Loek van Alphen, 1996	Revista: INFECTION AND IMMUNITY	

187 Nombre de la página:

Archivo:

Chickenpox Prevention and Treatment

https://web.archive.org/web/20180907094136/ https://www.cdc.gov/chickenpox/about/preven tion-treatment.html

Sitio web:

CDC

https://www.cdc.gov/chickenpox/about/prevention-treatment.html

Use non-aspirin medications, such as acetaminophen, to relieve fever from chickenpox. Do not use aspirin or aspirin-containing products to relieve fever from chickenpox. The use of aspirin in children with chickenpox has been associated with Reye's syndrome, a severe disease that affects the liver and brain and can cause death.

188 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 837-838.

189 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

Varicella is a highly contagious disease. Infectivity is postulated to occur by aerosol spread of virions from vesicular skin lesions, and possibly to a lesser extent from respiratory secretions.

190 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

In the immediate prevaccine era in the United States, an average of 4 million varicella cases occurred each year, which resulted in an average of 11,000 to 13,500 hospitalizations (4.1 to 5.0 hospitalizations per 100,000 population) and 100 to 150 deaths annually (0.4 to 0.6 per million population).

191 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 863.

192 Nombre de la página:

Archivo:

Chickenpox: public health management and guidance

http://archive.is/6d5YH

Sitio web:

GOV.UK

https://www.gov.uk/government/collections/chickenpox-public-health-management-andguidance

Chickenpox is not a notifiable disease in England and Wales.

193 Nombre de la página:

Preventing the spread of chickenpox

Archivo:

http://archive.is/JhxJr

Sitio web:

NHS

http://www.nhs.uk/Conditions/Chickenpox/Pages/Prevention.aspx

There is a vaccination against chickenpox, but it's only given to people who are at a very high risk of spreading the infection to vulnerable people. These include healthcare workers and people living with someone who has a weakened immune system

194

Nombre del documento:

Infectious diseases requiring notification in

https://www.health.gov.il/PublicationsFiles/ Disease1951 2010.pdf

Archivo:

https://drive.google.com/open?id=1QEXa9 ZV xDKvAdsUhN4ByWAfc7FbMjsH

Autor/año:

Israeli Ministry of Health, 2012

P 127, 129.

195

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

Surveillance data show a major decline in chickenpox incidence in the United States as a consequence of this program, including evidence for indirect protection among infants and adults, outside the vaccinated target age groups.

196

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 860.

197

Nombre de la página:

WHO vaccine-preventable diseases: monitoring system 2017

Archivo:

http://archive.is/KsGxL

WHO

Sitio web:

198

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

From the health care payer perspective, most studies have shown that universal childhood vaccination programs will not provide savings at the current price of the vaccine.

199

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1405:

Beyond this, the long-term risk of zoster associated with vaccine strains is still not clear. The situation will need close monitoring in the coming years to ensure an overall public health benefit from this intervention. As a consequence of this uncertainty, several countries (eg, the United Kingdom) still prefer to use varicella vaccine selectively—for

example, in high-risk patients and health-care workers - although these policies may change if the US policy proves successful and cost effective in the long term.

200 Nombre del documento: CDC Pink Book - Rubella

> https://drive.google.com/file/d/11JSySIkEL9HODpfuTATai JOwWXlIwJyK/view?usp=sharing

P 275-279.

201-220

201 Nombre del documento: Autor/año: CDC, 2011 CDC Pink Book - Rubella https://drive.google.com/file/d/11JSySIkEL9HODpfuTATai JQwWXlIwJyK/view?usp=sharing

P 276-277.

202 Nombre del documento:

CDC Pink Book - Rubella

https://drive.google.com/file/d/11JSySIkEL9HODpfuTATai JOwWXlIwJvK/view?usp=sharing

P 279.

203 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

The "Vaccines" book (Plotkin 2013 p. 694) sets the level of morbidity in Congenital Rubella Syndrome (CRS) at 4-8 cases per 10,000 births.

After that outbreak, CRS rates fell to 4 to 8 per 10,000 pregnancies until 1970, when the first vaccines were licensed.

This high rate is inconsistent with US CRS morbidity data in these years, as appears in the CDC's Pink Book (p. 279 [5]) and in the graph presented in the book 'Vaccines' itself (p. 712). These graphs show that in 1969-70 about 65-67 cases of CRS were reported in the US, while the birth rate was about 3.7 million births per year.

204 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

Rubella vaccination started in Sweden in 1982.

Before 1974, a yearly average of 14 CRS cases was recorded in Sweden; there were 2 cases per year between 1975 and 1985, and there have been no cases since 1985.

205 Nombre del documento:

Infectious diseases requiring notification in

https://www.health.gov.il/PublicationsFiles/

Disease1951 2010.pdf

Autor/año:

Israeli Ministry of Health, 2012

Archivo:

https://drive.google.com/open?id=1OEXa9 ZV xDKvAdsUhN4ByWAfc7FbMjsH

Autor/año:

CDC, 2011

Autor/año:

CDC, 2011

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 700:

The protective efficacy of rubella vaccination has been assessed (1) by observation of vaccinees and control subjects during natural epidemics and (2) by intranasal challenge of vaccinated volunteers with unattenuated or attenuated viruses. No double-blind efficacy study has been done, but there is much evidence for effectiveness.

207

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 711:

Rubella vaccine has had spectacular success in the United States, in terms of the number of persons vaccinated and the declining numbers of rubella cases reported. Since the licensing of the vaccine in 1969, no major epidemic of rubella has occurred, despite the previously observed 6 to 9 year cycle.

208

Nombre del documento:

CDC Pink Book - Rubella

Autor/año: CDC, 2011

https://drive.google.com/file/d/11JSySIkEL9HODpfuTATai JQwWXlIwJyK/view?usp=sharing

P 281:

Follow-up studies indicate that one dose of vaccine confers long-term, probably lifelong, protection.

209

Nombre del documento:

CDC Pink Book - Rubella

Autor/año: CDC, 2011

https://drive.google.com/file/d/11JSySIkEL9HODpfuTATai JQwWXlIwJyK/view?usp=sharing

P 276:

Prevention of CRS is the main objective of rubella vaccination programs in the United States.

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 710:

The goal of rubella vaccination programs is the prevention of the intrauterine infection that causes CRS, and, incidentally, the occasional complication of the disease in adults

210

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 716.

211

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

In 1982, Sweden adopted a two-stage vaccination scheme involving the use of MMR at two ages: 18 months and 12 years. [...] Before 1974, a yearly average of 14 CRS cases was recorded in Sweden; there were 2 cases per year between 1975 and 1985, and there have been no cases since 1985.

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 712

The Finns vaccinate with MMR at 14 to 18 months and at 6 years. Since 1986, no case of CRS has been reported. The last indigenous rubella case occurred in 1996. In 1997 and 1998, rubella has thus been eliminated from Finland.

213

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 712:

The policy of vaccinating schoolgirls was adopted by the British in 1970. During subsequent years, the number of reported rubella cases decreased only slightly, although the reported cases of CRS decreased approximately 75%. [...] Since October 1988, rubella vaccine as part of MMR has been recommended to all infants, and in 1994, a large-scale vaccination campaign was conducted with MR combined vaccine. Congenital rubella and terminations of pregnancy for rubella decreased markedly in England and Wales, with only one CRS case reported in 1995.

214

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 711:

The provinces of Canada adopted a policy either of mass vaccination of infants or of selective vaccination of preschool-age girls. Total rubella incidence dropped in the provinces that adopted mass vaccination of infants but was not much changed in those adopting vaccination of preschool-age girls. However, reported CRS decreased throughout Canada. As of 1983, all provinces give vaccine to infants and also to 12 year old girls who have not been immunized previously.

215

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 419:

Although mumps generally is viewed as an acute, relatively benign communicable disease of childhood, it gained notoriety as an illness substantially affecting armies during times of mobilization.

216

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 419-425.

Nombre del documento:

CDC Pink Book – Mumps

https://drive.google.com/file/d/1U1YBF2qTfjCbyi3hlFKAB EDnmxJxhCqh/view?usp=sharing

P 206-208.

217

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 443.

Nombre del documento:

Infectious diseases requiring notification in Israel

Archivo:

https://drive.google.com/open?id=1QEXa9 ZV_xDKvAdsUhN4BvWAfc7FbMjsH

Autor/año:

CDC, 2011

https://www.health.gov.il/PublicationsFiles/ Disease1951 2010.pdf

Autor/año:

Israeli Ministry of Health, 2012

P 125,127.

218

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 429:

In the US, mumps vaccine was first licensed in 1967 and has been administered as MMR since 1971. The ACIP first recommended MMR vaccine in 1977 and modified this to a two-dose schedule in 1989.

219

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

The effectiveness of mumps vaccines determined in field studies is lower than efficacy determined in clinical trials.

220

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

In the US, reported cases of mumps decreased from more than 185,000 in the prevaccine era to 2,982 by 1985, a decrease of more than 98%. By 2003, only 231 cases were reported, an all-time low

221-240

221

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 437-438.

222

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 426:

Indeed, since the 1989 implementation of a two-dose vaccination schedule in the US, reported mumps cases have decreased dramatically, although large mumps outbreaks still occur even in fully vaccinated populations, indicating that complete protection against mumps using current vaccines and vaccination schedules may not be feasible.

223

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 444.

224

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 439:

In Japan, the inclusion of mumps vaccine as part of the national immunization program was halted and has yet to resume;

225

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1404:

Mumps notifications fell by more than 95% after introduction of the vaccine in the United States (it was licensed in 1967 and recommended universally for children in 1977), which is appreciably greater than the product of coverage and efficacy and hence a clear indication of indirect protection.

226

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 357-358.

227

Nombre del documento:

CDC Pink Book - Measles

https://drive.google.com/file/d/1Yh8xUeOHSeX78GGs8DdWDFCm-hiKlSDz/view?usp=sharing

P 177-178.

228

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 356.

229

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 353:

Although subclinical infection with boosting of antibody may occur with subsequent exposure, immunity after natural infection is believed to be lifelong.

230

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 358

In the United States in the prevaccine era, approximately 500,000 cases of measles were reported each year, but, in reality, an entire birth cohort of approximately 4 million persons was infected annually. Associated with these cases were an estimated 500 deaths...

231

Nombre de la página:

Complications of measles

Archivo:

Autor/año:

CDC, 2011

http://archive.is/cTbri

Sitio web:

CDC

https://www.cdc.gov/measles/about/complications.html

For every 1,000 children who get measles, one or two will die from it.

232	Nombre de la página: Measles notifications and deaths in England and Wales: 1940 to 2016 https://www.gov.uk/government/publications/measles-deaths-by-age-group-from-1980-to-2013-ons-data/measles-notifications-and-deaths-in-england-and-wales-1940-to-2013 Sitio web: Public Health England	Archivo: http://archive.is/8YVzg
	Birth data of the National Bureau of Statistics Nombre de la página: Trends in births and deaths over the last century http://visual.ons.gov.uk/birthsanddeaths/ Sitio web: UK Office for National statistics	Archivo: http://archive.is/i0yx9

233	Nombre de la página (hebreo): Birth data in Israel		Archivo: http://archive.is/yCIfs
	Sitio web: https://tinyurl.com/y8z7v573		
	Nombre del documento: Infectious diseases requiring notification in Israel https://www.health.gov.il/PublicationsFiles/ Disease1951_2010.pdf	Archivo: https://drive.google.com/open?id=1QEXa9 ZV_xDKvAdsUhN4ByWAfc7FbMjsH	
	Autor/año: Israeli Ministry of Health, 2012		
	Measles mortality data on p 123.		

234	Nombre del artículo: Effect of vaccination programmes on mortality burden among children and young adults in the Netherlands during the 20th century: a historical analysis		PMID: 26873665
	Autor principal/año: Maarten van Wijhe, 2016	Revista: Lancet Infectious Diseases	
	P 6: For measles, the contribution to the all-cause mortality burden reduced steadily over the prevaccination period, so once vaccination was introduced in 1976, the mortality burden was already too low to note a clear effect of vaccination.		

235	Nombre abreviado: Plotkin 2013 - Vaccines (6th edition)
	P 353.

236	Nombre abreviado: Plotkin 2013 - Vaccines (6th edition)
	P 353:subacute sclerosing panencephalitis (SSPE) (1 per 100,000 cases)

The graph on page 374 shows about 45 cases of SSPE in the United States in 1969 (even before the level of measles fell, given the time lag between measles and the onset of SSPE).

237

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 358:

Young age at infection contributes to the high risk of serious complications and death. Also, malnutrition, especially vitamin A deficiency, may be an important factor leading to the marked severity of measles in the developing world because of defects in cellular (and possibly humoral) immunity.

238

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 365-366.

239

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

D 360.

With overall incidence of measles in the United States at record low levels and no evidence of increasing incidence among previously vaccinated persons, waning immunity does not appear to constitute a problem. Although secondary vaccine failures have been documented, taken collectively, the serologic and epidemiologic data during the past 35 years indicate that vaccine provides long-term immunity.

240

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 381

As vaccination coverage increases among successive birth cohorts, measles transmission decreases, reducing the risk of measles even among unvaccinated persons. At some vaccine- induced immunity level lower than 100%, measles virus transmission is interrupted.

[...⁻

Mathematical models have estimated the herd immunity threshold for measles in the United States at 92% to 95%.

[...]

Experience in industrialized countries has shown that a single dose of measles vaccine, widely administered, can reduce measles transmission, but a two-dose strategy is necessary for elimination of indigenous transmission.

P 365:

Measles vaccine provides both personal immunity to prevent disease when exposed to measles virus and population immunity through decreased intensity of transmission as the proportion of immune persons in a population increases. The population immunity effect decreases the risk of measles among immunized as well as unimmunized persons.

241-253

241	Nombre del artículo: Correlates of Vaccine-Induced Immunity		PMID: 18558875
	Autor principal/año: Stanley A. Plotkin, 2008	Revista: Clinical Infectious Dise	ases

P 5:

A remark in passing: it has become cliche' to say that vaccines prevent only disease, not infection. Although that may be often the case, it is not a general truth. If the presence of antibodies is sufficient to prevent colonization of mucosal surfaces, vaccines can produce "sterile" immunity. Vaccines against polio, measles, rubella, Hib, pneumococcus, meningococcus, and probably human papillomavirus are all capable of preventing infection as well as disease.

Nombre del artículo:

Control of pertussis—Lessons learnt from a 10-year surveillance programme in Sweden

PMID: 19679218

Autor principal/año: Rose-Marie Carlsson, 2009 Revista: Vaccine

P 5:

Mild-to-moderate cases in semi-immune individualsmayhave a shorter period of contagiousness, but they contribute to the spread of disease because they often go unrecognised and the infected individuals continue with their daily activities in day-care centres, schools and workplaces.

243

Nombre abreviado:

Carlsson 2009

P 1

In 1979, whole-cell pertussis (wP) vaccine was withdrawn from the Swedish childhood vaccination programme because of decreasing effectiveness and international concerns about safety.

244 Nombre abreviado:

Carlsson 2009

P 5.

Nombre del artículo:

Surveillance of infant pertussis in Sweden 1998–2012; severity of disease in relation to the national vaccination programme

PMID:

25695476

Autor principal/año:

Revista:

Rose-Marie Carlsson, 2015

Euro surveillance

P 1:

Pertussis decreased in non-vaccinated infants (2003 to 2012, p < 0.001), indicating herd immunity, both in those too young to be vaccinated and those older than three months.

245

Nombre abreviado:

Carlsson 2009

P 9

The Swedish enhanced surveillance project is sponsored by the aP vaccine manufacturers GlaxoSmithKline (Rixensart, Belgium), Sanofi Pasteur and Sanofi Pasteur MSD (Lyon, France).

Nombre abreviado:

Carlsson 2015

P 8

Financial support was obtained from the National Institute of Allergy and Infectious Diseases, Contract no. N01-AI-15125, from the European Commission, Contract n° QLK2-CT-2001-01819; Eupertstrain, and from the following manufacturers an

unrestricted grant: GlaxoSmithKline Vaccines, Wavre, Belgium, Sanofi Pasteur, Lyon, France, and Sanofi Pasteur MSD, Lyon, France.

246

Nombre abreviado:

Carlsson 2009

P 1:

There is also a well-established child healthcare system in Sweden, with 98–99% vaccination coverage in infancy. The coverage for the three-dose pertussis vaccination at 3, 5 and 12 months of age rapidly reached this level because the introduction of the diphtheria–tetanus–aP (DTaP) vaccine only involved a switch from DT vaccine to DTaP, and this coverage has remained unchanged during the subsequent switch to multivalent combinations including aP.

247

Nombre abreviado:

Carlsson 2015

P 3, chart 2.

248

Nombre abreviado:

Carlsson 2009

P 7:

Of the eight deaths in unvaccinated infants during the 10-year Swedish surveillance project [...] Examination of the Swedish national registry of deaths indicates that there were only three pertussis deaths in infants aged 3–11 months during the 10-year period before introduction of aP vaccination. The relevance of the difference between the two periods is uncertain...

249

Nombre abreviado:

Carlsson 2009

P 3-4:

The Swedish surveillance project was established as a continuation of an efficacy trial reporting procedure, including passive reporting from laboratories and the use of the same telephone questionnaire. This is in contrast to the active and prospective case finding in a previous efficacy trial, and the difference in reported rates between these two trials clearly indicates an almost 10-fold difference between active and passive case detection.

It is therefore likely that there has been under-reporting of pertussis cases following the introduction of aP vaccination in Sweden, and the degree of under-reporting within the country may vary.

250

Nombre abreviado:

Carlsson 2009

P 8:

While it is well established that wP or aP vaccination significantly reduces the overall disease burden, generalisations about the impact of vaccination on pertussis epidemiology are difficult to make because countries differ in many respects, including vaccination schedule, vaccination coverage, types of vaccines used, surveillance systems employed, crowding, mixing patterns and exposure to infection.

Nombre del artículo:

The relationship between mucosal immunity, nasopharyngeal carriage, asymptomatic transmission and the resurgence of Bordetella pertussis

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5580413/pdf/f1000research-6-12588.pdf

PMID: 28928960

Archivo:

https://drive.google.com/open?id=1b Cru-8-TfSy2uwMt01noQ_yY3B-6laEB

Autor principal/año: Revista: Christopher Gill, 2017 F1000 Research

P 1

The incidence of whooping cough in the US has been rising slowly since the 1970s, but the pace of this has accelerated sharply since acellular pertussis vaccines replaced the earlier whole cell vaccines in the late 1990s. A similar trend occurred in many other countries, including the UK, Canada, Australia, Ireland, and Spain, following the switch to acellular vaccines.

P 3, chart 1

252

Nombre del artículo:

Seroprevalence of Pertussis in the Netherlands: Evidence for Increased Circulation of Bordetella pertussis

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2995730/pdf/pone.0014183.pdf

PMID: 21152071

Archivo:

https://drive.google.com/open?id=1uIkUYGherxA7I8LGwKvOnMdql9aFXy3f

Autor principal/año: Revista: Sabine C. de Greeff, 2010 PLOS One

P 2:

Our results show that, although the changes in the vaccination program have reduced pertussis morbidity in childhood, they have not affected the increased infection rate in adolescent and adult pertussis.

253

Nombre abreviado:

Gill 2017

P 10:

...mathematical models that include no impact on disease transmission cannot explain the observed epidemiologic data.

Capítulo 10: Los misterios de la polio

1-20

1	Nombre del artículo: From Emergence to Eradication: The Epidemiology of Poliomyelitis Deconstructed https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2991634/pdf/kwq320.pdf		PMID: 20978089		
	Autor principal/año: Neal Nathanson, 2010	Revista: American Journal of Epidemiology			
	P 2.	P 2.			
2	http://archive.is/L7Mv5				
3	The institutional description of the history of polio appears in many sources, for example - Nombre del artículo: The Poliomyelitis Story: A Scientific Hegira https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2589894/pdf/yjbm00092-0018.pdf				
	Autor principal/año: Dorothy M. Horstmann, 1985				
	P 1-2.				
	Or Nombre del artículo: History of polio vaccination https://www.ncbi.nlm.nih.gov/pn 108.pdf	nc/articles/PMC3782271/pdf/WJV-1-	PMID: 24175215		
	Autor principal/año: Anda Baicus, 2012	Revista: World Journal of Virology			
	P 1-2.				
4	Título del libro: Vaccines (6 th edition) Published by Elsevier Saunders https://www.elsevier.com/books/	/vaccines/plotkin/978-1-4557-0090-5			
	Autor principal/año: Stanley Plotkin, 2013				
	D 572:				

5	Nombre del artículo: Poliomyelitis Problems		PMID: <u>14796117</u>
	Autor principal/año: Archibald L. Hoyne, 1951	Revista: Medical clinics of North America	

and scientific study of the agent began.

Fortunately, in 1908 Karl Landsteiner and Eric Popper isolated the virus of poliomyelitis,

P 1:

Notwithstanding the intensive studies of investigators, very little information of practical value has been added to our knowledge of poliomyelitis during the past forty years.

6 Nombre del artículo: PMID: Clinical concepts of poliomyelitis 18148242

Autor principal/año: Revista: EB Shaw, 1949 Pediatrics

P 1:

Every aspect of poliomyelitis has been subjected to intensive study during the last two or three decades, in spite of which the clinician has not been presented with any inescapably sound doctrine regarding its epidemiology and transmission, its precise pathogenesis, or the details of diagnosis and treatment.

7 Nombre del artículo: Paralytic consequences of poliomyelitis infection in different parts of the world and in different population groups https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1525657/pdf/amjphnation0 0428-0010.pdf

Autor principal/año: Revista:

Albert B. Sabin, 1951 American Journal of Public Health

Citing Sigmund Freud, P 15:

In one of these letters Freud wrote: "Even lectures I have given up, in order not to be forced to tell something that I only hope to learn some day."

8 Nombre del artículo: PMID: Innate host barriers to viral trafficking and population diversity: lessons 20951871 learned from poliovirus

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3234684/pdf/nihms338421.

PMID.

14885514

pdf

Autor principal/año: Revista:

Julie K. Pfeiffer, 2010 Advances in Virus Research

During research to develop the vaccines, many questions were asked: Why did certain people develop paralysis? How does the virus move from the gut to the CNS? What limits viral trafficking to the CNS in the vast majority of infected individuals? Despite over 100 years of poliovirus research, many of these questions remain unanswered.

9			PMID: 400274
	Autor principal/año: Neal Nathanson, 1979	Revista: American Journal of Epidemiology	

10	Nombre del artículo: From Emergence to Eradication: The Epidemiology of Poliomyelitis Deconstructed https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2991634/pdf/kwq320.pdf		PMID: 20978089
	Autor principal/año: Neal Nathanson, 2010	Revista: American Journal of Epidemiology	

11 Nombre abreviado:

Nathanson 2010

PMID: 20978089

...polio is one of the few major diseases whose appearance in epidemic guise was so recent that it was very well documented, together with its emergence as a worldwide scourge.

12 Nombre abreviado:

Nathanson 2010

PMID: 20978089

P 3, Figure 1.

13 Nombre del artículo:

The Epidemiology Of Poliomyelitis

PMID: 20242791

Problems at Home and Among the Armed Forces Abroad

Autor principal/año:

Revista: Albert B. Sabin, 1947 **JAMA**

...the main problem in the epidemiology of poliomyelitis concerns the cause or causes of the sudden appearance in certain parts of the world of large numbers of paralytic cases.

Nombre abreviado:

Nathanson 2010

PMID: 20978089

Beginning around 1880, a series of outbreaks of infantile paralysis were reported from several Scandinavian countries and the United States... Most remarkable is the almost simultaneous appearance of outbreaks in European countries and the United States.

14 Nombre abreviado:

Nathanson 2010

PMID: 20978089

P 2:

The disease's striking presentation, in which previously healthy infants underwent an acute febrile illness followed by localized paralysis, would have made outbreaks conspicuous. However, few if any cases were reported until late in the 19th century.

15 Nombre del artículo:

The Epidemiology Of Poliomyelitis

PMID:

Problems at Home and Among the Armed Forces Abroad

20242791

Autor principal/año: Revista: Albert B. Sabin, 1947 **JAMA**

the bulk of the evidence suggests that the epidemic outbursts, of the type which have occurred especially in the United States and a few other countries in the past thirty to forty years, are events that could not readily have been missed in the past.

16 Nombre del artículo:

The Poliomyelitis Story: A Scientific Hegira

PMID: 2994307

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2589894/pdf/yjbm00092-0018.pdf

Autor principal/año:

Dorothy M. Horstmann, 1985

The Yale Journal Of Biology And Medicine

P 2:

...epidemics emerged only in economically advanced countries of the world while in the underdeveloped areas the disease remained endemic;

17 Nombre del artículo:

PMID:

The Epidemiology Of Poliomyelitis

Problems at Home and Among the Armed Forces Abroad

20242791

Autor principal/año: Albert B. Sabin, 1947 Revista: JAMA

P 7:

Why did paralytic poliomyelitis become an epidemic disease only a little more than fifty years ago, and as such why does it seem to be affecting more and more the countries in which sanitation and hygiene, along with the general standard of living, are presumably making the greatest advances, while other large parts of the world, regardless of latitude, are still relatively unaffected?

18 Nombre del artículo:

PMID:

The Epidemiology Of Poliomyelitis

<u>20242791</u>

Problems at Home and Among the Armed Forces Abroad

Autor principal/año: Revista: Albert B. Sabin, 1947 JAMA

P 6:

.China, the Fiji Islands, Africa and certain other regions, in which only sporadic cases but no epidemics were known to occur...

19 Nombre del artículo:

PMID:

The Epidemiology Of Poliomyelitis

20242791

Problems at Home and Among the Armed Forces Abroad

Autor principal/año: Albert B. Sabin, 1947 Revista: JAMA

P 1:

...cities like Peiping, Tientsin and Shanghai, occupying approximately the same latitude in China, in which only rare sporadic cases have been recorded thus far, despite the presence in these cities for many years now of excellent western trained physicians who could not have missed such outbreaks in the native population if they had occurred.

Nombre del artículo:

PMID:

Poliomyelitis Problems

14796117

Autor principal/año: Archibald L. Hovne, 1951 Revista: Medical clinics of North America

D 2

I have been told by Chinese physicians that they had never seen poliomyelitis in their own country.

21-40

21	Nombre del artículo:	PMID:
	The Epidemiology Of Poliomyelitis	<u>20242791</u>
	Problems at Home and Among the Armed Forces Abroad	

Autor principal/año: Albert B. Sabin, 1947	Revista: JAMA
P 6-7.	

The Epidemiology Of Poliomyelitis

Problems at Home and Among the Armed Forces Abroad

PMID: 20242791

Autor principal/año: Albert B. Sabin, 1947 Revista: **JAMA**

Poliomyelitis has occurred among American troops in certain foreign countries, especially the Middle East, the Philippine Islands and during the past summer Japan and North China, in numbers and under circumstances that raise puzzling questions.

23 Nombre del artículo:

Poliomyelitis In British And American Troops In The Middle East: The Isolation Of VirusFrom Human Faeces

https://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC2284416&blo btype=pdf

Autor principal/año: Revista: John R. Paul, 1944 **BMJ**

P 1:

In 1941 a total of 74 cases were notified as acute poliomyelitis or encephalitis in the M.E.F., and of these 19 were fatal; in 1942 there were 32 cases, with 14 deaths. The rate among American soldiers stationed in the Middle East (during the first 10 months of 1943) has been more than 10 times that recorded in the United States for a similar period of time.

24 Nombre del artículo:

The Epidemiology Of Poliomyelitis

Problems at Home and Among the Armed Forces Abroad

PMID: 20242791

Autor principal/año: Revista: Albert B. Sabin, 1947 **JAMA**

P 7:

This past summer I had occasion to observe an outbreak of poliomyelitis among American marines stationed in the Tientsin area of North China. Four men died, 1 was severely paralyzed and at least 25 others had nonparalytic attacks. There was no evidence of an outbreak of poliomyelitis in the native population at the time, and Dr. Grice, a British physician in practice in Tientsin for twenty-five years, informed me that while he not infrequently saw paralytic poliomyelitis in children in the foreign colony he rarely saw the disease among the Chinese.

25 Nombre abreviado: Nathanson 2010

PMID: 20978089

P 25:

In the 1950s, Casablanca had 2 sizeable populations, native Moroccans and Europeans. During the period 1947–1953, there were cases of paralytic poliomyelitis in both populations, but the attack rate was 20-fold higher in the European sector.

Epidemiology Of Acute Poliomyelitis

In India Command

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(45)90883-X/fulltext?code=lancet-site

Autor principal/año: Revista: Douglas McAlpine, 1945 Lancet

P 1, Tabla 1.

Nombre del artículo:

Epidemiology Of Acute Poliomyelitis

In India Command

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(45)90883-X/fulltext?code=lancet-site

A/Tuntext: code—tancet-site

Autor principal/año: Revista: Douglas McAlpine, 1945 Lancet

P 1, Tabla 3.

Nombre del artículo:

Epidemiology Of Acute Poliomyelitis

In India Command

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(45)90883-X/fulltext?code=lancet-site

Autor principal/año: Revista: Douglas McAlpine, 1945 Lancet

P 1, Tabla 1 and 3. In addition:

British Army at Home: For 1943 and 1944 the incidence of acute poliomyelitis was 0 02 per 1000

Nombre del artículo:

Poliomyelitis

 $\underline{https://jamanetwork.com/journals/jama/article-abstract/296121}$

Autor principal/año: Revista: Hart E. Van Riper, 1947 JAMA

P 1:

The period of evolution from sporadic to epidemic poliomyelitis corresponds roughly with the institution of widespread measures for improved sanitation. This interesting coincidence has led to the hypothesis that the virus is more widespread in areas where the sporadic disease predominates, making possible frequent exposures of the young infant to virus during the time when he still retains a high titer of passive immunity from his mother. Exposure to the virus under these conditions would surely stimulate further resistance to poliomyelitis and only occasionally result in the production of the frank disease. This theory might explain the infrequent cases of poliomyelitis in young children as they occurred in the early history of the disease in Europe and the United States. But, in regions where epidemics predominate, people are exposed to the virus less frequently and at a later period in life, when they have lost all or most of the passive immunity acquired from the mother. Thus there results a greater chance for the development of frank disease among older age groups rather than an increased resistance.

Paralytic consequences of poliomyelitis infection in different parts of the world and in different population groups

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1525657/pdf/amjphnation00428-0010.pdf

PMID: 14885514

Autor principal/año: Revista:

Albert B. Sabin, 1951 American Journal of Public Health

P 15

In general, the poorer the population, its standard of living and sanitation, the more extensively is poliomyelitis virus disseminated among them and the lower is the incidence of paralytic poliomyelitis when virulent strains of virus come their way.

31 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

D 31.

Polioviruses probably circulated in an uninterrupted endemic manner for many centuries, infecting new cohorts of susceptible infants continuously, almost all early in life, when maternally derived antibody transferred from mother to newborn still provided some protection.

A change from endemic transmission to periodic epidemics was first observed in some temperate-climate countries (eg, Norway, Sweden, and the United States) late in the 19th century and at the beginning of the 20th century... The generally accepted explanation, supported by numerous studies, is that, in a temperate-zone climate with increased economic development and correspondingly improved resources for community sanitation and household hygiene, exposure to polioviruses was postponed to later in life.

32 Nombre abreviado:

Nathanson 2010

PMID: 20978089

P 2:

The most probable hypothesis is that outbreaks were associated with an increase in the age at which poliovirus infection was occurring (4). In the pre-epidemic era, enteric infections were so ubiquitous that most infants were infected within 6–12 months, at a time when they had circulating antibodies passively derived from their nursing mothers. Although serum antibodies did not prevent enteric infection, they were sufficient to preclude viremia, thereby avoiding invasion of the central nervous system and paralysis. The result was the acquisition of active immunity under the cover of passive protection. However, with the advent of improved personal hygiene and public sanitation, the transmission of enteric infections was delayed so that some infants were first infected after 12 months of age, when levels of passive antibodies had waned, reducing the barrier against invasion of the central nervous system.

Nombre abreviado:

Nathanson 2010

PMID: 20978089

Nathanson himself refers to it as a "hypothesis."

P 2:

The most probable hypothesis is that...

Nombre del artículo:

PMID:

The epidemiology of poliomyelitis: enigmas surrounding its appearance, epidemicity, and disappearance

400274

Autor principal/año: Revista:

Neal Nathanson, 1979 American Journal of Epidemiology

Nathanson calls it the "central dogma", P 1:

In fact, an explanation was developed, which can be considered the "central dogma" of poliomyelitis epidemiology.

35	Nombre del artículo: Studies On The Development Of Natural Immunity To Poliomyelitis In Louisiana		PMID: 13827179
	Autor principal/año: Henry M. Gelfand, 1960	Revista: Journal of Immunology	
	P 4, Tabla 6.		
	Trombie del articule.		PMID: 14885514
	Autor principal/año: Albert B. Sabin, 1951	Revista: American Journal of Public Health	
	P 10: While the time of disappearance of placentally transmitted antibody generally depends on the original concentration, the majority of infants are devoid of placentally transmitted antibody at 5 to 6 months of age.		
Similar findings were received in Israel in 1960 - Nombre del artículo: Epidemiology of Poliomyelitis in Israel, 1952-59 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC255531-0059.pdf		Israel, 1952-59	PMID: 13814376
	Autor principal/año: A. Michael Davies, 1960	Revista: Bulletin of the World Health Organization	1
P 4.			

36 Nombre del artículo:

Paralytic consequences of poliomyelitis infection in different parts of the world and in different population groups

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1525657/pdf/amjphnation00428-0010.pdf

Autor principal/año: Revista:

Albert B. Sabin, 1951 American Journal of Public Health

P 11

It is evident from these data that neither among the lower income groups in the United States nor in the Far East or Egypt were Lansing antibodies (and presumably infection) acquired to any significant extent during the period of diminishing placentally transmitted antibody. The hypothesis of extensive immunization as a result of modified or subclinical infection among certain population groups during the first year of life therefore became untenable.

PMID:

14885514

Nombre de la página: Vaccines and Immunization - Polio Sitio web: Museum of Healthcare http://www.museumofhealthcare.ca/explore/exhibits/vaccinati ons/polio.html Archivo: http://archive.is/VR6Aa

Thus, over time, a growing percentage of children, as well as young adults, particularly among the more hygienic middle class in small towns and new suburban areas during the postwar "baby boom," were vulnerable to the poliovirus, which had a greater chance of invading the nervous system and causing paralytic damage.

38 Título del libro:

Dirt and Disease: Polio Before FDR

https://www.amazon.com/Dirt-Disease-Medicine-American-

Society/dp/0813517869/ref=sr 1 1?s=books&ie=UTF8&qid=1476620110&sr=1-

1&keywords=9780813517865

Autor principal/año: Publicador :

Naomi Rogers, 1992 Rutgers University Press

39 Título del libro:

Dirt and Disease: Polio Before FDR

https://www.amazon.com/Dirt-Disease-Medicine-American-

Society/dp/0813517869/ref=sr 1 1?s=books&ie=UTF8&qid=1476620110&sr=1-

1&keywords=9780813517865

Autor principal/año: Publicador :

Naomi Rogers, 1992 Rutgers University Press

P 165:

During the 1920s and 1930s the public and the scientific community developed a new image of polio. Until then polio, seen as a children's illness that rarely attached adults, was associated with immigrants and urban slums.

40 Título del libro:

Dirt and Disease: Polio Before FDR

https://www.amazon.com/Dirt-Disease-Medicine-American-

Society/dp/0813517869/ref=sr 1 1?s=books&ie=UTF8&qid=1476620110&sr=1-

1&keywords=9780813517865

Autor principal/año: Publicador :

Naomi Rogers, 1992 Rutgers University Press

P 9-10:

The scenes show narrow streets lined with dirty and unsanitary pushcarts, the latter filled with fly-specked cakes and candy and decaying fruit... all are touched by many hands before they are finally eaten; there are uncovered garbage cans near which cats and children play and squabble over crusts of bread and other tid-bits.

41-60

41	Nombre del artículo: In Reaction to Zika Outbreak, Echoes of Polio	Fecha: Aug 29, 2016
	Sitio web: NYTIMES http://www.nytimes.com/2016/08/30/health/zika-outbreak-echoes-of-polio.html	Archivo: http://archive.is/qp0YD

The first child to be paralyzed lived in a modest Italian neighborhood east of the Gowanus in Brooklyn. Polio soon jumped to Pigtown, a gritty pig-farming area, and most of the first 20 cases were in Italian children.

Infant Paralysis Starts a Cleanup

Fecha: July 1, 1916

Sitio web:

NYTIMES

http://newspaperarchive.com/us/new-york/new-york/new-york-times/1916/07-01/page-7

...forty-seven [deaths] occurring since last Saturday, forty-two in Brooklyn and five in Manhattan. Italians living in crowded tenements have been the chief sufferers...

The infected area contains many old tenements and garbage and ashes are deposited in the halls. It is reported that these areas are infested with cats and the garbage and ash piles draw flies. With the co-operation of the various departments these areas are being cleaned up.

43 Título del libro:

Murderous Contagion: A Human History of Disease

https://www.amazon.com/Murderous-Contagion-Human-History-Disease/dp/1782069437

Autor principal/año: Publicador :

Mary Dobson, 2015 Quercus Publishing

But in the summer of 1916 it became clear that the epidemic, while striking hardest at the young, affected both rich and poor, long-time residents as well as recent immigrants.

44 Título del libro:

Dirt and Disease: Polio Before FDR

https://www.amazon.com/Dirt-Disease-Medicine-American-

Society/dp/0813517869/ref=sr 1 1?s=books&ie=UTF8&qid=1476620110&sr=1-

1&keywords=9780813517865

Autor principal/año: Publicador :

Naomi Rogers, 1992 Rutgers University Press

P 10:

Poliomyelitis paralyzed infants and children. Their economic or sanitary conditions seemed to make little difference; rich or poor, clean or dirty, no child seemed immune.

45 Nombre del artículo:

Notes Of An Epidemic Of Acute Anterior Poliomyelitis

https://jamanetwork.com/journals/jama/article-abstract/458738

Autor principal/año: Revista: Charles S. Caverly, 1896 JAMA

P 1:

That the general sanitary surroundings and methods of living were in anywise responsible for the outbreak is also more than doubtful, since the disease showed no partiality to that class of the population whose habits and surroundings are the most unsanitary. The so-called laboring classes were oftenest affected, but not out of proportion to their numbers. These classes here, whether among the farming population or in the mills and quarries, have usually pure air, food and water. Hence, general sanitary conditions did not seem to have any influence on the epidemic.

46 Nombre del artículo:

The Occurrence Of Infantile Paralysis In Massachusetts In 1907

https://archive.org/details/b22431779

Autor principal/año: Revista:

Robert W. Lovett, 1908 Boston Medical and Surgical Journal

P 6-7·

The reports on the conditions of the house in which the patients lived are of interest. One

hundred and fifteen lived in detached houses; 110 in tenements. As to the influence of dampness, 99 lived on the first floor; 65 on the second; 12 on the third; and 6 in the upper stories; 20 occupied the whole house. Sanitary conditions were described as exceptionally good in 21. Good, in 123. Fair, in 55. Poor or bad, in 23... The house was screened in 133 cases, and not screened or insufficiently so in 80... Analyzing these data for what they are worth, it would seem that it was not an affection confined to the lower classes.

47 Nombre del artículo:

An Epidemic Of Infantile Paralysis In Western Massachusetts In 1908 https://archive.org/details/bostonmedicalsur1611mass

Autor principal/año: Revista:

Herbert C. Emerson, 1909 Boston Medical and Surgical Journal

P 118:

Investigation of the home conditions of each case shows that sanitary conditions were found to be excellent in 4 cases, good in 17, fair in 31 and bad in 17. Forty-one of the cases lived in detached houses, 17 in two-tenement and 3 in three-tenement houses, while but 8 lived in houses having four or more tenements...

The sanitary arrangements in the houses showed that 23 houses had water closets connected with the sewer and 46 had earth closets; that the sink water from 30 houses was carried into the sewer and in 39 cases it was disposed of in various ways on the land nearby or in pipes to the nearest brook, pond, etc.

48 Título del libro:

Preventive Medicine and Hygiene

https://drive.google.com/open?id=1ONdl0AG5blbi8mJM0vMupllagVoL0T4D

Autor principal/año: Publicador:

Milton J. Rosenau, 1918 D Appleton and Company

P 340:

From the standpoint of prevention it is important to note that social and hygienic conditions apparently have no influence whatever in determining the infection. All classes are affected in about equal proportion.

49 Nombre del artículo:

PMID:

A Survey Of Neutralizing Antibodies To Poliomyelitis Virus In Cairo,

Egypt

14933381

Autor principal/año: Revista:

John R. Paul, 1952 American Journal of Epidemiology

P 4-5.

50 Nombre del artículo:

The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año:

Revista:

Tiberio A. Swartz, 2008 Israel Center for Disease Control (ICDC), Ministry of Health

This indicated the presence of an almost constantly moderate endemicity (Levenstein K, 1937) that varied between 1.7 and 0.3 per 100,000 population during the whole reporting period. An exception were the epidemic years 1928, 1929, 1934 and 1939, when the attack rates ranged between 2.1 and 4.1 per 100,000.

51 Nombre del artículo:

The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año: Tiberio A. Swartz, 2008	Revista: Israel Center for Disease Control (ICDC), Ministry of Health
P 43, Figure 4.1	

The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año:

Revista:

Tiberio A. Swartz, 2008

Israel Center for Disease Control (ICDC), Ministry of Health

This pattern, common to the other countries in the geopolitical area, was the result of poor sanitation which favored the community transmission of infection in a slowly growing population, and to a low level of family hygiene which supported the intrafamilial spread of fecal-oral transmitted infectious diseases. The result was infection in early life, which led to immunity to polio in the majority of the population. This maintained an endemic state which prevented massive spread.

53 Nombre del artículo:

The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año:

Revista:

Tiberio A. Swartz, 2008

Israel Center for Disease Control (ICDC), Ministry of Health

This population was severely affected by the disease, as expressed by an exceedingly high attack rate of 271.0 per 100,000, recorded in the year following immigration, as compared with 122.0 per 100,000 in the veteran Israeli residents.

54 Nombre del artículo:

The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año:

Revista:

Tiberio A. Swartz, 2008

Israel Center for Disease Control (ICDC), Ministry of Health

There were high attack rates, which ranged between 268.0 per 100,000 in kibbutz settlements and 107.0 per 100,000 in towns, respectively. Quite strikingly, similarly high rates occurred in kibbutz and immigrant camp populations, in spite of the marked differences in terms of housing, sanitation and nutrition.

55

Nombre del artículo:

The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año:

Revista:

Tiberio A. Swartz, 2008

Israel Center for Disease Control (ICDC), Ministry of Health

P 52-54.

56

Nombre del artículo:

The Poliomyelitis Story: A Scientific Hegira

PMID: 2994307

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2589894/pdf/vjbm00092-0018.pdf

Autor principal/año:

Revista:

Dorothy M. Horstmann, 1985

The Yale Journal Of Biology And Medicine

P 11:

Estimates based on the findings suggested incidence rates comparable to those during the peak years in the United States before the introduction of vaccine in 1955.

57

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 606:

Lower socioeconomic status has been shown to be a risk for paralytic poliomyelitis in developing countries, probably because children belonging to the lower socioeconomic group experience more intense exposure to poliovirus (ie, a higher virus inoculum, which has been shown in experimental studies to be a risk factor for paralytic disease).

58

Nombre del documento:

Poliovirus infection case definition summary

https://www.health.gov.au/internet/main/publishing.nsf/Content/cda-phlncd-polio.htm/\$FILE/polio.pdf

Autor principal/año:

Archivo:

Public Health Laboratory Network (Australia), 2000

https://drive.google.com/open?id=1RCX0f4JIg DWhu4Ypvf55CUPB8b1FJg3f

P 1

The risk of infection is directly correlated with poor hygiene and poor sanitation and overcrowding, typically among inadequately vaccinated populations. This is a major health problem in the developing world causing mortality and morbidity among thousands of children annually.

59

Nombre del artículo:

PMID:

17110580

New Strategies for the Elimination of Polio from India http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.654.6533&rep=rep1&type=pdf

Autor principal/año: Revista: Nicholas C. Grassly, 2006 Science

P 3:

High population densities and poor sanitation therefore appear to explain the persistence of polio. These factors act to facilitate the transmission not only of poliovirus but also of other enteroviruses and diarrhea...

60

Nombre del artículo:

PMID: 2994307

The Poliomyelitis Story: A Scientific Hegira https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2589894/pdf/yjbm00092-

0018.pdf

Autor principal/año: Revista:

Dorothy M. Horstmann, 1985

The Yale Journal Of Biology And Medicine

Because in third-world countries few cases of poliomyelitis are reported and epidemics do not occur, it has been assumed that the wide dissemination of the virus resulted in immunizing infections in the first years of life at a price of only rare paralytic cases. This assessment proved false...

61-80

61	Nombre del artículo: The Poliomyelitis Story: A Scientific Hegira https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2589894/pdf/yjbm00092-0018.pdf	PMID: 2994307	
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Autor principal/año: Revista:

Dorothy M. Horstmann, 1985 The Yale Journal Of Biology And Medicine

The likely explanation of these patterns is thought to be related to ways of life - to an improved sanitary environment in industrialized countries which protected young children from early exposure to the virus, allowing a build-up in the number of susceptibles among whom epidemics could get under way. In contrast, in the underdeveloped, largely tropical countries of the world where the sanitary environment remains poor, infection and immunity develop in the first few years of life. Thus there are not enough susceptibles for an epidemic to occur, and cases remain confined to the youngest age group.

62 Nombre del artículo: PMID: Poisoning as The Cause of Poliomyelitis 14771968 Autor principal/año: Revista: Ralph R. Scobey, 1950 Archives of Pediatrics P 29. One has only to examine critically the literature of the past and it will be found that poliomyelitis beyond doubt existed, but that it was designated by many names. The writer had found individual cases and epidemics of paralytic diseases listed by nearly 200 names prior to 1890.

63	Nombre del artículo: Is the Cause of Poliomyelitis Alw	ays the Same?	PMID: 13066184
	Autor principal/año: Ralph R. Scobey, 1953	Revista: Archives of Pediatrics	
	P 3-7.		

64 Nombre del artículo: PMID: Nonpolio Causes of Polio-like Paralytic Syndromes 6740077 Autor principal/año: Revista: JHS Gear, 1984 Reviews of Infectious Diseases P 1-2.

65	Nombre del artículo: Nonpolio Causes of Polio-like Par	culo: of Polio-like Paralytic Syndromes	
	Autor principal/año: JHS Gear, 1984	Revista: Reviews of Infectious Diseases	
	P 2-3.		

66	Nombre del artículo: Poliomyelitis-The Los Angeles Epidemic Of 1934 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1753761/pdf/calwestmed00	PMID: 18743375
	403-0040.pdf	

Autor principal/año: Revista:
RW Meals, 1950 Revista: California And Western Medicine

Part II, p 2:

We were interested in the long list of mistaken diagnoses reported by Brady and Lenarsky but found, on checking our own experiences that we had seen in this and other epidemics fifty seven different conditions suspected of being poliomyelitis.

Nombre del artículo:
Poliomyelitis-The Los Angeles Epidemic Of 1934

18743375

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1753761/pdf/calwestmed00403-0040.pdf

Autor principal/año: Revista:

RW Meals, 1950 California And Western Medicine

Part II, p 7:

In the Chicago outbreaks of 1916 and 1917, almost every conceivable disease and condition was reported by physicians as poliomyelitis.

Nombre del artículo: Poliomyelitis Problems PMID: 14796117

Autor principal/año: Revista:

Archibald L. Hoyne, 1951 Medical clinics of North America

P 7:

In the midst of an epidemic a great variety of diseases and conditions have been confused with poliomyelitis. Among them are some that have been observed by the writer and which will merely be mentioned here. They are: practically all forms of bacterial meningitis but particularly tuberculosis, tetanus, rheumatic fever, mononucleosis, brain abscess, brain tumor, trichinosis, mumps meningoencephalitis, lymphocytic choriomeningitis, transverse myelitis, lead poisoning, Guillain-Barre syndrome, laryngeal diphtheria, scurvy, tonsillitis, postdiphtheritic paralysis, acute pharyngitis, diabetes and hysteria; also osteomyelitis, a foreign body in the plantar surface of the foot causing a limp, appendicitis and fracture of the fibula, skull fracture and spontaneous subarachnoid hemorrhage.

P 5:

It is frequently stated that no two cases of poliomyelitis are exactly alike

Nombre del artículo:
Acute Poliomyelitis With Special Reference To Early Symptomatology And Contact Histories
https://www.jstor.org/stable/25361797?

Autor principal/año: Revista: Douglas McAlpine, 1947 BMJ

P 1, 3.

70 Nombre del artículo: PMID: Clinical concepts of poliomyelitis 18148242

Autor principal/año: Revista: EB Shaw, 1949 Pediatrics

P 1

Every aspect of poliomyelitis has been subjected to intensive study during the last two or three decades, in spite of which the clinician has not been presented with any inescapably sound doctrine regarding its epidemiology and transmission, its precise pathogenesis, or the details of diagnosis and treatment.

71	Nombre del artículo: Report Of A Possibly Milk-Born Epidemic Of Infantile Paralysis		
Autor principal/año: John C. Dingman, 1916		Revista: New York State Journal of Medicine	

72 Nombre del artículo: An Outbreak Of Poliomyelitis Apparently Milk Borne https://jamanetwork.com/journals/jama/article-abstract/242504 Autor principal/año: Revista: AC Knapp, 1926 **JAMA**

73 Nombre del artículo: An Institutional Outbreak Of Poliomyelitis Apparently Due To A Streptococcus In Milk https://www.jstor.org/stable/30083744 Autor principal/año: Revista: Edward C. Rosenow, 1932 Journal of Infectious Diseases

74	Título del libro: Poliomyelitis In All Its Aspects		
	Autor principal/año: John Ruhrah , 1917		Publicador : LEA & FEBIGER
	P 57: The fact [is] that the disease seems to spread radially from an infected center so that the most recent cases are generally found to be the farthest away from the center geographically.		
	Título del libro: Acute Poliomyelitis (Heine-Medin's Disease)		
	Autor principal/año: Ivar Wickman, 1913	Publicador: The Journal of Nervous and Mental Disease Publishing Company	
	P 112:		

75	Nombre del artículo: Dangers In The Manufacture Of P https://www.jstor.org/stable/41829	
Year: Revista: Monthly Review of the		Revista: Monthly Review of the U.S. Bureau of Labor Statistics

person to person.

The Swedish epidemic of 1905 thus demonstrated that the mode in which the disease spreads both within the large epidemic centers and within the individual components which constitutes them, so far as it was possible to determine, was essentially analogous to that established for a number of other infectious diseases, in which transmission takes place from

76	Título del libro: Before Silent Spring: Pesticides	s and Public Health in Pre-DDT America	
	Autor principal/año: James Whorton, 1974	Publicador : Princeton University Press	
	P 39-40: An incomplete list of arsenic-tinted items compiled by the Medical Society of London in the early 18805, for example, enumerated paper, fancy and surface coloured, in sheets for		

covering cardboard boxes; for labels of all kinds; for advertisement cards, playing cards, wrappers for sweetmeats, cosaques, etc.; for the ornamentation of children's toys; for covering-children's and other books; for lamp shades, paperhangings for walls and other purposes; artificial leaves and flowers; wax ornaments for Christmas trees and other purposes; printed or woven fabrics intended for use as garments; printed or woven fabrics intended for use as curtains or coverings for furniture; children's toys, particularly inflated india-rubber balls with dry colour inside, painted india-rubber dolls, stands and rockers of rocking-horses and the like, glass balls (hollow); distemper colour for decorative purposes; oil paint for the same; lithographer's colour printing; decorated tin plates, including painted labels used by butchers and others to advertise the price of provisions; japanned goods generally; Venetian and other blinds; American or leather cloth; printed table baizes; carpets, floorcloth, linoleum, book cloth and fancy bindings. To this list may be added coloured soaps, sweetmeats and false malachite. Arsenic is also used in the preparation of skins for stuffing and of some preservatives used by anatomists." Other lists, though less lengthy, often turned up additional arsenical products. The renowned British toxicologist Robert Christison observed that not only was Scheele's green used to make sweetmeats more appetizing, but that it was also added to preserves and to apple tarts, and that several children had been made ill by the latter.' Others' pointed out that the green cakes in water color sets generally contained arsenic, as did dental fillings, and that people had been injured by arsenical stockings, veils, cosmetics, concert tickets, fly papers, stuffed animals, even money.

77

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador :

James Whorton, 1974 Princeton University Press

P 49-51:

The respect in which Fowler's solution was held can be best appreciated by an enumeration of the conditions for which it was regularly prescribed. These included anemia, headache, dyspepsia, eczema, psoriasis, all other chronic skin diseases, neuralgia, chorea, epilepsy, whooping cough, asthma, bronchitis, emphysema, pulmonary tuberculosis, malaria, and cancer. In addition, Fowler's solution was suggested, at one time or another, for cholera, yellow fever, syphilis, diabetes, angina pectoris, tic douloureux, gout, arthritis, rheumatism, constipation, morning sickness, melancholia, impotence, fits of sneezing, warts, boils, and, for the careless traveler in the Orient, cobra bites.

78

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador :

James Whorton, 1974 Princeton University Press

P 41

The real leadership of the campaign against arsenical manufactures was assumed by the physicians of Massachusetts, most prominent among these Yankee meddlers being a foursome of Bostonians: Frank Winthrop Draper, medical examiner (coroner) of Boston and lecturer at Harvard Medical School; James Jackson Putnam, professor of neurology at Harvard; Frederick Cheever Shattuck, professor of clinical medicine; and William Barker Hills, the medical school's chemistry professor. With a diligence befitting Harvard men, these four delivered lectures and published papers on the dangers of arsenic in the household, with the express purpose of informing the citizenry, through their physicians, of products to be avoided.

79

Nombre del artículo:

On The Character Of The Evidence As To The Injuriousness Of Arsenic As A Domestic Poison

https://jamanetwork.com/journals/jama/article-abstract/466612

Autor principal/año: James J. Putnam, 1891	Revista: JAMA
P 3.	

On The Character Of The Evidence As To The Injuriousness Of Arsenic As A Domestic Poison

https://jamanetwork.com/journals/jama/article-abstract/466612

Autor principal/año: Revista: James J. Putnam, 1891 **JAMA**

These results conclusively show: first, that the community is exposed to arsenical contamination on a very large scale.

81-100

81 Título del libro:

Encyclopedia of Pest Management

https://books.google.co.il/books?id=ytFoAcwI4sQC&pg=PA377&lpg=PA377#v=onepage& q&f=false

Autor principal/año: Publicador: David Pimentel, 2013 **CRC Press**

The Colorado potato beetle, provides a prime example. It appeared as a devastating pest of potato in Iowa and Nebraska in 1861, having transferred from a native weed to an introduced relative, the potato. The beetle spread rapidly eastward, reaching the Atlantic coast in 1874, despite the use of traditional nonchemical means of control. In 1867, farmers in the west discovered that the Colorado potato beetle could be controlled with Paris green, an arsenical. Paris green was in general use by 1880 and became the first widely used pesticide in North America.

82 Título del libro: War on Bugs

https://www.amazon.com/War-Bugs-Will-Allen/dp/1933392460

Autor principal/año: Publicador: Will Allen, 2007 **CRC Press**

Chapter 14.

83 Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Publicador: Autor principal/año: Princeton University Press James Whorton, 1974

P 23:

This decline did not leave the field uncontested to Paris green, for shortly before 1900 the most effective arsenical insecticide of all had been discovered, during the campaign against the gypsy moth. A leaf-eating insect native to Europe, the moth was first brought to the New World by Leopold Trouvelot, a French-born Harvard astronomer with a side-interest in silkworm breeding. Some experiments dealing with the latter subject seemed to Trouvelot to require gypsy moths, and so in 1869 he imported a number of gypsy moth eggs and cared for them until the insects reached maturity. The moths wasted little time asserting their

independence, and soon escaped from Trouvelot's home in Medford, Massachusetts. Twenty years later, in 1889, their descendants, in the form of caterpillars, returned to Medford, in numbers that "were so enormous that the trees were completely stripped of their leaves, the crawling caterpillars covered the sidewalks, the trunks of the shade trees, the fences and the sides of the houses, entering the houses and getting into the food and into the beds. They were killed in countless numbers by the inhabitants who swept them up into piles, poured kerosene over them and set them on fire. Thousands upon thousands were crushed under the feet of pedestrians, and a pungent and filthy stench arose from their decaying bodies. The numbers were so great that in the still, summer nights the sound of their feeding could plainly be heard, while the pattering of the excremental pellets on the ground sounded like rain.

Nombre del artículo: Historical use of lead arsenate insecticides, resulting soil contamination and implications for remediation https://drive.google.com/open?id=1aQjZsfRp8Qyjjyp4qvJx3db0a Lead Author: Archivo: https://archive.is/M0jdl

D 1

Francis J. Peryea

These properties were useful to farmers, with the consequence that LA was rapidly adopted for insecticidal use throughout the world. Lead arsenate initially was prepared by farmers at home by reacting soluble lead salts with sodium arsenate, a practice that continued in some countries through the 1930s and likely 1940s. Lead arsenate pastes and powders also were sold commercially. Their formulations became more refined over time.

85	Nombre del artículo: Historical use of lead arsenate insecticides, resulting soil contamination and implications for remediation https://drive.google.com/open?id=1aQjZsfRp8Qyjjyp4qvJx3db0a n68Tsid	Archivo: http://archive.is/M0jdl
	Lead Author: Francis J. Peryea	

P 1-2:

Lead arsenate insecticide was used in Australia, Canada, New Zealand, and the USA (Peryea and Kammereck, 1997). It also was used in England (Gratwick, 1965), and was the principal arsenical pesticide used in France and also was used in North Africa (Balachowsky and Mesnil, 1936). Lead arsenate likely was used in many other countries, particularly where codling moth was a pest of apples.

86	Nombre del artículo: Is Acute Poliomyelitis Unusually Prevalent This Season?	
	Autor principal/año: James J. Putnam, 1893	Revista: Boston Medical and Surgical Journal

87	Nombre de la página: Massachusetts U-Pick Farms	Archivo: http://archive.is/gvyA7
	Sitio web: PickYourOwn.org http://www.pickyourown.org/MAharvestcalendar.htm#apples	
	Nombre de la página: Pick Your Own Apples At Parlee Farms	Archivo: http://archive.is/L570h

Sitio web: PARLEE FARMS

http://parleefarms.com/apples

Nombre del artículo:

Is Acute Poliomyelitis Unusually Prevalent This Season?

Autor principal/año: Revista:

James J. Putnam, 1893 Boston Medical and Surgical Journal

P 2:

...that the patients did not come to any extent, from any one locality, but from different parts of the large area of the suburbs of Boston... Very few of the patients came from Boston proper;

89 Nombre del artículo:

Notes Of An Epidemic Of Acute Anterior Poliomyelitis

https://jamanetwork.com/journals/jama/article-abstract/458738

Autor principal/año: Revista: Charles S. Caverly, 1896 JAMA

P 1

The epidemic, as I have indicated, invaded our valley in the early summer of 1894. It prevailed with increasing severity during July, apparently reached its climax about the first of August, and steadily declined until about the first of October, the last case occurring early in that month.

90 Nombre del artículo:

Growing Apples In Vermont

https://vermonthistory.org/images/stories/articles/histor

icroots/growingapplesinvermont.pdf

Autor principal/año: Revista:
Barbara Bellows, 1997 Historic roots

Р3

In the 1880s Vermont farmers were looking for new crops to grow. Some planted large apple orchards and hoped they would make a lot of money selling the fruit to markets in the big cities.

91 Nombre de la página:

Vermont Seasonality Calendar

Sitio web:

Vermont Agency of Agriculture

http://agriculture.vermont.gov/buy local/harvest calendar

Archivo:

https://drive.google.com/open?id=

ItYY12oINmO0LV jq5vw

http://archive.is/EDfEH

92 Nombre del documento:

ATSDR - Arsenic Toxicity

http://www.atsdr.cdc.gov/csem/arsenic/docs/arsenic

.pdf

Archivo:

https://drive.google.com/open?id=17

uL KUUCnrOv-

Archivo:

1Ioz5WpggWaI-

zfAP9QUkh zOoInWjXQ

Autor/año:

CDC, 2009

P 47.

Nombre del documento:

ATSDR - Lead Toxicity

http://www.atsdr.cdc.gov/csem/lead/docs/lead.pdf

Archivo:

https://drive.google.com/open?id=1K

Autor/año:
CDC, 2009
P. 45.

Nombre del artículo:
On The Character Of The Evidence As To The Injuriousness Of Arsenic As
A Domestic Poison
https://jamanetwork.com/journals/jama/article-abstract/466612
Autor principal/año:
James J. Putnam, 1891

P 3.

94 Nombre del artículo:

The Occurrence Of Infantile Paralysis In Massachusetts In 1907 https://archive.org/details/b22431779

Autor principal/año: Revista:

Robert W. Lovett, 1908 Boston Medical and Surgical Journal

P 3

Vulpian produced, experimentally, paralysis of the extensors and lesions resembling those of poliomyelitis in a dog by lead poisoning, and in a case of lead poisoning found pronounced poliomyelitis with colloid degeneration arid cell atrophy. Phillippe and Gauthard report a case of anterior poliomyelitis from lead poisoning and Obrastoff one from arsenical poisoning. Onuf reported the case of a painter with flaccid paralysis of both legs, in whom autopsy showed lesions characteristic of the disease.

Nombre del artículo:
Report Of An Unusual Case Of Lead Paralysis With Autopsy
.https://ia800201.us.archive.org/21/items/journalofnervous27ameruoft/journ
alofnervous27ameruoft.pdf

Autor principal/año:
B. Onof, 1900

Revista:
Journal of Nervous and Mental Disease

P 155-156.

Nombre del artículo:
Poisoning as The Cause of Poliomyelitis

Autor principal/año:
Ralph R. Scobey, 1950

P 2-3.

RMID:
14771968

Revista:
Archives of Pediatrics

PMID:
Poliomyelitis Problems

Autor principal/año:
Archibald L. Hoyne, 1951

Revista:
Medical clinics of North America

P 7:

In the midst of an epidemic a great variety of diseases and conditions have been confused with poliomyelitis. Among them are some that have been observed by the writer and which will merely be mentioned here. They are: practically all forms of bacterial meningitis but particularly tuberculosis, tetanus... lead poisoning...

98	Nombre del artículo: Fatal Lead Poisoning Simulating Poliomyelitis		PMID: 14958999
	Autor principal/año: Andrew F. Braff, 1952	Revista: US Armed Forces Medical Journal	

99 PMID: Nombre del artículo: 14958999 Fatal Lead Poisoning Simulating Poliomyelitis Autor principal/año: Revista: Andrew F. Braff, 1952 US Armed Forces Medical Journal Lead poisoning is easily confused with poliomyelitis of the bulbo-spinal type.

100 Nombre del artículo:

The History of Lead Arsenate Use in Apple Production: Comparison of its Impact in Virginia with Other States

Autor principal/año: Revista: Michael J. Weaver, 2008 Journal of Pesticide Safety Education

In 1919 they discovered that common washing practices did not adequately remove arsenic residues from produce. A study conducted by the Virginia Agricultural Experiment Station (Hough et al., 1931) concluded that three sprays of lead arsenate applied in May and June did not require removal of spray residue at harvest time. However, when a third or fourth spray of lead arsenate was applied in July, followed by dry weather, excessive residues remained on the apples at harvest. Wiping or brushing apples removed only about one-third of the total arsenical residues.

101-120

101 Nombre del artículo:

The History of Lead Arsenate Use in Apple Production: Comparison of its Impact in Virginia with Other States

Autor principal/año: Revista: Michael J. Weaver, 2008 Journal of Pesticide Safety Education

The search for substitutes for LA began in earnest when it was discovered in 1919 that contemporary practices for washing produce were failing to adequately remove As residues (Shepard, 1939). Unfortunately, all of the tested alternative materials were found to provide less effective insect control or were more toxic to plants and animals. No adequate substitutes were found until 1947, when the synthetic organic insecticide dichlorodiphenyltrichloroethane (DDT) was introduced.

102	Nombre del artículo: Arsenic-laced soil lingers where children play in Washington state	Fecha: Nov 4, 2015
	Sitio web: PBS http://www.pbs.org/newshour/updates/arsenic-laced-soil-lingers-where-children-play-in-washington/	Archivo: http://archive.is/r5x3h

103 Nombre del documento:

Arsenic Contamination in Vermont's Private Wells

http://www.middlebury.edu/media/view/270347/original/es401 arsenic final report.pdf

Autor principal/año: Archivo:

Peter Ryan, 2010 https://drive.google.com/open?id=1 y5C67E8mXGhMMLZS

uwMVSdrz8-brcI

P 13:

High arsenic levels were found in small pockets throughout the state (Map 1-1). The most notable collection of high arsenic results were in Rutland and Bennington counties.

104 Nombre del artículo:

'Do Not Eat Those Apples; They've Been On The Ground!': Polio Epidemics And Preventive Measures, Sweden 1880s-1940s

PMID: 19750602

Autor principal/año: Revista:

Per Axelsson, 2009 Asclepio. Revista de Historia de la Medicina y de la Ciencia

P 8:

Medin considered polio to be an acute infectious disease, affecting the nervous system, that could cause epidemics, but he did not consider it to be contagious.

105 | Nombre del artículo:

'Do Not Eat Those Apples; They've Been On The Ground!': Polio Epidemics And Preventive Measures, Sweden 1880s-1940s

PMID: 19750602

Autor principal/año: Revista:

Per Axelsson, 2009 Asclepio. Revista de Historia de la Medicina y de la Ciencia

P 7

As late as 1911 some physicians in Sweden still argued that polio was a disease caused by miasma. The theory of miasma implied that disease was not caused by contagions but by putrefaction, i.e. «bad air» and should be combated with cleaner environments which often meant improved hygiene and sanitation.

106 | Título del libro:

Acute Poliomyelitis (Heine-Medin's Disease)

Autor principal/año: Publicador :

Ivar Wickman, 1913 The Journal of Nervous and Mental Disease Publishing

Company

P 112:

Infantile paralysis is of an infectious, but not of a contagious nature. As a matter of fact, no indisputable instance of contagion could be proved.

107

Nombre del artículo:

Is Acute Poliomyelitis Unusually Prevalent This Season?

Autor principal/año: Revista:

James J. Putnam, 1893 Boston Medical and Surgical Journal

P 2:

To what is the unfavorable influence of the summer due? It may be an affair of weather, as such, though obviously heat, pure and simple, is not the important factor; or the weather may act as favoring some other influence, perhaps bacterial in character. The reasonableness of this latter view is now conceded by many good observers; but it is certain that its advocates are still far from having made good their claim.

108

Nombre del artículo:

Is Acute Poliomyelitis Unusually Prevalent This Season?

Autor principal/año: Revista:

James J. Putnam, 1893 Boston Medical and Surgical Journal

It is noteworthy, as against any strongly marked epidemic influence that the patients did not come to any extent, from any one locality, but from different parts of the large area of the suburbs of Boston.

109

Nombre del artículo:

NOTES OF AN EPIDEMIC OF ACUTE ANTERIOR

POLIOMYELITIS

https://jamanetwork.com/journals/jama/article-abstract/458738

Autor principal/año: Revista: Charles S. Caverly, 1896 **JAMA**

P 3:

There was a general absence of infectious disease as an etiologic factor in this epidemic. The element of contagion does not enter into the etiology either. I find but a single instance in which more than one member of a family had the disease, and as it usually occurred in families of more than one child, and as no efforts were made at isolation, it is very certain that it was non-contagious.

110

Nombre del artículo:

Notes Of An Epidemic Of Acute Anterior Poliomyelitis https://jamanetwork.com/journals/jama/article-abstract/458738

Autor principal/año: Revista: Charles S. Caverly, 1896 **JAMA**

P 5:

That a disease occasionally prevails epidemically suggests a specific poison, a definite toxin, and this phase of the etiology of poliomyelitis has recently received attention from foreign observers as well as from Dana, Putnam and others in this country. Thus far, however, there does not seem to have been any substantial progress made toward isolating any specific microorganism peculiar to this disease.

111

Nombre del artículo:

An Epidemic Of Infantile Paralysis In Western Massachusetts In 1908 https://archive.org/details/bostonmedicalsur1611mass

Autor principal/año: Revista:

Herbert C. Emerson, 1909 Boston Medical and Surgical Journal

With regards to the contagiousness of the disease, the investigation of this group of cases

suggests that the disease is but mildly contagious to say the most. A large number of children were in intimate contact with those that were sick, and of these children an insignificant minority developed the disease... the circumstances were particularly favorable to the investigation of points of contact between sick and well and of the detection of contagion.

112

Nombre del artículo:

The Occurrence Of Infantile Paralysis In Massachusetts In 1907 https://archive.org/details/b22431779

Autor principal/año: Revista

Robert W. Lovett, 1908 Boston Medical and Surgical Journal

P 4:

Following up still further the evidence of contagion: Other cases in the family were reported in 11 instances; other cases in the same house in 9 instances; other cases among acquaintances in 20 instances. That is, in 40 cases (17%), there was reason to look into the question of contagion.

113

Nombre del artículo:

An Epidemic Of Infantile Paralysis In Western Massachusetts In 1908 https://archive.org/details/bostonmedicalsur1611mass

Autor principal/año: Revista:

Herbert C. Emerson, 1909 Boston Medical and Surgical Journal

P 118:

Although the cause of the disease is not known, it can undoubtedly be classed as infectious, as its distribution and incidence in localities are similar to those of other infectious diseases and strongly suggest a common cause.

Nombre del artículo:

The Occurrence Of Infantile Paralysis In Massachusetts In 1907 https://archive.org/details/b22431779

Autor principal/año: Revista:

Robert W. Lovett, 1908 Boston Medical and Surgical Journal

P 2:

That anterior poliomyelitis is an infectious disease is the commonly received opinion. Since it has been seen that this cannot be regarded as established by bacterial evidence so far collected, the other evidence in favor of this view will next be investigated....

114

Nombre del artículo:

The Occurrence Of Infantile Paralysis In Massachusetts In 1907 https://archive.org/details/b22431779

Autor principal/año: Revista:

Robert W. Lovett, 1908 Boston Medical and Surgical Journal

P 4:

This evidence tends rather toward supporting the contagious character of the disease, as established by its uneven distribution, extending from foci and not evenly scattered through the state; by its extension from Pittsfield along the lines of most frequent travel, and by the fact that there was rarely a case in one town without the occurrence of a case in the adjacent town or towns.

The Epidemiology Of Acute Poliomyelitis

Autor principal/año: Revista:

L. Emmet Holt, 1908 American Journal of Medical Sciences

P 652:

In all we have collected a total of 40 instances, comprising 96 cases, in which more than I case occurred in a family or household.

116 Nombre del artículo:

The Epidemiology Of Acute Poliomyelitis

Autor principal/año:

L. Emmet Holt, 1908 American Journal of Medical Sciences

P 662:

The occurrence of epidemics and the relation of certain groups of cases to one another in these epidemics place beyond question the statement that acute poliomyelitis is an infectious disease.

117

Nombre del artículo:

The Epidemiology Of Acute Poliomyelitis

Autor principal/año: Revista:

L. Emmet Holt, 1908 American Journal of Medical Sciences

Whether we can go farther and state that the disease is communicable is an open question. After carefully considering all the evidence brought together in this paper, we cannot resist the conclusion that the disease is communicable, although only to a very slight degree.

118 Cases from the medical literature of paralysis as a result of spoiled or poisoned food -

PMID:

Nombre del artículo:

Poisoning as The Cause of Poliomyelitis

14771968

Autor principal/año:

Revista:

Ralph R. Scobey, 1950 Archives of Pediatrics

P 7-17.

119

Nombre del artículo:

An Account Of The Epidemic Outbreak Of Arsenical Poisoning

Autor principal/año: Revista: Ernest Septimus Reynolds, 1901 **BMJ**

120

Nombre del artículo:

Death in the beer-glass: the Manchester arsenic-in-beer epidemic of 1900-1 and the long-term poisoning of beer

http://www.breweryhistory.com/journal/archive/132/Death in a beerglass.pdf

Autor principal/año: Revista:

Matthew Copping, 2009 Journal of the Brewery History Society

121-140

121	Nombre del artículo: Jamaica Ginger Paralysis Forty-seven-Year Follow-up		PMID: 666613
	Autor principal/año: John P. Morgan, 1978	Revista: Archives of	Neurology
	Nombre del artículo: The Jamaica ginger paralysis		PMID: 6750161
	Autor principal/año: John P. Morgan, 1982	Revista: JAMA	

122	Título del libro: Paralyzed with Fear https://www.amazon.com/Paralyse	ed-Fear-Story-Gareth-Williams/dp/1137299754
	Autor principal/año: Gareth Williams, 2013	Publicador : Palgrave Macmillan
	P 13.	

123	Título del libro: Acute Poliomyelitis (Heine-Medin's Disease)	
	Autor principal/año: Ivar Wickman, 1913	Publicador: The Journal of Nervous and Mental Disease Publishing Company
	Chapter 8.	

124	Título del libro: Acute Poliomyelitis (Heine-Medin's Disease)	
	Autor principal/año: Ivar Wickman, 1913	Publicador: The Journal of Nervous and Mental Disease Publishing Company
	P 123.	

125	Título del libro: Acute Poliomyelitis (Heine-Medin's Disease)	
	Autor principal/año: Ivar Wickman, 1913	Publicador: The Journal of Nervous and Mental Disease Publishing Company
	,	y for direct contact of patient with patient to occur. Indeed, the

disease seems more often to be propagated through the mediation of the healthy. As in many other epidemic maladies, spread occurs in Heine-Medin's disease by transmission from person to person.

126	Título del libro: Acute Poliomyelitis (Heine-Medir	n's Disease)
	Autor principal/año: Ivar Wickman, 1913	Publicador :

	The Journal of Nervous and Mental Disease Publishing Company
P 116 and after.	

127 For example, here -Nombre de la página:

Polio Hall of Fame

Sitio web:

Wikipedia

https://en.wikipedia.org/wiki/Polio Hall of Fame

Archivo:

http://archive.is/nAps3

PMID:

2994307

Ivar Wickman - Discovered the epidemic character of polio (1907) and coined the term Heine-Medin disease.

Nombre del artículo:

The Poliomyelitis Story: A Scientific Hegira

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2589894/pdf/yjbm00092-

0018.pdf

Autor principal/año:

Revista:

Dorothy M. Horstmann, 1985 The Yale Journal Of Biology And Medicine

Wickman's meticulous investigations led him to conclude that the mild cases were as contagious as the paralytic ones and were responsible for wide dissemination of the agent. This was a tremendously important discovery made...

128 Título del libro:

Acute Poliomyelitis (Heine-Medin's Disease)

Autor principal/año:

Ivar Wickman, 1913 The Journal of Nervous and Mental Disease Publishing

Company

P 125-126:

Acute poliomyelitis must therefore, be included among the contagious diseases. The lateness of the recognition of this fact is due partly to the smallness of former epidemics and partly to two factors which nullified all earlier investigations of epidemic conditions; viz., first, abortive types were not considered, and, second, the possibility of infection through healthy virus carriers was not realized.

129 Título del libro:

Acute Poliomyelitis (Heine-Medin's Disease)

Autor principal/año: Publicador:

Ivar Wickman, 1913 The Journal of Nervous and Mental Disease Publishing

Company

P 126-127.

130 Título del libro:

Acute Poliomyelitis (Heine-Medin's Disease)

Autor principal/año:

Ivar Wickman, 1913 The Journal of Nervous and Mental Disease Publishing

Company

P 125:

The intimate association of the disease with the principal highways was clearly demonstrable. The relation to main roads and railways was especially striking in districts in which the cases were scattered, either singly or in small groups. A study of the local

conditions showed that dissemination must be due to the busy traffic which permitted more frequent communication between the people.

131

Título del libro:

Polio: from Emergence to Eradication

Autor principal/año: Matthew Smallman-Reynor, 2006 Publicador:

Oxford University Press

P 95:

The geographical distribution of poliomyelitis activity in the epidemic of 1905 is mapped in Figure 4.5... A striking feature of the epidemic pattern is the particular involvement of the southern counties of the country (map B), with the principal areas of poliomyelitis activity limited to six scattered, and geographically restricted, epidemic foci (map A)... As a rule, the infected localities were of a distinctly rural nature, with the epidemic demonstrating a marked aversion for the larger urban centers of Stockholm (ten cases). Goteborg (zero cases) and Malmo (zero cases).

132

Título del libro:

Introduction to Epidemiology (7th edition)

Autor principal/año: Publicador:

Ray M. Merrill, 2017 Jones and Bartlet Learning

P 475:

It is known that polio seems to occur in rural areas as much as, if not more than, in large cities, and Scandinavia was quite rural at the time. Less exposure to a disease led to the population's having less immunity to the disease. There seemed to be higher immunity in city dwellers and lower immunity in rural populations.

133

Nombre del artículo:

The Epidemiology Of Poliomyelitis With Reference To Its Mode Of Spread

Autor principal/año: Revista: W. Lloyd Aycock, 1926 JAMA

P 1-2

...with concentration of population and, as has been assumed, greater person to person contact, there is a widespread distribution of the virus, resulting not in greater incidence than in rural sections, as is true of the common contact diseases, but in a widespread immunization.

134

Nombre del artículo:

The Epidemiology Of Poliomyelitis With Reference To Its Mode Of Spread

Autor principal/año: Revista: W. Lloyd Aycock, 1926 JAMA

P 2

In view of the fact that there is no theoretical reason why persons in rural life should be more prone to exhibit the paralytic form of the disease, it would seem perhaps more reasonable to believe that the immunization in concentrated populations may be due to subinfective doses rather than to a mild attack of the disease.

The Epidemiology Of Poliomyelitis With Reference To Its Mode Of Spread

Autor principal/año: Revista: W. Lloyd Aycock, 1926 JAMA

P 1

The proportion of cases ascribed to direct contact, made up largely of multiple cases in families, has been stated at around 5 per cent. It has been observed that the onsets of multiple cases in families as a rule so nearly coincide that they probably represent in the majority of instances simultaneous infection. When allowance is made for this, the proportion of direct contact cases is reduced to an extremely small figure.

136 Nombre del artículo:

The Epidemiology Of Poliomyelitis With Reference To Its Mode Of Spread

Autor principal/año: Revista: W. Lloyd Aycock, 1926 JAMA

P 4-5.

137 Nombre del artículo:

Poliomyelitis Problems

PMID: 14796117

Autor principal/año: Revista:

Archibald L. Hoyne, 1951 | Medical clinics of North America

P 13:

There is little to indicate that isolation has been a controlling influence in the spread of the disease during epidemics... Since the virus may be found in the intestinal tract for thirty-five days or possibly longer after onset of the disease it would seem logical to disinfect all body discharges before their disposal. However, in the Cook County Contagious Disease Hospital where the latter procedure has not been used there has never been a doctor, intern, nurse or any other member of the personnel who contracted poliomyelitis within a period of at least thirty-five years, nor has any patient ever developed poliomyelitis after admission to the hospital.

138 | Título del libro:

Acute Poliomyelitis (Heine-Medin's Disease)

Autor principal/año:
Ivar Wickman, 1913
Publicador:
The Journal of Nervous and Mental Disease Publishing
Company

P 121:

This center contained 18 cases; ten of these were abortive and presented pronounced general symptoms... Only for six children, occupying four houses, could no contact with the other 52 who attended school be traced.

139 | Título del libro:

Acute Poliomyelitis (Heine-Medin's Disease)

Autor principal/año:
Ivar Wickman, 1913
Publicador:
The Journal of Nervous and Mental Disease Publishing
Company

P 120:

It was impossible to find, how the disease penetrated the island.

140	Título del libro: Acute Poliomyelitis (Heine-Medin's Disease)	
	Autor principal/año: Ivar Wickman, 1913	Publicador: The Journal of Nervous and Mental Disease Publishing Company
	P 129-130.	

141-160

141 Título del libro:

Infantile Paralysis In Vermont

https://archive.org/details/infantileparalys00cave

Autor principal/año: Publicador: Charles S. Caverly, 1925 Burlington, Vermont State Department Of Public Health

Referring to the polio epidemic in Vermont in 1912, p 88:

This once more emphasizes the rather slight contagiousness of the disease

Referring to the polio epidemic in Vermont in 1916-17, p 150:

While, therefore, contact infection seems to be increasingly traceable, it must still be considered a disease of rather low contagiousness.

And p. 167:

These figures corroborate the statement made before that while the disease is a communicable disease, it is one of low contagiousness.

And this, even though he is well aware of Wickman's theory, p. 158:

Infantile Paralysis is generally recognized as a contagious disease and one that may be spread innocently by persons who have no clinical symptoms, in other words, by "abortive cases" or "healthy carriers."

142

Nombre del artículo:

The Epidemiology Of Poliomyelitis With Reference To Its Mode Of Spread

Autor principal/año: Revista: W. Lloyd Aycock, 1926 **JAMA**

...transmission in such instances is not usually through direct contact between the individuals, nor through the intervention of missed cases or healthy carriers, but through some indirect means. This is illustrated by a recent outbreak, the epidemiologic evidence of which pointed to milk as the means of transmission.

143 Título del libro:

Acute Poliomyelitis (Heine-Medin's Disease)

Autor principal/año: Publicador: Ivar Wickman, 1913 The Journal of Nervous and Mental Disease Publishing Company

P 126:

All the patients were supplied with milk by the farmer. The houses were separated from one another by one to two kilometers; and in five cases the illness began on the same day. Under these circumstances it seems to me extremely probable that the milk conveyed the infection.

144	Nombre del artículo: Milestones in Early Poliomyelitis Research (1840 to 1949)		PMID: 10233910
	Autor principal/año: Hans J. Eggers, 1999	Revista: Journal Of Virology	
	P 1		

145 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 573:

Fortunately, in 1908 Karl Landsteiner and Eric Popper isolated the virus of poliomyelitis, and scientific study of the agent began.

146 Nombre del artículo: PMID: Milestones in Early Poliomyelitis Research (1840 to 1949) 10233910 Autor principal/año: Revista: Hans J. Eggers, 1999 Journal Of Virology P 1

147 For example -Nombre del artículo: The Transmission Of Acute Poliomyelitis To Monkeys Revista: Autor principal/año: Simon Flexner, 1909 **JAMA**

148 Título del libro: Polio: An American Story Autor principal/año: Publicador: David M. Oshinsky, 2006 Oxford University Press P 17: In the long run, monkeys would prove invaluable to the polio story. More than 100,000 would be sacrificed in the fifty-year quest for a vaccine.

149	For example, here - Nombre de la página: Polio Hall of Fame	
	Sitio web: Wikipedia https://en.wikipedia.org/wiki/Polio Hall of Fame	Archivo: http://archive.is/nAps3

150	Nombre del artículo: The Occurrence Of Infantile Paralysis In Massachusetts In 1907 https://archive.org/details/b22431779	
	Autor principal/año: Robert W. Lovett, 1908	Revista: Boston Medical and Surgical Journal
	P 3.	

151 | Por ejemplo -

Nombre del artículo:

Epidemic Poliomyelitis In Monkeys

Autor principal/año: Revista: Simon Flexner, 1910 JAMA

P 2

Brief mention should be made of other species of animals that have been employed for inoculation. Besides many rabbits and guinea-pigs, 1 horse, 2 calves, 3 goats, 3 pigs, 3 sheep, 6 rats, 6 mice, 6 dogs and 4 cats have had active virus introduced into the brain, but without causing any appreciable effect whatever. These animals have been under observation many weeks.

152 | Por ejemplo -

Nombre del artículo:

Does the Spinal Fluid from Human Poliomyelitis Contain the Specific Infective Agent?

Autor principal/año: Revista: HL Abramson, 1917 JAMA

153 Nombre de la página:

Polio - Diagnostic Methods

Sitio web: Archivo:

CDC website

https://www.cdc.gov/polio/us/lab-testing/diagnostic.html

http://archive.is/hDbJu

Virus isolation in culture is the most sensitive method to diagnose poliovirus infection. Poliovirus is most likely to be isolated from stool specimens. It may also be isolated from pharyngeal swabs. Isolation is less likely from blood or CSF.

154 Nombre del artículo:

Poliomyelitis

Autor principal/año: Revista:
John A. Toomey, 1941 Journal of Pediatrics

P 1

There has been a vast amount of research in poliomyelitis Most of the experiments have been done on M. rhesus monkeys, animals not susceptible to this disease.

155 Título del libro:

Preventive Medicine and Hygiene

 $\underline{https://drive.google.com/open?id=1ONdl0AG5blbj8mJM0vMupllqgVoL0T4D}$

Autor principal/año: Publicador:

Milton J. Rosenau, 1918 D Appleton and Company

P 341:

Monkeys have so far never been known to contract the disease spontaneously, even though they are kept in intimate association with infected monkeys.

medium of flowing sewage.

Nombre del artículo: Poliomyelitis Autor principal/año: John A. Toomey, 1941 P 5: The natural disease never acts like an upper respiratory infection in the experimental

animal for no animal gets the disease from another, no matter how intimately exposed.

Nombre del artículo: Poliomyelitic Virus In Urban Sewage https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2135110/pdf/765.pdf Autor principal/año: John R. Paul, 1940 Revista: Journal of Experimental Medicine P 13: In two out of three large urban epidemics of poliomyelitis the virus of this disease has been detected in samples of sewage. From one of the sites it was found repeatedly. Both positive sites were located in the vicinity of isolation hospitals, and we believe that the

Nombre del artículo:
Sewage as a carrier and disseminator of Poliomyelitis Virus

Autor principal/año:
C. Kling, 1942

Revista:
Acta Medica Scandinavica

findings indicate that this virus can be transported, for short distances at least, through the

159	Nombre del artículo: Sewage as a carrier and disseminator of Poliomyelitis Virus	
	Autor principal/año: C. Kling, 1942	Revista: Acta Medica Scandinavica
	P 15.	

160	Nombre del artículo: Sewage as a carrier and disseminator of Poliomyelitis Virus	
	Autor principal/año: C. Kling, 1942	Revista: Acta Medica Scandinavica
	P 5: From these experiments it is apparent that we have succeeded in isolating the virus of poliomyelitis in a sample of sewage collected in Stockholm in the course of a minor epidemic of infantile paralysis.	

161-180

	161	Nombre del artículo: Sewage as a carrier and disseminator of Poliomyelitis Virus	
		Autor principal/año: C. Kling, 1942	Revista: Acta Medica Scandinavica

P 32:

...we know also the vehicle where the infectious agent, while the epidemic is going on and for some time after its end, dwells, i. e. the sewage.

162 Nombre del artículo:

Poliomyelitic Virus In Human Stools

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2135104/pdf/751.pdf

PMID: 19870996

Autor principal/año:

Revista:

James D. Trask, 1940 Journal of Experimental Medicine

163 Nombre del artículo:

Persistence Of Virus Excretion In The Stools Of Poliomyelitis Patients

Autor principal/año: Revista: Dorothy M. Horstmann, 1944 **JAMA**

164 Nombre del artículo:

Flies As Carriers Of Poliomyelitis Virus In Urban Epidemics

PMID: 17773978

Revista:

Autor principal/año: Albert A. Sabin, 1941 Science

165 Nombre del artículo:

Insects And Epidemiology Of Poliomyelitis

Autor principal/año: Revista: Albert A. Sabin, 1942 Science

The distinctly positive results which we obtained with collections of insects consisting only of flies, leaves no doubt that they are carriers of the virus.

166 Nombre del artículo:

Insects And Epidemiology Of Poliomyelitis

Autor principal/año: Revista: Albert A. Sabin, 1942 Science

It should be noted that we were unable to obtain positive results with Rhesus monkeys, and because Cynomolgi are needed, these studies will probably have to be postponed until importation from Java is again possible.

167 Nombre del artículo:

The Detection Of Poliomyelitis Virus In Flies Collected During

PMID: 19871302

Epidemics Of Poliomyelitis

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2135360/pdf/531.pdf

Autor principal/año: Revista:

James D. Trask, 1943 Journal of Experimental Medicine

168 Nombre del artículo:

Poliomyelitis Virus In Fly-Contaminated Food Collected At An

PMID:

Epidemic

Autor principal/año: Revista: Robert Ward, 1945 Science

17735530

Nombre del artículo: Poliomyelitis Virus In Fly-Contaminated Food Collected At An Epidemic Autor principal/año: Robert Ward, 1945 PAI: Poliomyelitis virus has been detected in food exposed to flies at homes of poliomyelitis patients within an epidemic area.

Nombre del artículo: Poliomyelitis

Autor principal/año: Revista:
John A. Toomey, 1941 Journal of Pediatrics

P 25:

Most of the experiments described during this period have been made in animals given the disease by injecting virus intranasally, intratheeally, intrasciatically, or by some other artificial avenue of approach. If the virus enters the human being by way of the gastrointestinal tract, practically all except the broader conclusions, especially those that have to do with pathogenesis and the explanation of symptoms, have to be discarded in toto.

171 Nombre del artículo: PMID: Poisoning as The Cause of Poliomyelitis 14771968

Autor principal/año: Revista: Ralph R. Scobey, 1950 Revisto: Archives of Pediatrics

Part II P 5:

The views as to the portal of entry and communicability rest fundamentally and entirely on findings from experiments on monkeys. To some of us it does not appear to square with the facts obtained by epidemiological studies of the disease among human beings. It seems to elastic, too restful. On epidemiological grounds alone, it appears conceivable that poliomyelitis is not caused by a living microorganism or a virus, but by a toxin.

172 Nombre del artículo:

A Study Of The Origin Of An Epidemic Of Poliomyelitis

Autor principal/año: Revista: Martha L. Smith, 1945 JAMA

P 6:

Yet, in spite of the comparative ease with which poliomyelitis may be experimentally transferred to monkeys from these reservoirs, it has not been established that the virus in such form gives rise to the human disease. The possibility undoubtedly exists, but direct proof is still lacking.

173	Nombre del artículo: The Polioviruses Of Man	
	Autor principal/año: Stanley A. Plotkin, 1962	Revista: Annals of New York Academy of Sciences
	P 13, Tabla 10.	
	Nombre de la página: Pink Book - Polio	

Sitio web:

CDC

https://www.cdc.gov/vaccines/pubs/pinkbook/polio.html

Archivo:

http://archive.is/yvRRU

Humans are the only known reservoir of poliovirus, which is transmitted most frequently by persons with inapparent infections.

174 Nombre del artículo:

Notes Of An Epidemic Of Acute Anterior Poliomyelitis

https://jamanetwork.com/journals/jama/article-abstract/458738

Autor principal/año: Revista: Charles S. Caverly, 1896 JAMA

P 4:

During this epidemic and in the same geographical area, an acute nervous disease, paralytic in its nature, affected domestic animals. Horses, dogs and fowls died with these symptoms.

175

Nombre del artículo:

Notes Of An Epidemic Of Acute Anterior Poliomyelitis https://jamanetwork.com/journals/jama/article-abstract/458738

Autor principal/año: Revista: Charles S. Caverly, 1896 JAMA

P 4:

...says that the examination of a section of the lumbar portion of, the cord showed a granular degeneration and pigmentation of the ganglion cells of the anterior cornua, and atrophy of the anterior nerve roots." He further states that there was no meningitis in this case. Dr. Charles L. Dana, who made the examination of the fowl, with the aid of Dr. Dunham, of the Carnegie Laboratory, found "an acute poliomyelitis of the lumbar portion of the cord and no meningitis."

176 Nombre del artículo:

Notes Of An Epidemic Of Acute Anterior Poliomyelitis

https://jamanetwork.com/journals/jama/article-abstract/458738

Autor principal/año: Revista: Charles S. Caverly, 1896 JAMA

P 5

That domestic animals suffered with human beings in our epidemic is a noteworthy fact and one, so far as I can learn, hitherto unobserved. That such was the case can not be doubted.

177

Título del libro:

Infantile Paralysis In Vermont

https://archive.org/details/infantileparalys00cave

Autor principal/año: Publicador: Charles S. Caverly, 1925 Burlington, Vermont

State Department Of Public Health

P 51-53.

178

Título del libro:

Infantile Paralysis In Vermont

https://archive.org/details/infantileparalys00cave

Autor principal/año: Charles S. Caverly, 1925	Publicador: Burlington, Vermont State Department Of Public Health
P 110.	

179 Título del libro:

Infantile Paralysis In Vermont

https://archive.org/details/infantileparalys00cave

Autor principal/año: Publicador:

Charles S. Caverly, 1925 Burlington, Vermont

State Department Of Public Health

P 110:

Instances of paralysis among domestic animals have always been noted as accompanying our outbreaks of human infantile paralysis.

180 Nombre del artículo:

The Occurrence Of Infantile Paralysis In Massachusetts In 1908

Autor principal/año: Revista:

Robert W. Lovett, 1909 Boston Medical and Surgical Journal

P 1:

The attention of the State Board of Massachusetts has been called to the occurrence of infantile paralysis in a mother and daughter shortly after an epidemic of "leg weakness" in the chickens of the household, and the matter is under investigation.

181-200

181 Nombre del artículo:

The Occurrence Of Infantile Paralysis

In Massachusetts In 1910

Autor principal/año: Revista:

Robert W. Lovett, 1911 Boston Medical and Surgical Journal

Total, 34 homes out of 110 had illness, paralysis or death in 82 animals near the time of the human paralysis.

182 Título del libro:

A Manual On Infantile Paralysis With Modern Methods Of Treatment

Autor principal/año: Publicador:

Henry W. Frauenthal, 1914 FA Davis Company

P 8.

Título del libro:

A Manual On Infantile Paralysis With Modern Methods Of Treatment

Autor principal/año: Publicador:

Henry W. Frauenthal, 1914 FA Davis Company

P 10:

During the epidemic of 1000 cases in Minnesota in 1909 three colts were seen by Dr. H. W. Hill, epidemiologist of the Minnesota State Board of Health, ill with a disease "strongly analogous in clinical history and symptoms to the disease in the human."

184

Título del libro:

A Manual On Infantile Paralysis With Modern Methods Of Treatment

Autor principal/año: Publicador: Henry W. Frauenthal , 1914 FA Davis Company

P 10

In my veterinary practice of the past five or six years I have found a disease appearing among one- or two- year-old colts that shows a line of symptoms corresponding closely to anterior poliomyelitis in children. I have had from 5 to 10 cases a year during this time, always occurring during the summer months, and the majority of them during the month of August. The affected colts are usually found in the pasture unable to stand.

185

Título del libro:

A Manual On Infantile Paralysis With Modern Methods Of Treatment

Autor principal/año: Publicador: Henry W. Frauenthal , 1914 FA Davis Company

P 11:

The State of California had an epidemic of 100 known cases of poliomyelitis in 1910. The majority of these cases occurred in San Joaquin County, and according to the September, 1910, Bulletin of the California State Board of Health, "veterinarians report a considerable number of puzzling paralyses of colts in San Joaquin County, where the largest number of cases have occurred so far."

186

Título del libro:

A Manual On Infantile Paralysis With Modern Methods Of Treatment

Autor principal/año: Publicador: Henry W. Frauenthal , 1914 FA Davis Company

P 12-13:

Dr. A. R. Robertson, pathologist at Drake University Medical School, reported: "Examination of fowl paralyzed after three days' acute illness (one wing, both legs). Upon exposure of the spinal cord, a distinct area of softened cord, one inch in length, of the lower dorsal and upper lumbar regions was observed. Histological sections from the affected areas revealed numerous small hemorrhages in the anterior cornua and distinct collections of cells in perivascular and perilymph channels, and tissue spaces of the anterior horns. The histological picture was that of acute poliomyelitis in man."

187

Nombre del artículo:

The Occurrence Of Infantile Paralysis In Massachusetts In 1908

Autor principal/año: Revista: Robert W. Lovett, 1909 Boston Medical and Surgical Journal

P 1

It was noted by Wickman that in the Swedish epidemic of 1903 dogs were apparently affected in many instances with the children, but he was not convinced of the identity of the two affections.

Título del libro: Acute Poliomyelitis (Heine-Medin's Disease)

Autor principal/año: Publicador:

Ivar Wickman, 1913 The Journal of Nervous and Mental Disease Publishing

Company

P 132:

Caverley, Wickman. Peiper, and others have mentioned the appearance of paralysis in animals and in fowl coincident with epidemics among human beings. But the futile inoculation of these creatures shows their affliction has nothing in common with that in man.

189

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

190

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 48.

The farmer would be laughed at who undertook to manure his fields or his trees with a salt of lead or arsenic.

191

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 69 (citation from 1913):

...a prominent federal entomologist could admit... that "there exists, in this country, no regulation in force and no precaution is taken toward preventing accidents resulting from the use of arsenicals".

192

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 72-78.

193

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 **Princeton University Press**

The head of the Agriculture Department's Bureau of Entemology, C. V. Riley himself, was called upon to assure readers "how utterly groundless are any fears of injury" from sprayed produce.

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 84:

The Royal Commission Appointed to Inquire into Arsenical Poisoning from the Consumption of Beer and other Articles of Food and Drink was chaired by the most venerable figure in British science, the physicist Baron Kalvin, and staffed by several of the most prominent medical specialists in the nation.

195

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 86:

"Pending the establishment of official standards in respect of arsenic under the Sale of Food and Drugs Acts," the commissioners decided, the evidence we have received fully justifies us in pronouncing certain quantities of arsenic in beer and in other foods as liable to be deleterious, and at the same time capable of exclusion, with comparative ease, by the careful manufacturer. In our view it would be entirely proper that penalties should be imposed under the Sale of Food and Drugs Acts upon any vendor of beer or any other liquid food, if that liquid is shown by an adequate test to contain 1/100th of a grain or more of arsenic in the gallon; and with regard to solid food-no matter whether it is habitually consumed in large or in small quantities, or whether it is taken by itself ... or mixed with water or other substances . . .-if the substance is shown by an adequate test to contain 1/100th grain of arsenic or more in the pound."

196

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 86

The Commission's recommendation, furthermore, was informally adapted by the British government and the limit of 0.01 grain per pound or gallon soon came to be referred to as the "world tolerance" for arsenic as other nations recognized the importance and validity of the Royal Commission's work.

197

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 266, note 49:

In Germany, too, there was opposition to the use of arsenicals. The chemist von der Heide found in 1906 that grapes from German vines sprayed with lead arsenate contained as much as 0.2 mg. of arsenic per 100 g. (about 0.014 grain of arsenic per pound, or 40 percent above the "world tolerance."). This discovery prompted the German Imperial Health Commission to oppose the use of lead arsenate and, in fact, the compound was eventually prohibited (temporarily) from agricultural application in Germany. Other arsenical insecticides were apparently permitted, but only under close supervision, as was generally the case in other European countries.

198	Título del libro: Before Silent Spring: Pesticides and Public Health in Pre-DDT America	
	Autor principal/año: James Whorton, 1974	Publicador: Princeton University Press
	P 88-90.	

199 | Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 9N

Despite the failure to effectively control the use of arsenicals insecticides, French physicians recognized their situation as superior to that of America, where no attempt at control had yet been made.

200

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 85

...the scale of use of arsenical insecticides in Great Britain was never comparable to that of America, though it was sufficiently great to attract the Royal Commission's attention.

201-220

201	Nombre del documento: Green Book - Poliomyelitis https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/148141/Gren-Book-Chapter-26-Polio-updated-18-January-2013.pdf	
NHS, 2013		Archivo: https://drive.google.com/open?id=15wYdgB3upwPEHYP7XZkU VxQEAOXe1Lnb
	P 2, chart 26.1	

202 | Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 71:

Riley's sentiments had originally been expressed in an 1891 address to Boston's Lowell Institute and were at least questionable then. In later years, however, their frequent repetition would become dangerously misleading, for shortly after Riley's speech the average residues of arsenic on fruit and vegetables began to steadily increase. This increase was due, in part, to the growing numbers of farmers using arsenical insecticides.

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 **Princeton University Press**

P 69:

More than two decades later, a prominent federal entomologist could admit... to a foreign inquirer that, "there exist, in this country, no regulation in force and no precaution is taken toward preventing accidents resulting from the use of arsenicals."

204

Título del libro:

DDT – Scientists, Citizens and Public Policy

https://www.amazon.com/DDT-Scientists-Citizens-Princeton-Library/dp/0691613907

Autor principal/año: Publicador:

Thomas Dunlap, 1981 Princeton Legacy Library

P 42:

When insecticide residues became a problem in the 1920s, one agency of the department, the Bureau of Plant Industry, was recommending spraying schedules to kill insect pests; another agency, the Bureau of Chemistry (replaced by the Food and Drug Administration in 1927), was seizing produce, sometimes sprayed in strict accordance with the schedules, on the grounds that it was contaminated with poisonous chemicals. The Secretary of Agriculture had to satisfy the requirements and needs of public health without alienating the main political support of the department, the farmers.

205

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

Chapters 4-5.

206

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

The FDA significantly remained within the Department of Agriculture until 1940, however, so that activities such as spray-residue control continued to be hindered by the general Department emphasis on promoting agricultural prosperity.

207

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 126:

In less diffuse terms, what the Bureau of Chemistry committed itself to at the 1919 conference was a policy of educating fruit growers to the existence of a residue problem... while avoiding any publicizing of the problem outside of agricultural circles.

208	Título del libro: Before Silent Spring: Pesticides and Public Health in Pre-DDT America	
	Autor principal/año: James Whorton, 1974	Publicador: Princeton University Press
	P 133-136	

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 226:

In Czecho-Slovakia and Austria, newspaper articles and radio talks are telling the public that American apples are poisonous, and Poland has actually prohibited the entry of American apples.

210

Título del libro:

DDT – Scientists, Citizens and Public Policy

https://www.amazon.com/DDT-Scientists-Citizens-Princeton-Library/dp/0691613907

Autor principal/año: Publicador:

Thomas Dunlap, 1981 Princeton Legacy Library

P 48:

Paul Dunbar, then assistant commissioner of the FDA, admitted this in an article written in 1959. Our "objective," he said, "was to persuade all departmental agencies to cooperate in working out the [spray residue] problem and to refrain meanwhile from creating public alarm."

211

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 201:

Introducing this educational campaign, the FDA broke with its tradition of sheltering the residue problem in secrecy. Indeed, thanks to the activity of muckrakers, the secret was already out, and the "steady diet of arsenic and lead"... was soon being publicized, if more quietly, by the FDA as well.

212

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 158:

...Harvard toxicologist Joseph Aub... stressed the insidiousness of lead poisoning. "The more severe types of intoxication by lead are very easy to recognize," he noted, "but the mild manifestations are so protean in character and develop so irregularly that differentiation between absorption and true intoxication is often nearly impossible."

213

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

Dr. Frederick Tony, a physician in the Chicago Department of Public Health, testified in 1927 -

P 147

Q. Doctor, would it be possible for people to be poisoned by arsenate of lead on apples and pears and the doctor not know from where the poison obtained?

A. I think it is not only possible, but it would be very probable that the doctor would not realize the source of such a poison".

214 | Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 177:

Distribution of lead and arsenic was so complete that all members of industrialized populations carried at least traces of the metals in their tissues, and there was some serious scientific consideration being given the notion that these were normal physiological constituents.

215

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 246-247:

The FDA's original plan had been to continue under the old system of administrative tolerances until the final report of the Public Health Service could be published, after which a hearing would be announced." But, as Paul Dunbar, Campbell's successor as Commissioner of Food and Drugs, later related: "the war intervened and made it impossible for us to hold the necessary hearings to establish tolerances... The hearings were finally held in 1950, but offered, so far as lead arsenate was concerned, only a rehash of evidence that had been familiar to the FDA for years.

216

Título del libro:

Before Silent Spring: Pesticides and Public Health in Pre-DDT America

Autor principal/año: Publicador:

James Whorton, 1974 Princeton University Press

P 249:

Food and Drug Commissioner Paul Dunbar explained... "In general, arsenic and fluorine sprays have been replaced by DDT and other newer chemicals."

217

Nombre del artículo:

The Occurrence Of Infantile Paralysis In Massachusetts In 1907 https://archive.org/details/b22431779

Autor principal/año: Revista:

Robert W. Lovett, 1908 Boston Medical and Surgical Journal

P 6:

The disease is well recognized as one that attacks children in the first dentition and as one that prevails in the late summer and early fall.

218 Nombre del artículo:

Transmission Of Poliomyelitis Virus

PMID: 14889394

Autor principal/año:

Revista:

Albert B. Sabin, 1951 Journal of Pediatrics

P 8:

One of the important unsolved problems in poliomyelitis is why in temperate zones approximately 80 to 90 per cent of the cases occur during four months of the year in late summer and early autumn.

219

Nombre del artículo:

Present Concepts And Recent Advances In Acute Poliomyelitis

Autor principal/año: Revista:

John R. Paul, 1952 AMA Archive of Internal Medicine

P 8:

Thus, although it is agreed that poliomyelitis is a disease generally spread by personal contact, the situation is more complex than that, for in most parts of the world the prevalence of poliomyelitis is influenced or even dominated in a mysterious manner by season and climate. No satisfactory reason has as yet been proposed to explain the occurrence of epidemics of poliomyelitis in the temperate zones of the world at so much higher a rate in the summer than in the winter.

220

Nombre del artículo:

PMID:

The epidemiology of poliomyelitis: enigmas surrounding its appearance, epidemicity, and disappearance

<u>400274</u>

Autor principal/año: Revista:

Neal Nathanson, 1979 American Journal of Epidemiology

P 10:

Thus, looking at data for the whole country, the rates for the peak months (August and September) are over 35 times the rate for the low month (April). The regularity of this pattern over many years suggested that it was governed by a mechanism which should be ascertainable. Nevertheless, the underlying explanation has remained elusive.

221-240

221

Nombre del artículo:

PMID: 20978089

From Emergence to Eradication: The Epidemiology of Poliomyelitis Deconstructed

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2991634/pdf/kwq320.pdf

Autor principal/año: Revista:

Neal Nathanson, 2010 American Journal of Epidemiology

P 6

Although there is no definitive explanation for polio seasonality, there are some data worth pondering... However, until further studies are done, this hypothesis will remain speculative.

222 Nombre del artículo:

The Epidemiology Of Poliomyelitis

Problems at Home and Among the Armed Forces Abroad

PMID: 20242791

Autor principal/año: Albert B. Sabin, 1947

Revista: **JAMA**

P 4:

...it is remarkable that, unlike certain other infections of childhood, the epidemics of paralysis occur during the very months when the children are away from school.

223

Nombre del artículo:

PMID: 14796117

Poliomyelitis Problems

Revista:

Autor principal/año: Archibald L. Hoyne, 1951

Medical clinics of North America

P 2:

Considering that nearly all of the common acute infectious diseases predominate in the fall and winter or winter and spring, seasons when life is principally within doors and schools are in session, we are forced to ponder why poliomyelitis is epidemic in the summer.

224

Nombre del artículo:

PMID:

The epidemiology of poliomyelitis: enigmas surrounding its appearance, epidemicity, and disappearance

400274

Autor principal/año:

Revista:

Neal Nathanson, 1979

American Journal of Epidemiology

No good explanation was ever documented for the occurrence of epidemics, although this was one of the most feared features of poliomyelitis and of particular concern to health officers.

225

Nombre del artículo:

PMID:

Paralytic consequences of poliomyelitis infection in different parts of the world and in different population groups

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1525657/pdf/amjphnation

00428-0010.pdf

14885514

Autor principal/año:

Revista:

Albert B. Sabin, 1951

American Journal of Public Health

In New York City, for example, the attack rates during the five epidemic years have been 6 to 46 times higher than the mean annual rate for the 17 non-epidemic years between 1928 and 1947 (Table 4). The attack rate of 20.6 per 100,000 in the first London epidemic of 1947 was about ten times higher than the mean annual rate of 1.96 for the period of 1932 to 1946. The attack rate of 76.2 per 100,000 in the first Berlin epidemic of 1947 was 20 times higher than the mean annual rate for the period of 1928 to 1946.

226

Nombre del artículo:

PMID: 14885514

Paralytic consequences of poliomyelitis infection in different parts of the world and in different population groups

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1525657/pdf/amjphnation 00428-0010.pdf

Autor principal/año: Albert B. Sabin, 1951

Revista:

American Journal of Public Health

In 1928 Aycock pointed out that the accumulation of non-immunes cannot be a major

factor in the production of epidemics, because the age incidence was not found to vary materially from year to year, even during epidemics which occurred after a number of years of comparative freedom from the disease. Twenty years later, I showed that Aycock's observation was still valid, despite the fact that age selection patterns had changed over the years in certain communities.

PMID:

PMID:

400274

PMID: 14796117

PMID:

20978089

14885514

227

Nombre del artículo:

Paralytic consequences of poliomyelitis infection in different parts of the world and in different population groups

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1525657/pdf/amjphnation 00428-0010.pdf

Autor principal/año: Revista:

Albert B. Sabin, 1951 American Journal of Public Health

The conclusion seems inescapable that poliomyelitis epidemics are the result of the invasion of a community by strains of unusual virulence.

228

Nombre del artículo:

The epidemiology of poliomyelitis: enigmas surrounding its appearance, epidemicity, and disappearance

Autor principal/año: Revista:

Neal Nathanson, 1979 American Journal of Epidemiology

P 9-10:

However, no attempt was made to compare systematically a large number of isolates from epidemic and non-epidemic settings... The relative importance of virus virulence and of elevated infection rate in the production of epidemics therefore remains unknown.

229

Nombre del artículo: Poliomyelitis Problems

Revista:

Autor principal/año: Archibald L. Hoyne, 1951 Medical clinics of North America

One of the strangest features of this disease is that with the great advances in sanitation and higher scale of living poliomyelitis seems to thrive. In the meantime most of the other common contagious diseases have declined markedly, with the exception of measles.

230

Nombre del artículo:

From Emergence to Eradication: The Epidemiology of Poliomyelitis

Deconstructed

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2991634/pdf/kwq320.pdf

Autor principal/año: Revista:

Neal Nathanson, 2010 American Journal of Epidemiology

In the United States, beginning in the early 1900s, annual epidemics of poliomyelitis occurred with regularity until the introduction of IPV in 1955...

Nombre de la página:
The Effectiveness Of Immunizations

Sitio web:
HHS.GOV
https://archive.hhs.gov/nvpo/concepts/intro6.htm

Figure 6.

Nombre del documento:

Green Book - Poliomyelitis

 $\underline{https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/148141/Gre_en-Book-Chapter-26-Polio-updated-18-January-2013.pdf$

Autor/año: Archivo:

NHS, 2013 https://drive.google.com/open?id=15wYdgB3upwPEHYP7XZkU

VxQEAOXe1Lnb

P 2, chart 26.1

Nombre del artículo:

Epidemiology Of Poliomyelitis And Allied

Diseases--1963

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2604573/pdf/yjbm00599-0011.pdf

PMID: 14064722

Archivo:

https://drive.google.com/open?id=1fV_w0 3BSORQKex-hR7DkGZH44EXUwpTv

Autor principal/año: Revista:

Dorothy M. Horstmann, 1963 | Yale Journal of Biology and Medicine

P 2

...not until the 1940's in Japan, Czechoslovakia, the Union of South Africa, the Netherlands, Great Britain and Germany; and in France, Belgium, and most of the U.S.S.R. after 1950.

Nombre del artículo:

The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año: Revista:

Tiberio A. Swartz, 2008 | Israel Center for Disease Control (ICDC), Ministry of Health

P 40·

This period was the most critical in the Israeli experience, with the disease suddenly occurring in high numbers, and continuing in an uninterrupted series of epidemic events called at that time "the everlasting epidemic". This new pattern of the disease was similar to that observed in western countries...

235 On Geigy's ties to the Nazi regime -

Nombre de la página:

Chemical firms exploited Nazi links, probe found

Sitio web:

HHS.GOV

Archivo:

http://archive.is/xzpeP

http://www.swissinfo.ch/eng/chemical-firms-exploited-nazi-links--probe-found/2218350

JR Geigy, Ciba, Sandoz and Hoffmann-La Roche - put their own interests ahead of humanitarian concerns in their dealing with the Nazis.

... All the companies concerned owned factories in Germany between 1933 and 1945, as well as in wartime-occupied Poland, and were important suppliers of chemicals, dyes and pharmaceuticals for the Third Reich... The ICE found the firms also had extensive contacts

among the Nazis: "Geigy maintained particularly good relations Claus Ungewitter, the Reich commissioner for chemicals ...

The report also singled out Geigy and Roche for using forced labour at their plants in Germany.

It said at least 33 Dutch and French labourers were forced to work for Geigy between 1943 and 1945, while at least 61 prisoners-of-war and 150 foreign labourers were forced to work at the Roche plant...

It said the companies' claims that they were cut off from their subsidiaries in Germany were patently false: "senior managers at the parent company in Switzerland were aware that forced labour was being used... As a rule they were not worried or uneasy about the situation, and as long as production was maintained they had no thoughts of intervening.

236

Título del libro:

DDT - Scientists, Citizens and Public Policy

https://www.amazon.com/DDT-Scientists-Citizens-Princeton-Library/dp/0691613907

Autor principal/año: Publicador:

Thomas Dunlap, 1981 Princeton Legacy Library

P 76:

Earlier insecticides had been confined by their high cost and low efficiency, to farms and orchards. DDT's combination of high toxicity to many insects. low mammalian toxicity, low cost, and suitability

for aerial spraying invited its use in areas that had been, before World War II, free of insecticides.

237

Título del libro:

The Ethics of Intensification: Agricultural Development and Cultural Change https://books.google.co.il/books?id=0K8qkYZdx7cC&pg=PA66#v=onepage&q&f=false

Autor principal/año: Publicador: Julie Eckinger, 2008 Springer

P 66:

Safe to use in his context meant that the person exposed to DDT was unlikely to suffer acute illness. Later the criteria for "safety" underwent substantial change.

238

Nombre del documento:

Pharmacologic And Toxicologic Aspects Of DDT

Autor principal/año: Archivo

AMA Council On Pharmacy And https://drive.google.com/open?id=1nOgsZm np2lZuTWbEBB4jW1eiPccKlvfb

P 2:

[DDT] acts primarily on the nervous system of the insect... the facts that small amounts are required and that its action is prolonged increase its value.

239

Nombre del artículo:

Present Position of DDT in the Control of Insects of Medical Importance

Autor principal/año: Revista:

Fred C. Bishopp, 1946 American Journal of Public Health

P 6

The solvent or carrier evaporates, leaving the surfaces covered with minute crystals of DDT. Insects that crawl over these surfaces or otherwise come in contact with them during the next 3 to 12 months are killed.

240	Nombre del artículo: DDT and Silent Spring: Fifty Years After		
	Autor principal/año: Cristóbal S. Berry-Caban , 2011	Revista: Journal of Military and Veterans' Health	
	P 1-2.		

241-260

241

Nombre del artículo:

DDT Poisonins and the Elusive "Virus X:" A New Cause for Gastro-Enteritis

Revista: Autor principal/año: Morton S. Biskind, 1949 American Journal of Digestive Diseases

P 1:

Not only is it used in households with reckless abandon, so that sprays and aerosols are inhaled, the solutions are permitted to contaminate the skin, bedding and other textiles are saturated, and food and food utensils are contaminated, but DDT is also widely used in restaurants and food processing establishments and as an insecticide on crops. Cattle, sheep and other food animals are extensively dusted with it and large areas are indiscriminately sprayed from airplanes for mosquito control.

Pictures of DDT spraying:

https://www.gettyimages.com/photos/spray-ddt

242

Nombre de la página:

The DDT Collector

Sitio web:

Science History Institute

https://www.chemheritage.org/distillations/article/ddtcollector

Archivo:

https://web.archive.org/web/ 201809<u>26062552/https://ww</u> w.sciencehistory.org/distillat ions/article/ddt-collector

A sprayer-toting soldier stands guard on cans of Flit. Introduced by Standard Oil in 1923, the original Flit used mineral oil to exterminate flies and mosquitoes; DDT was added to the mix in the late 1940s.

243

Nombre del artículo:

The Amount of DDT Found In The Milk Of Cows Following Spraying

Autor principal/año: Revista:

D. E. Howell, 1947 Journal of Dairy Science

Four lots of cattle were sprayed with DDT to determine the amount of this material that may appear in the milk following recommended and excessive treatment. All animals tested excreted some DDT in the milk.

244

Nombre del artículo:

Public Health Aspects Of The New Insecticides

Autor principal/año: Revista:

Morton S. Biskind, 1953 American Journal of Digestive Diseases

Unfortunately, today contamination of food is virtually universal. Even if the farmer does not use the new insecticides (and few do not), it is a rare food that escapes contact with

insecticides in storage, shipment, processing plants, warehouses and stores. Dendy, for instance, bought milk and meat on the open market in Texas, from July through December. Every specimen of these staples was found to contain DDT, from less than 0.5 p. p. m. to 13.8 p. p. m. in milk and from 3.1 p. p. m. in lean meat to 68.5 p. p. m. in fat meat.

245 Nombre del artículo:

THE PERCUTANEOUS ABSORPTION OF DDT (2,2-BIS (P-CHLOROPHENYL 1, 1)

-1, TRICHLOROETHANE) IN LABORATORY ANIMALS

Autor principal/año: Revista:

John H. Drayze, 1944 Journal of Pharmacology and Experimental Therapeutics

P 8:

The above data indicate that the unlimited use of DDT solutions on the skin is not free of danger; however, some solutions of DDT have been found safe for restricted use.

246

Nombre del artículo:

Acute And Subacute Toxicity of DDT (2,2,-bis(p-CHLOROPHENYL-1, 1, 1-) TRICHLOROETHANE) TO LABORATORY ANIMALS

Autor principal/año: Revista:

Geoffrey Woodard, 1944 Journal of Pharmacology and Experimental Therapeutics

DDT is capable of causing subacute toxicity when given in small amounts in the diet for periods of from 3 days to 20 weeks.

247

Nombre del artículo:

Acute And Subacute Toxicity of DDT (2,2,-bis(p-CHLOROPHENYL-1, 1, 1-) TRICHLOROETHANE) TO LABORATORY ANIMALS

Autor principal/año: Revista:

Geoffrey Woodard, 1944 Journal of Pharmacology and Experimental Therapeutics

Characteristic of DDT poisoning is the wide variation in individual susceptibility, making the estimate of a safely tolerated dose extremely difficult.

248

Nombre del artículo:

DDT Poisonins and the Elusive "Virus X:" A New Cause for Gastro-Enteritis

Autor principal/año: Revista:

Morton S. Biskind, 1949 American Journal of Digestive Diseases

In 1944, Smith and Stohlman of the National Institute of Health, after an extensive study on the cumulative toxicity of DDT, pointed out, "The toxicity of DDT combined with its cumulative action and absorbability from the skin places a definite health hazard on its use."

249

Nombre del artículo:

A Case of D.D.T. Poisoning in Man

Autor principal/año: Revista: V. B. Wigglesworth, 1945 **BMJ**

250

Nombre del artículo:

DDT Poisoning In Man

Autor principal/año:	Revista:
I. M. Mackerras, 1946	The Medical Journal Of Australia
P 400.	

251 Nombre del artículo: D.D.T. Poisoning In Man A Suspected Case Autor principal/año: Revista: A. M. G. Campbell, 1949 Lancet

252 Nombre del artículo: TOXIC EFFECTS OF 2,2-bis (p-CHLORPHENY) 1,1,1-TRICHLORETHANE (D.D.T.) IN MAN Autor principal/año: Revista: R. A. M. Case, 1945 BMJ P 2, Experimental

253	Nombre del artículo: TOXIC EFFECTS OF 2,2-bis (p-CHLORPHENY) 1,1,1-TRICHLORETHANE (D.D.T IN MAN	
	Autor principal/año: R. A. M. Case, 1945	Revista: BMJ
	P 3.	

254 Nombre del artículo:

TOXIC EFFECTS OF 2,2-bis (p-CHLORPHENY) 1,1,1-TRICHLORETHANE (D.D.T.) IN MAN

Autor principal/año: Revista: R. A. M. Case, 1945 BMJ

P 1-2:

...it is likely that a substance known to be toxic to mammals, shown to be toxic to man under certain conditions, and in wide use may produce subclinical manifestations, not at present recognized, which will lower the health-level and efficiency of workers at risk, and that the rapidly growing use of D.D.T. will extend into circumstances where human intoxication is likely to occur.

255 Nombre del artículo:

TOXIC EFFECTS OF 2,2-bis (p-CHLORPHENY) 1,1,1-TRICHLORETHANE (D.D.T.) IN MAN

Revista: Autor principal/año: R. A. M. Case, 1945 **BMJ**

It should be stressed that these experiments only show D.D.T. distemper to be toxic under special conditions, possibly rather more severe than would obtain in practice, and do not form the basis for any condemnation of the widespread use of D.D.T. if proper precautions are taken, particularly in the avoidance of oil contamination. They do, however, emphasize that D.D.T. intoxication in human beings is a hazard to be considered and guarded against.

256 Nombre del artículo: Present Position of DDT in the Control of Insects of Medical Importance

1	Autor principal/año: Fred C. Bishopp, 1946	Revista: American Journal of Public Health

257 Nombre del artículo: Present Position of DDT in the Control of Insects of Medical Importance Revista: Autor principal/año: Fred C. Bishopp, 1946 American Journal of Public Health P 2: DDT is a nerve poison, as indicated by the early appearance of muscular tremors and other symptoms.

258	Nombre del artículo: Present Position of DDT in the Control of Insects of Medical Importance	
	Autor principal/año: Fred C. Bishopp, 1946	Revista: American Journal of Public Health
	P 2: DDT must not be allowed to get into foods or to be ingested accidentally.	

259 Nombre del artículo: Present Position of DDT in the Control of Insects of Medical Importance Autor principal/año: Revista: Fred C. Bishopp, 1946 American Journal of Public Health One of the outstanding characteristics of DDT is its persistence. In fact, this is perhaps the major element in making it superior to many other insecticides. This persistence, however, makes it necessary to use care when applying it on crops or products intended for food or

260	Nombre del documento: Pharmacologic And Toxicologic Aspects Of DDT			
	Autor principal/año: AMA Council On Pharmacy And Chemistry, 1951 Archivo: https://drive.google.com/open?id np2IZuTWbEBB4jW1eiPccKlvf			
	P 2: DDT must be applied cautiously to food crops, which require treatment after the development of the edible portion of the plant, if residues at the time of harvest are to be avoided It should not be used on dairy cattle or animals being prepared for slaughter since there is a danger of accumulation of the substance in the milk and tissues of treated animals.			

261-280

feed.

261	Nombre del documento: Pharmacologic And Toxicologic Aspects Of DDT		
Autor principal/año: AMA Council On Pharmacy And Chemistry, 1951		Archivo: https://drive.google.com/open?id=1nOgsZm np2lZuTWbEBB4jW1eiPccKlvfb	
	P 2:		

DDT is a "cerebrospinal" poison which acts primarily on the central nervous system in man and higher animals as contrasted with its apparent peripheral action in insects. The principal systemic effects in higher animals are disturbances of the central nervous system characterized by hyperexcitability, generalized tremors, spastic or flaccid paralysis and convulsions.

262

Nombre del documento:

Pharmacologic And Toxicologic Aspects Of DDT

Autor principal/año:

Archivo:

AMA Council On Pharmacy And Chemistry, 1951

https://drive.google.com/open?id=1nOgsZm

np2lZuTWbEBB4jW1eiPccKlvfb

P 3:

Chronic poisoning may result from prolonged ingestion or exposure to small amounts of DDT... As in acute poisoning, there are wide individual variations in susceptibility regardless of the route of administration; this makes it difficult to establish safe tolerance levels applicable to all individuals

263

Nombre del artículo:

Fred C. Bishopp, 1946

Present Position of DDT in the Control of Insects of Medical Importance

Autor principal/año:

Revista: American Journal of Public Health

P 1-2:

From the work of these pharmacologists the following very general conclusions can be

10. When used as recommended for the control of human parasites and household insects, DDT insecticides are not harmful to human health.

Nombre del artículo:

THE TOXICITY OF 29,2-bis (P-CHLORPHENYL) 1,,1-TRICHLORETHANE (D.D.T.)

Autor principal/año: Revista: G. R. Cameron, 1945 **BMJ**

D.D.T. is tolerated in fairly large amounts when administered as single or repeated doses. Toxic levels are not easily reached when dilute solutions suitable for insecticidal purposes are employed. Danger to health is likely to arise only from careless use of concentrates.

264

Nombre del artículo:

Present Position of DDT in the Control of Insects of Medical Importance

Autor principal/año: Revista:

Fred C. Bishopp, 1946 American Journal of Public Health

The question of safety in labeling and handling DDT is dealt with in a release of the Food and Drug Administration of November 5, 1945. The position is taken that the degree of toxicity of DDT does not place it with the caustic poisons and hence -labeling it "poison" with skull and crossbones is not necessary.

265

Título del libro:

DDT - Scientists, Citizens and Public Policy

https://www.amazon.com/DDT-Scientists-Citizens-Princeton-Library/dp/0691613907

Autor principal/año: Publicador:

Thomas Dunlap, 1981 Princeton Legacy Library

P 59:

The official debate over regulatory policy for DDT was, however, conditioned by a factor unique in the history of insecticide regulation: DDT was first used during World War II; by the time it entered the civilian market it already had a reputation for effectiveness, power, and safety unmatched by any other material.

P 63:

As soon as production exceeded military requirements the War Production Board allowed the surplus to be used for experiments; it released DDT for general civilian use on 1 August 1945.

266

Nombre del artículo:

Statement on Clinical Intoxication From DDT and Other New Insecticides

PMID: 14832501

Autor principal/año: Morton S. Biskind, 1950

Journal of Insurance Medicine

Part 1, p 1:

Since shortly after the last war, a large number of cases had been observed by physicians all over the country... The condition was of unknown origin... [and] was widely attributed to a "virus X". As with all other physicians, a large number of my patients had this condition. I, like others, found it extremely puzzling; it resembled no infectious process I was acquainted with...

267

Nombre del artículo:

DDT Poisonins and the Elusive "Virus X:" A New Cause for Gastro-Enteritis

Revista:

Autor principal/año:

Revista:

Morton S. Biskind, 1949

American Journal of Digestive Diseases

Altogether data have 'been accumulated on more than 200 cases of the "virus X" syndrome in which the condition followed immediately on known exposure to DDT.

268

Nombre del artículo:

DDT Poisonins and the Elusive "Virus X:" A New Cause for Gastro-Enteritis

Autor principal/año:

Revista:

Morton S. Biskind, 1949

American Journal of Digestive Diseases

The high incidence, the usual absence of a febrile reaction, the persistence and erratic recurrence of the symptoms, the lack of observable inflammatory lesions, and the resistance even to palliative therapy, suggested an intoxication rather than an infection. Investigation for possible etiologic agents soon led to consideration of DDT.

269

Nombre del artículo:

DDT Poisonins and the Elusive "Virus X:" A New Cause for Gastro-Enteritis

Autor principal/año:

Revista:

Morton S. Biskind, 1949

American Journal of Digestive Diseases

P 1.

270

Nombre del artículo:

DDT Poisonins and the Elusive "Virus X:" A New Cause for Gastro-Enteritis

Autor principal/año:

Revista:

Morton S. Biskind, 1949

American Journal of Digestive Diseases

P 2.

Nombre del artículo: Statement on Clinical Intoxication	Nombre del artículo: Statement on Clinical Intoxication From DDT and Other New Insecticides	
Autor principal/año: Morton S. Biskind, 1950	Revista: Journal of Insurance Medicine	
Part 1, p2.		

271 Nombre del artículo: DDT Poisonins and the Elusive "Virus X:" A New Cause for Gastro-Enteritis Autor principal/año: Revista: Morton S. Biskind, 1949 American Journal of Digestive Diseases P 3-4.

272 Nombre del artículo:

DDT Poisonins and the Elusive "Virus X:" A New Cause for Gastro-Enteritis

Autor principal/año: Revista: Morton S. Biskind, 1949 American Journal of Digestive Diseases

P 4:

To anyone with even a rudimentary knowledge of toxicology, it exceeds all limits of credibility that a compound lethal for insects, fish, birds, chickens, rats, guinea pigs, rabbits, dogs, cats, goats, sheep, horses, cattle and monkeys would be nontoxic for human beings.

273 Nombre del artículo:

Public Health Aspects Of The New Insecticides

Autor principal/año: Revista: Morton S. Biskind, 1953 American Journal of Digestive Diseases

Since the last war there have been a number of curious changes in the incidence of certain ailments and the development of new syndromes never before observed. A most significant feature of this situation is that both man and all his domestic animals have simultaneously been affected.

274 Nombre del artículo:

Public Health Aspects Of The New Insecticides

Autor principal/año: Revista: Morton S. Biskind, 1953 American Journal of Digestive Diseases

...these conditions is mentioned in the comprehensive U. S. Department of Agriculture Handbook, "Keeping Livestock Healthy," published in 1942. This coincidence alone should have been sufficient to rouse a suspicion that something new that is common both to man and his domestic animals, has been operating in their environment during the period these changes have occurred.

275	Nombre del artículo: Public Health Aspects Of The New Insecticides	
	Autor principal/año: Morton S. Biskind, 1953	Revista: American Journal of Digestive Diseases
	P 4:	

...studies by Lillie and his collaborators (74, 75) of the National Institutes of Health, published in 1944 and 1947 respectively, which showed that DDT may produce degeneration of the anterior horn cells of the spinal cord in animals. These changes do not occur regularly in exposed animals any more than they do in human beings, but they do appear often enough to be significant.

276

Nombre del artículo:

DDT Poisonins and the Elusive "Virus X:" A New Cause for Gastro-Enteritis

Autor principal/año: Revista:

Morton S. Biskind, 1949 American Journal of Digestive Diseases

P 5:

A Siamese cat dusted with DDT developed convulsions in a few hours and died some days later with paralysis of the hind limbs.

277

Nombre del artículo:

Public Health Aspects Of The New Insecticides

Autor principal/año: Revista:

Morton S. Biskind, 1953 American Journal of Digestive Diseases

P 4

When the population is exposed to a chemical agent known to produce in animals lesions in the spinal cord resembling those in human polio, and thereafter the latter disease increases sharply in incidence and maintains its epidemic character year after year, is it unreasonable to suspect an etiologic relationship?

278

Nombre del artículo:

Public Health Aspects Of The New Insecticides

Autor principal/año: Revista:

Morton S. Biskind, 1953 American Journal of Digestive Diseases

P 4

In the Philippines and elsewhere in the Far East American troops, who used vast quantities of DDT as insecticides, had a high incidence of poliomyelitis, while it was extremely low in the surrounding native population.

279

Nombre del artículo:

Present Concepts And Recent Advances In Acute Poliomyelitis

Autor principal/año: Revista:

John R. Paul, 1952 AMA Archive of Internal Medicine

P 8:

It is not known whether the disease may be spread by agents other than infected persons, as, for instance, by insects or contaminated food or water. Theoretically these agents might be "eliminated" by the introduction of "improved sanitary measures." One recognizes that food or flies or cockroaches could on occasion be infectious, but no evidence exists that such insects are an essential link in the chain, comparable with mosquitoes when they carry the parasite of malaria or the virus of yellow fever.

280

Título del libro:

DDT - Scientists, Citizens and Public Policy

https://www.amazon.com/DDT-Scientists-Citizens-Princeton-Library/dp/0691613907

Autor principal/año: Publicador:

Thomas Dunlap, 1981 Princeton Legacy Library

P 65:

In desperation, some towns even sprayed DDT in an effort to combat polio.

281-300

281 Nombre del artículo:

The Epidemiology of Poliomyelitis in Africa

Autor principal/año: Archivo:

James Gear, 1958 https://drive.google.com/open?id=1F-IcUN-b22YEghe-

3I4Pldwk4vwDA3xe

P 5

The systemic spraying of villages and towns with DDT, BHC and similar long-acting insecticides has not hastened the end of an epidemic, nor indeed has it prevented the onset of an epidemic.

282

Nombre del artículo:

Statement on Clinical Intoxication From DDT and Other New Insecticides 1483

PMID: <u>14832501</u>

Autor principal/año: Revista:

Morton S. Biskind, 1950 Journal of Insurance Medicine

Part 2, p 2:

Wherever DDT had been used extensively against polio, not only was there an epidemic of the syndrome I have described but the incidence of polio continued to rise and in fact appeared where it had not been before.

283

Nombre del artículo:

Statement on Clinical Intoxication From DDT and Other New Insecticides

PMID: 14832501

Autor principal/año: Revista:

Morton S. Biskind, 1950 Journal of Insurance Medicine

Part 2, p 2:

This is not surprising since it is known that not only can DDT poisoning produce a condition that may easily be mistaken for polio in an epidemic but also being a nerve poison itself, may damage cells in the spinal cord and thus increase the susceptibility to the virus.

284

Nombre del artículo:

Public Health Aspects Of The New Insecticides

Autor principal/año: Revista

Morton S. Biskind, 1953 American Journal of Digestive Diseases

P 1:

Soon after the introduction of DDT for widespread use as a household, public health and agricultural insecticide, it became evident that virtually all forms of insects were propagating strains completely resistant to this compound. This led to a frantic search for more and more potent insecticides (which also turned out to be more and more toxic for animals and man). One after another new compounds were introduced, the total list being very *long* indeed.

285

Nombre del artículo:

PMID:

Statement on Clinical Intoxication From DDT and Other New Insecticides

14832501

Autor principal/año: Morton S. Biskind, 1950	Revista: Journal of Insurance Medicine	
Part 2 p 5, Por ejemplo parathion.		
Nombre del artículo: Public Health Aspects Of The New Insecticides		
Autor principal/año: Revista: Morton S. Biskind, 1953 Revista: American Journal of Digestive Diseases		
P 7 – Chlordane is 10-times more poisonous than DDT.		

286 Nombre del artículo:

Public Health Aspects Of The New Insecticides

Autor principal/año: Revista:

Morton S. Biskind, 1953 American Journal of Digestive Diseases

In agriculture alone 232 million pounds were used in the United States in 1951 and 252 million pounds in 1952.

287

Nombre del artículo:

PMID:

Statement on Clinical Intoxication From DDT and Other New Insecticides 14832501

Autor principal/año: Revista:

Morton S. Biskind, 1950 Journal of Insurance Medicine

Part 2, p 5:

Virtually all studies on the toxicity of the various insecticides have been made on the individual substances. However, this in no way reflects what happens in in actual practice, for today in a single day's diet we may readily be exposed to DDT, BHC, chlordane, chlorinated camphene, methoxychlor, and parathion as well as some lead and arsenic. How many simultaneous insults can the human body take?

288 Nombre del artículo:

Possible Hazards From The Use of DDT

https://ajph.aphapublications.org/doi/pdf/10.2 105/AJPH.39.7.925

Archivo:

https://drive.google.com/open?id=1n3Ni yviMKqjEFbZ9PzowYd0R-2L6DA6t

Autor principal/año:

Editorial (unsigned), 1949 American Journal of Public Health

DDT the great bug-killer may turn out to be one of the most devastating biological weapons ever loosed by a people upon themselves... DDT is slowly poisoning large numbers of Americans, especially children.

289

Nombre del artículo:

Archivo:

Possible Hazards From The Use of DDT https://ajph.aphapublications.org/doi/pdf/10.2 105/AJPH.39.7.925

https://drive.google.com/open?id=1n3Ni yviMKqiEFbZ9PzowYd0R-2L6DA6t

Revista: Autor principal/año:

Editorial (unsigned), 1949 American Journal of Public Health

This statement pointed out that the toxicity of DDT for man "has been given full consideration in making recommendations for its use. There is no evidence that the use of DDT in accordance with the recommendations of the various federal agencies has ever caused human sickness due to DDT itself... "Statements that DDT is responsible for

causing the so-called 'virus X disease' of man and 'X disease' of cattle are totally without foundation. Both of these diseases were recognized before the utilization of DDT as an insecticide."

290

Nombre del artículo:

Archivo:

Possible Hazards From The Use of DDT https://ajph.aphapublications.org/doi/pdf/10.2 105/AJPH.39.7.925

https://drive.google.com/open?id=1n3Ni yviMKqjEFbZ9PzowYd0R-2L6DA6t

Autor principal/año: Revista: Editorial (unsigned), 1949 Americar

American Journal of Public Health

P 2

In April it urged that "this insecticide not be applied to animals producing milk for human consumption. In the light of current information the Bureau also advises that safer materials be used for insect control in places where the milk might be contaminated, such as dairy barns, milk rooms, rooms containing dairy feed, or in similar situations on the farm. Nor should DDT be used for fly control in milk-processing plants... It would seem desirable to obtain more extensive data as to the actual presence of DDT in milk by methods now available; but, all in all, the situation seems to be well in hand and the public adequately protected.

291

Nombre del artículo:

Public Health Aspects Of The New Insecticides

Autor principal/año: Revista:

Morton S. Biskind, 1953 American Journal of Digestive Diseases

P 2

The relationship was promptly denied by government officials, who provided no evidence to contest the author's observations but relied solely on the prestige of government authority and sheer numbers of experts to bolster their position.

292

Nombre de la página:

Select Committee to Investigate the Use of Chemicals in Food and Cosmetics (1950-52)

Sitio web:

Archives.GOV

 $\underline{https://www.archives.gov/legislative/guide/house/chapter-22-select-food-and-cosmetics.html}$

The committee was authorized to inquire into the extent and the effect of the use of chemicals, synthetics, pesticides, and insecticides in the production and preparation of food products and to determine the effects of such use on the public and upon agricultural stability.

293

Nombre del artículo:

PMID:

Statement on Clinical Intoxication From DDT and Other New Insecticides

14832501

Autor principal/año: Revista:

Morton S. Biskind, 1950 Journal of Insurance Medicine

This is Dr. Biskind's testimony in congress.

294

Nombre del artículo:

Public Health Aspects Of The New Insecticides

Autor principal/año: Revista

Morton S. Biskind, 1953 American Journal of Digestive Diseases

P 2:

Yet, far from admitting a causal relationship so obvious that in any other field of biology it would be instantly accepted, virtually the entire apparatus of communication, lay and scientific alike, has been devoted to denying, concealing, suppressing, distorting and attempts to convert into its opposite, the overwhelming evidence. Libel, slander and economic boycott have not been overlooked in this campaign.

295

Nombre del artículo: Probers into Chemical Sprays Smeared by Lobby Fecha:

Sep 9, 1951

Author:

Newspaper:

Louis Bromfield

Cleveland Plain Dealer

P 2:

The hirelings at least of the chemical companies and their lobbyists are doing their best to cripple or suppress the inquiries of Mr. Delaney's committee... The committee investigations have given rise to one of the most extraordinary smear campaigns in our history. Mr. Delaney has been blackguarded and those who testified that we know nothing of the effects of the strange, new poisons have been called liars, fools and virtually threatened with blackmail.

296

Nombre del artículo: Poliomyelitis Problems

PMID:

<u>14796117</u>

Autor principal/año:

Revista:

Archibald L. Hoyne, 1951

Medical clinics of North America

P 14:

A SUMMARY OF PROBLEMS:

- 1. Still unknown etiologic agent.
- 2. Warm weather prevalence, unusual for a communicable disease.
- 3. Undetermined manner of transmission.
- 4. Susceptibility in the exceptionally well nourished.
- 5. Variability of symptoms.
- 6. Lack of a practicable laboratory diagnostic test.
- 7. Diagnostic difficulties added by the "new virus."
- 8. Reliable measures for prevention.
- 9. Dependable methods for treatment.
- 10. Question whether isolation of poliomyelitis patients is an effective means of controlling the disease.

297

Nombre del artículo:

PMID:

Transmission Of Poliomyelitis Virus

14889394

Autor principal/año:

Revista:

Albert B. Sabin, 1951

Journal of Pediatrics

298

Nombre del artículo:

Transmission Of Poliomyelitis Virus

PMID: 14889394

Autor principal/año:

Revista:

Albert B. Sabin, 1951

Journal of Pediatrics

P 1:

Although flies have been found to be contaminated with virus, there has been no reliable evidence of spread by insects, water, food or sewage...

Nombre del artículo:

Present Concepts And Recent Advances In Acute Poliomyelitis

Autor principal/año: Revista:

John R. Paul, 1952 AMA Archive of Internal Medicine

P 7:

...there is agreement among students of poliomyelitis that not enough is known about the factors responsible for the spread of poliomyelitis to enable elimination of the virus from a community.

300

Nombre del artículo:

Epidemiology Of Poliomyelitis And Allied

Diseases--1963 https://www.ncbi.nlm.nih.gov/pmc/articles/P

MC2604573/pdf/vibm00599-0011.pdf

PMID: 14064722

Archivo:

https://drive.google.com/open?id=1fV_w0 3BSOROKex-hR7DkGZH44EXUwpTv

Autor principal/año:

Revista:

Dorothy M. Horstmann, 1963

Yale Journal of Biology and Medicine

As with so many contact infections, the exact manner in which polioviruses are transmitted from one person to another is imperfectly understood.

301-320

301

Nombre del artículo:

Transmission Of Poliomyelitis Virus

PMID: 14889394

Autor principal/año:

Revista:

Albert B. Sabin, 1951 Journal of Pediatrics

If the introduction of the virus into the mouth by means of the hands or other materials is of basic importance in the transmission of poliomyelitis, can we regard the period of communicability as being for only a few days before and a few days to a week after onset of symptoms, when, by our present methods, the virus is still readily demonstrable in the stools of approximately 50 per cent of individuals during the third and fourth weeks? How much reliance should we place on the epidemiological observations which place the "infectious period" at four to five days before and after onset of symptoms, when it is realized that these conclusions are based on tracing extrafamilial secondary cases to presumably single contacts with patients who became sick and had to go to bed?

302

Nombre del artículo:

Epidemiology Of Poliomyelitis And Allied Diseases--1963

https://www.ncbi.nlm.nih.gov/pmc/articles/P

MC2604573/pdf/yjbm00599-0011.pdf

PMID: 14064722

Archivo:

https://drive.google.com/open?id=1fV_w0 3BSORQKex-hR7DkGZH44EXUwpTv

Autor principal/año:

Revista:

Dorothy M. Horstmann, 1963

Yale Journal of Biology and Medicine

P 4.

The main portal of exit is the intestinal tract, and large quantities of virus can be found in the feces often for many weeks and occasionally for many months... Epidemiologic evidence indicates that a case is most infectious during the early phase of infection, sometime before onset of symptoms or in the first few days of the clinical disease.

Nombre del artículo:

Present Concepts And Recent Advances In Acute Poliomyelitis

Autor principal/año: Revista:

John R. Paul, 1952 AMA Archive of Internal Medicine

P 1:

Eventually the new facts should find more clinical application than can be assigned to them now, for one must still admit that there are no more immediate measures available for the prevention and cure of the acute disease than existed in the times of Medin and Wickman, 80 and 40 years ago, respectively.

304

Nombre del artículo:

Poliomyelitis Problems

PMID: 14796117

Autor principal/año: Revista:

Archibald L. Hoyne, 1951 Medical clinics of North America

P 1-2:

Notwithstanding the intensive studies of investigators, very little information of practical value has been added to our knowledge of poliomyelitis during the past forty years... One might almost be tempted to make the contradictory statement that the more we learn about poliomyelitis, the less we know.

305

Nombre del artículo:

The cultivation of the poliomyelitis viruses in

tissue culture

https://assets.nobelprize.org/uploads/2018/06/enders-robbins-weller-

<u>lecture.pdf?</u> ga=2.149573750.1715530293.1537951684-1754545531.1537951684

Autor principal/año:

John F. Enders, 1952

Nombre del artículo:

Present Concepts And Recent Advances In Acute Poliomyelitis

Autor principal/año: Revista:

John R. Paul, 1952 AMA Archive of Internal Medicine

P 3:

In these recent discoveries it is possible that we have witnessed the end of what might be termed "the monkey era" in poliomyelitis research. This is no great loss, for the expense of maintaining monkey colonies for poliomyelitis research has been great. Also it is heartening to realize that the way is now open for many laboratories to engage in certain clinical and epidemiological investigations on poliomyelitis which have been denied to them in the past because of expense and other difficulties. Scores of new investigators can now enter the poliomyelitis field, and new impetus can be given to such work all over the world. All this stems from the discovery that a tissue-culture tube may be substituted for a monkey.

306

Nombre del artículo:

Archivo:

The Present Status of Polio Vaccines

https://drive.google.com/open?id=13MEzjI

rvcvuzbltwTqBhGiOm8nZln2I4

Autor principal/año: Revista:

Herbert Ratner, 1960 Illinois Medical Journal

Ratner and colleagues discuss a change in the diagnostic criterion and note that it has been implemented since 1955 (Ratner 1960, p. 5). An official report states that the change was implemented (at least) since 1958 (PSU 1962, p. 2).

307 Nombre del artículo:

Archivo: The Present Status of Polio Vaccines

https://drive.google.com/open?id=13MEzjI rvcvuzbltwTqBhGiOm8nZln2I4

Autor principal/año: Revista:

Herbert Ratner, 1960 Illinois Medical Journal

Furthermore, diagnostic procedures have continued to be refined. Coxsackie virus in factions and aseptic meningitis have been distinguished from paralytic poliomyelitis. Prior to 1954 large numbers of that; cases undoubtedly were mislabeled as paralytic poliomyelitis.

308 Nombre del artículo:

The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año: Revista:

Tiberio A. Swartz, 2008 Israel Center for Disease Control (ICDC), Ministry of Health

309 Nombre del artículo:

Epidemiology of Poliomyelitis in Israel, 1952-59

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2555311/pdf/bullwho003

27-0059.pdf

Revista: Autor principal/año:

A. Michael Davies, 1960 Bulletin of the World Health Organization

...in 1957-59 only proved paralytic cases have been included in the statistics.

310 Nombre del documento:

Green Book - Poliomyelitis

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/148141/Gre en-Book-Chapter-26-Polio-updated-18-January-2013.pdf

Autor/año:

Archivo: NHS, 2013

https://drive.google.com/open?id=15wYdgB3upwPEHYP7XZkU

VxQEAOXe1Lnb

Chapter 26

311 Nombre del artículo:

Surveillance of Poliomyelitis in the United States, 1958-61

19316432

PMID:

PMID:

13814376

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1915173/pdf/pubhealthre

porig00096-0009.pdf

Autor principal/año: Revista:

PSU, 1962 Public Health Reports

In 1955, the National Foundation for Infantile Paralysis sponsored an immunization program for first- and second-grade school children who were primarily 7 and 8 years old. These children comprised essentially the only population group that received vaccine during the spring and summer of 1955.

~ . —	Nombre del artículo: Exit Poliomyelitis-What Next?	

Autor principal/año: Revista:

Sven Gard, 1961 Yale Journal Of Biology And Medicine

P 2:

This dramatic drop in case incidence to less than 1% in four years was not expected. Even with a wild hope for a 100% protective effect-which actually seems to have materialized-one could not have anticipated a concomitant drastic reduction in attack rates among non-vaccinated persons.

313	For example, in Houston, 1958 - Nombre del artículo: Effectiveness of Salk Vaccine Analysis of Virologically Confirmed Cases of Paralytic and Nonparalytic Poliomyelitis Autor principal/año: Joseph L. Melnick, 1961 Revista: JAMA	
	Or, in Detroit, 1958 - Nombre del artículo: Laboratory Data On The Detroit Poliomyelitis Epidemic - 1958	
	Autor principal/año: Gordon C. Brown, 1960	Revista: JAMA

314 Nombre del artículo:

Use Of Poliomyelitis Vaccine Under Epidemic Conditions Report Of Outbreak Of Poliomyelitis Among Naval Personnel And Dependents In Hawaii

Autor principal/año: Revista: Robert S. Poos, 1956 JAMA

P 8:

After the mass vaccination program, attack rates were lower in vaccinees than in the unvaccinated population, although this difference was not statistically significant.

315 Nombre del artículo: Archivo

The Present Status of Polio Vaccines

https://drive.google.com/open?id=13MEzjI
rvcvuzbltwTqBhGiOm8nZln2I4

Autor principal/año: Revista:
Herbert Ratner, 1960 Illinois Medical Journal

P 6

We repeated this study of 1955 and 1956 by projecting the same type of statistical analysis into 1957. Lo and behold, we found that two doses of Salk vaccine was not nearly as effective in 1957 as we thought it was in 1956. Instead of 83 per cent effectiveness we found only about 24 per cent.

316 Nombre del artículo: Archivo:

The Present Status of Polio Vaccines https://drive.google.com/open?id=13MEzjI rvcvuzbltwTqBhGiOm8nZln2I4

Autor principal/año: Revista:

Herbert Ratner, 1960 Illinois Medical Journal

P 7

At present, I am an agnostic as far as the efficacy of the Salk vaccine is concerned because I do not know how effective it is. I believe it has some degree of effectiveness, but I do not know the extent because I cannot get proper denominators.

317	Nombre del artículo:	Archivo:
	The Present Status of Polio Vaccines	https://drive.google.com/open?id=13MEzjI
		rvevuzbltwTqBhGiOm8nZln2I4

Autor principal/año: Herbert Ratner, 1960	Revista: Illinois Medical Journal		
P 7: If notice antibodies mean anything in respect to protection, then I am forced to conclude			

If polio antibodies mean anything, in respect to protection, then I am forced to conclude that much of the Salk vaccine we have been using is useless.

318 Nombre del artículo: Paralytic poliomyelitis in Massachusetts, 1959 Autor principal/año: Revista: Sumner Berkovich, 1961 NEJM P 2, Tabla 1.

319	9 Nombre del artículo: Paralytic poliomyelitis in Massachusetts, 1959			
	Autor principal/año: Revista: Sumner Berkovich, 1961 NEJM			
	P 2: Effectiveness of the vaccine in Massachusetts cannot be accurately evaluated, since the total number in each age group who had received three or more doses is unknown. However, that it did not provide the expected protection is apparent"			

320	Nombre del artículo: Paralytic poliomyelitis in Massachusetts, 1959	
	Autor principal/año: Sumner Berkovich, 1961	Revista: NEJM
	P 4-5.	

321-340

321	Por ejemplo - Nombre del artículo: The Influence Of Natural And Artificially Induced Immunity On Alimentary Infections With Polioviruses Autor principal/año: John P. Fox, 1958 Revista: American Journal of Public Health P 11: De novo development of antibody induced by the vaccine was excellent in children possessing one or two types of heterologous antibody but among triple negatives ne quarter and a half, respectively, developed no antibody after the booster to types 1 a viruses.			
Nombre del artículo: Influence Of Vaccination With Formalin Inactivated Vaccine Upon Gastrointestinal Infection With Polioviruses		~	PMID: 14415906	
	Autor principal/año: Revista: Martha Lipson. Lepow, 1960 American Journal of Public Health			
P 10: Our failure to find any clear-cut differences between the vaccinated and unvachildren either in regard to the presence of antibody or levels of antibody is so				

disturbing. Some doubt might be raised concerning the potency of the vaccines used in the population studied. One might also regard these data as emphasizing the importance of giving more than two doses of vaccine.

322 Nombre del artículo:

Paralytic poliomyelitis in Massachusetts, 1959

Autor principal/año: Revista: Sumner Berkovich, 1961 NEJM

P 5.

323 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 574:

Although the results of the historical Francis trial were positive, the Cutter incident led to a change in manufacturing processes that lowered the immunogenicity of the early vaccine.

324

Nombre del artículo: Archivo:

The Present Status of Polio Vaccines https://drive.google.com/open?id=13MEzjI

rvcvuzbltwTqBhGiOm8nZln2I4

PMID:

13814376

Autor principal/año: Revista:

Herbert Ratner, 1960 Illinois Medical Journal

Р 4·

A scientific examination of the data, and the manner in which the data were manipulated, will reveal that the true effectiveness of the present Salk vaccine is unknown and greatly overrated.

325

Nombre del artículo:

The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año: Rev

Revista:

Tiberio A. Swartz, 2008 | Israel Center for Disease Control (ICDC), Ministry of Health

P 42 Tabla 4.1, P 56 Tabla 5.1.

326

Nombre del artículo:

Epidemiology of Poliomyelitis in Israel, 1952-59

 $\underline{https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2555311/pdf/bullwho003}$

27-0059.pdf

Autor principal/año:

Revista:

A. Michael Davies, 1960 Bulletin of the World Health Organization

P 16:

The 1957 drop in incidence affected all age-groups, not merely those vaccinated, and although 1958 should have brought a wider age span of susceptible infants, especially to type 1 virus, there was no change in the age pattern of cases.

327

Nombre del artículo:

The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año:

Revista:

Tiberio A. Swartz, 2008

Israel Center for Disease Control (ICDC), Ministry of Health

P 67

The partial vaccination program, implemented exclusively during the first half of 1957, was probably not associated with the low morbidity recorded during the year.

Nombre del artículo:
The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año:
Tiberio A. Swartz, 2008 | Revista:
Israel Center for Disease Control (ICDC), Ministry of Health

P 66:
...the polio vaccine produced in Israel in 1957 and used until mid-1958, performed poorly in potency tests and induced low seroconversion rates.

Nombre del artículo: The Epidemiology of Polio in Israel - An Historical Perspective Autor principal/año: Tiberio A. Swartz, 2008 Revista: Israel Center for Disease Control (ICDC), Ministry of Health P 67: The limited morbidity of 1959 and 1960 coincided with the implementation of a better vaccination program with an improved vaccine. The role of vaccination in the prevention

of polio virus activity at that time cannot be excluded.

330	Nombre del artículo: An Outbreak Of Poliomyelitis I Attenuated Type 1 Vaccine In I	n Israel In 1961 And The Use Of ts Control
	Autor principal/año: Jacob Yofe, 1962	Revista: American Journal of Epidemiology
	P 16, Tabla 6.	

331	Nombre del artículo: Epidemiology of Poliomyelitis in Israel, 1952-59 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2555311/pdf/bullwho003	
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332	In Israel – Nombre del artículo: An Outbreak Of Poliomyelitis In Israel In 1961 And The Use Of Attenuated Type 1 Vaccine In Its Control Autor principal/año: Jacob Yofe, 1962 Revista: American Journal of Epidemiology P 6: During the third week of May, type 1 attenuated vaccine prepared from Sabin's LSc, 2 ab strain was obtained through the courtesy of Wyeth Laboratories. It was decided to feed vaccine to all children born from January 1, 1957, down to 4 days of age.		
	In USA – Título del libro: Jonas Salk: A Life https://www.amazon.com/Jonas-Salk-Charlotte-DeCroes-Jacobs/dp/0199334412/		
	Autor principal/año: Charlotte DeCroes Jacobs, 2015		Publicador: Oxford University Press

P 226:

Among those few who sided with Salk in opposition to the oral vaccine was the director of the Communicable Disease Center, Alex Langmuir. The number of polio cases had fallen to 2 percent of that prior to the field trial. He saw no reason to revaccinate those who had received the Salk vaccine. O'Connor agreed and held a press conference at which he vehemently opposed revaccination and leveled his guns at the surgeon general. Saying Terry was "flying in the face of facts and for reasons

that might not best be questioned," O'Connor accused him of "withholding from the public the true picture of the need...to promote the preferential sale of the second vaccine to do what's already been done by one....Half-truths and nonscientific innuendos and implications" had no place where the health of the public was concerned. He sent a letter to the editor of Washington Star, decrying the advice to revaccinate those already protected with the killed vaccine. "There is no sane or scientific basis." Yet widespread oral vaccination continued.

In USA -

Título del libro:

Jonas Salk (Makers of Modern Science)

https://www.amazon.com/Jonas-Salk-Makers-Modern-Science/dp/0816028052/

Autor principal/año: Publicador: Victoria Sherrow, 1993 Facts on File

P 93

Within a few years, however, Sabin's became the vaccine of choice in the United States. April 24, 1960, known as "Sabin Oral Sunday," marked the first day that people in the United States received Sabin's vaccine. As of 1961 communities throughout the country were holding SOS-Sabin Oral Sunday-campaigns, and people lined up at schools or other places to receive their vaccine on a sugar cube. Local officials and medical societies encouraged people to take oral vaccine, even if they were already vaccinated by injection.

Nombre del artículo:

Two Voluntary Mass Immunization Programs Using Sabin Oral Vaccine

Autor principal/año: Revista: Richard B. Johns, 1963 JAMA

P 5, Tabla1:

An example of a Sabine-vaccine vaccination operation in two counties in Arizona in 1961. Children aged 6-14 were vaccinated at a rate of over 95% during the operation. These are exactly the ages vaccinated with the Salk vaccine.

Nombre del artículo:

A Survey of Immunization Levels After an Oral Poliovaccine Program in Cleveland

Autor principal/año: Revista: Martha L. Lepow, 1964 JAMA

P 5, Tabla 3:

Vaccination operation in the Cleveland area, Ohio, in 1962. Similarly, the vast majority of Sabin vaccinees were previously vaccinated with the Salk vaccine.

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 593:

Despite incomplete application of the vaccine, polio incidence fell 95% between the introduction of the vaccine in 1955 and its abandonment in 1961.

Nombre del artículo: The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año:
Tiberio A. Swartz, 2008

Revista:
Israel Center for Disease Control (ICDC), Ministry of Health

P 56 Tabla 5.1, P 42 Tabla 4.1.

Nombre del artículo:

Final Report of Poliomyelitis Epidemic in Detroit and Wayne County, 1958

PMID: 13771906

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1929571/pdf/pubhealthreporig00119-0058.pdf

Autor principal/año:

Revista:

Joseph G. Molner, 1960

Public Health Reports

P 5 chart 2, p 9 remarks to Tabla 8.

336 Nombre del artículo:

Laboratory Data On The Detroit Poliomyelitis Epidemic - 1958

Autor principal/año: Revista: Gordon C. Brown, 1960 JAMA

P 1:

Virological laboratory tests were carried out on 1,060 persons, probably the greatest percentage of victims of a large epidemic of poliomyelitis ever to be subjected to laboratory investigation.

337 Nombre del artículo:

Laboratory Data On The Detroit Poliomyelitis Epidemic - 1958

Autor principal/año: Revista: Gordon C. Brown, 1960 JAMA

P 2, Tablas 1 and 2.

338 Nombre del artículo:

Laboratory Data On The Detroit Poliomyelitis Epidemic - 1958

Autor principal/año: Revista: Gordon C. Brown, 1960 JAMA

P 1:

Specimens from paralytic patients were retested if the findings had been negative for virus on the first attempt.

339 Nombre del artículo:

Preliminary Report And Observations On The 1956 Poliomyelitis Outbreak In Chicago

Autor principal/año: Revista: Herman N. Bundesen, 1957 JAMA

P 1

Of the 1,111 cases, virology reports have been received on 651. Of these 651 cases, a poliomyelitis virus has been successfully isolated from 412.

340 Nombre del artículo:

Effectiveness of Salk Vaccine

Analysis of Virologically Confirmed Cases of

Paralytic and Nonparalytic Poliomyelitis

Autor principal/año:	Revista:	
Joseph L. Melnick, 1961	JAMA	

P 1

Of the 126 cases which were diagnosed clinically as paralytic poliomyelitis, 102 yielded a virus in monkey kidney cultures. Of the viruses isolated, all but 2 were polioviruses... In the same period, 125 cases diagnosed as aseptic meningitis were studied... Of these, only 23 were polioviruses...

341-360

Nombre del artículo: Nonpolioviruses and Paralytic Disease https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1575072/pdf/califmed001 57-0049.pdf Autor principal/año: Robert L. Magoffin, 1962 Revista: California Medicine P 4: In etiologic studies of clinical paralytic poliomyelitis in California, poliovirus was recovered from about 80 per cent of the patients under five years of age, as compared with 60 to 65 per cent of older children and adults.

342	Nombre del artículo: Surveillance of Poliomyelitis in the United States, 1958-61 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1915173/pdf/pubhealthre-porig00096-0009.pdf		PMID: 19316432
	Autor principal/año: PSU, 1962	Revista: Public Health Reports	
	P 9, Tabla 9.		

343	Nombre del artículo: Epidemiology of Poliomyelitis in Israel, 1952-59 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2555311/pdf/bullwho00327-0059.pdf		PMID: 13814376
	Autor principal/año: A. Michael Davies, 1960	Revista: Bulletin of the World Health Organization	
	P 17, Tabla 19.		

344	In Kazakhstan, 1959, fecal samples from polio patients were tested in parallel with the introduction of the Sabin vaccine: only 16 out of 39 patients with paralysis in May-June 1959 were found to have polio virus in their feces.	Archivo: https://drive.google.com/open?id=1HoFd5 6xRmtStwV8CJyn_OxlPVVwdQ0DK https://drive.google.com/open?id=1fFx_Tl cKcnVMXX2QC3Ln-TSrr6bjXuuh
Czechoslovakia https://babel.hathitrust.org/cg015009662027;view=1up;sed Autor principal/año:	Report on a visit to the USSR, Poland and	
	Autor principal/año: Dorothy M. Horstmann, 1959	Revista: WHO

P 40-41.	

345 Nombre del artículo: PMID: Nonpolioviruses and Paralytic Disease 14468369 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1575072/pdf/califmed001 57-0049.pdf Revista: Autor principal/año: Robert L. Magoffin, 1962 California Medicine P 2-6. Nombre del artículo: PMID: A Study Of Certain Nonpoliomyelitis And Poliomyelitis Enterovirus 13538759 Autor principal/año: Revista: William McD. Hammon, 1958 **JAMA**

Nombre del artículo: A Study Of Certain Nonpoliomyelitis And Poliomyelitis Enterovirus Infections PMID: 13538759

Autor principal/año: Revista: William McD. Hammon, 1958 JAMA

P 3-6, quote from p 6:

It should be emphasized that these illnesses had been diagnosed as clinical paralytic poliomyelitis by a team of experienced poliomyelitis clinicians engaged in a research evaluation. We refer to these illnesses now as paralytic poliomyelitis-like because there is essentially no laboratory evidence of a poliovirus infection. This distinction is made because of the formerly held concept that this type of paralytic disease is only caused by one of the three types of poliovirus.

347	Nombre del artículo: A Study Of Certain Nonpoliomyelitis And Poliomyelitis Enterovirus Infections		PMID: 13538759
	Autor principal/año: William McD. Hammon, 1958	Revista: JAMA	
	P 6: Whether the enteroviruses isolated in all six cases were the respective etiological age		gical agents is

Whether the enteroviruses isolated in all six cases were the respective etiological agents is not unequivocally established.

348		Nombre del artículo: A Study Of Certain Nonpoliomyelit Infections	is And Poliomyelitis Enterovirus	PMID: 13538759
		Autor principal/año: William McD. Hammon, 1958	Revista: JAMA	
	P 6: In other words, there may exist strains of enteroviruses which, with opportune conditions act like polioviruses in man and produce an occasional paralytic illness that clinically cannot be differentiated from paralytic poliomyelitis.			

349	Nombre del artículo: A Study Of Certain Nonpoliomyelitis And Poliomyelitis Enterovirus Infections	PMID: 13538759
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Autor principal/año:	Revista:
William McD. Hammon, 1958	JAMA

P 7:

These paralytic and nonparalytic illnesses cannot be expected to be prevented by the present poliomyelitis vaccine and may be considered vaccine failures unless the exact etiology is established.

350 Nombre del artículo:

Epidemiology Of Poliomyelitis And Allied Diseases--1963

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2604573/pdf/yjbm00599-0011.pdf

PMID: 14064722

Archivo:

https://drive.google.com/open?id=1fV_w0 3BSORQKex-hR7DkGZH44EXUwpTv

Autor principal/año:

Dorothy M. Horstmann, 1963

Revista:

Yale Journal of Biology and Medicine

P 9:

The inactivated vaccine, since its introduction in 1955, has greatly reduced the incidence of paralytic poliomyelitis in countries in which its use has been extensive. This has been accomplished by inducing serologic immunity in vaccinees, which prevents CNS invasion. However the extent to which the inactivated vaccine has suppressed the circulation of wild polioviruses and the incidence of inapparent intestinal infection is not well documented... This is not surprising, for although the vaccine induces antibody formation, it does not provide a significant barrier to intestinal infection with either wild or vaccine strains.

351 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 631:

Continued use of OPV will induce effective intestinal immunity, thereby enhancing community resistance to transmission of imported wild poliovirus.

352 Nombre del artículo:

Epidemiology Of Poliomyelitis And Allied Diseases--1963

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2604573/pdf/yjbm00599-0011.pdf

PMID: 14064722

Archivo:

https://drive.google.com/open?id=1fV_w0 3BSORQKex-hR7DkGZH44EXUwpTv

Autor principal/año:

Revista:

Dorothy M. Horstmann, 1963

Yale Journal of Biology and Medicine

ρa

In contrast, inapparent infection, either natural or oral vaccine induced, does result in a marked degree of resistance to intestinal multiplication of virus, although in neither case is this resistance absolute.

353

Nombre del artículo:

The Influence Of Natural And Artificially Induced Immunity On Alimentary Infections With Polioviruses

PMID: 13571484

Annicitary infections with Followings.

Autor principal/año: Revista:
John P. Fox, 1958 American Journal of Public Health

Þα

At that time, no evidence could be found that primary vaccination had influenced either the occurrence or course of alimentary infections in any way, whereas it was already clear that immunity resulting from natural infection did exert a significantly limiting effect.

354 Nombre del artículo:

The Influence Of Natural And Artificially Induced Immunity On Alimentary Infections With Polioviruses

PMID: 13571484

Autor principal/año:

Revista: John P. Fox, 1958 American Journal of Public Health

Infected but vaccinated children appeared to be just as effective sources for intrahousehold spread of virus as did unvaccinated children.

355

Nombre del artículo:

The Influence Of Natural And Artificially Induced Immunity On Alimentary Infections With Polioviruses

PMID: 13571484

Autor principal/año: Revista:

John P. Fox, 1958 American Journal of Public Health

P 9:

Among children without natural immunity there was little variation in the duration of excretion in relation to vaccination... Rather surprisingly, however, tests for the amount of virus present in the first virus-positive specimen revealed nearly as much virus (4.2 mean long infectivity) in stools from children with prior natural immunity as in those, whether vaccinated or not, without natural immunity (4.0 to 4.9 mean log infectivity).

356

Nombre del artículo:

The Influence Of Natural And Artificially Induced Immunity On Alimentary Infections With Polioviruses

PMID:

13571484

Autor principal/año:

Revista:

John P. Fox, 1958

American Journal of Public Health

P 11:

...it is concluded that widespread use of Salk vaccine should not by any reasonable mechanism influence poliovirus dissemination.

357

Nombre del artículo:

Influence Of Vaccination With Formalin Inactivated Vaccine Upon Gastrointestinal Infection With Polioviruses

PMID:

14415906

Autor principal/año:

Revista:

Martha Lipson Lepow, 1960

American Journal of Public Health

The results of this study would indicate that the prior administration of one or two doses of inactivated poliomyelitis vaccine does not reduce the susceptibility of the lower gastrointestinal tract of man to poliovirus infection. These results are in accord with those of Fox, Davis, Koprowski, and Sabin... Vaccination cannot be expected to decrease significantly the number of persons in the community suffering from inapparent poliovirus infections. Therefore, the opportunities of becoming infected will be the same as before vaccine was used, although paralytic disease can be expected to be less frequent.

358

Nombre del artículo:

Influence Of Vaccination With Formalin Inactivated Vaccine Upon Gastrointestinal Infection With Polioviruses

PMID:

14415906

Autor principal/año:

Revista:

Martha Lipson Lepow, 1960

American Journal of Public Health

The observations of Koprowski and Sabin with avirulent viruses, and Fox with natural infection provide more direct evidence concerning this question. They indicate that

antibody, either acquired passively from the mother or resulting from vaccination with killed vaccine, has no effect upon the susceptibility of the bowel.

359

Nombre del artículo:

Influence Of Vaccination With Formalin Inactivated Vaccine Upon Gastrointestinal Infection With Polioviruses PMID: 14415906

Autor principal/año:

Revista:

Martha Lipson Lepow, 1960

American Journal of Public Health

P 11:

It is concluded that immunization with killed poliomyelitis vaccines cannot be expected to decrease the numbers of persons in the community with alimentary poliovirus infection. Thus, vaccination, while of value to the persons immunized, is unlikely to provide protection to those not vaccinated.

360

Nombre del documento:

Polio - The Beginning Of The End

Autor/año: WHO, 1997

Archivo:

https://drive.google.com/open?id=1r0R4dlS UiB6jOtNta-FvrKDD-gFlzW9h

P 20:

Inactivated polio vaccine (IPV) works by producing protective antibodies in the blood—thus preventing the spread of poliovirus to the central nervous system. However, it induces only very low-level immunity to poliovirus inside the gut. As a result, it provides individual protection against polio paralysis but only marginally reduces the spread of wild poliovirus. In a person immunized with IPV, wild virus can still multiply inside the intestines and be shed in stools. Because of this, IPV could not be used to eradicate polio.

361-380

361

Nombre del artículo:

Exit Poliomyelitis-What Next?

Autor principal/año:

Revista:

Sven Gard, 1961

Yale Journal Of Biology And Medicine

P 8

In any event, Salk was inclined to regard the reduced attack rates as an effect of the vaccination, reasoning as follows. If oropharyngeal secretions are more important for transmission of virus in communities where contact with sewage or feces is less likely, and if vaccination has little or no effect upon fecal virus but does have a significant effect upon pharyngeal virus, then it is conceivable that spread of virus may be diminished by effective vaccination...

362

Nombre del artículo:

Exit Poliomyelitis-What Next?

Autor principal/año:

Revista:

Sven Gard, 1961 Yale Journal Of Biology And Medicine

P 8

The evidence supporting the first if seems at best equivocal and as regards the second if, evidence was at the time entirely lacking.

363

Nombre del artículo:

Exit Poliomyelitis-What Next? Autor principal/año: Revista: Sven Gard, 1961 Yale Journal Of Biology And Medicine The New Orleans group in their studies on the spread of virus found no evidence to support the theory that oropharyngeal secretions are more important than fecal excretion where the spread of the virus is concerned. In fact, some of their observations spoke decidedly in favor of the assumption of predominantly fecal spread. Our own observations on the decisive importance of the age of the excreter point in the same direction. Nombre del artículo: PMID: The Influence Of Natural And Artificially Induced Immunity On 13571484 Alimentary Infections With Polioviruses Autor principal/año: Revista: John P. Fox, 1958 American Journal of Public Health P 10: This has led to renewed consideration of the possibility that pharyngeal virus is more important than fecal virus and that vaccination may influence upper alimentary or pharyngeal infection even though it has no effect on the process at a lower level. The

364

Título del libro:

Vaccines (6th edition)

Published by Elsevier Saunders

available data do not seem to support this idea.

https://www.elsevier.com/books/vaccines/plotkin/978-1-4557-0090-5

365

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 586:

Thus, in epidemiological settings where the primary mode of interhuman transmission in affected communities is oral to oral (vs. fecal to oral), IPV can effectively terminate transmission.

366

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 588:

The evidence for herd immunity comes from countries where oral-to-oral transmission was probably the dominant mode of interhuman poliovirus transmission. It is less clear if IPV is able to induce herd immunity in countries where the fecal-to-oral route is thought to be the primary role in transmission.

367

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 587.

368

Nombre del artículo:

The Poliomyelitis Story: A Scientific Hegira

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2589894/pdf/yjbm00092-

0018.pdf

Autor principal/año:

Revista:

Dorothy M. Horstmann, 1985

The Yale Journal Of Biology And Medicine

PMID:

2994307

P 10:

In three countries, Sweden, Finland, and Holland, where only IPV has been used and close to 100 percent of the population has been immunized, virtual elimination of the indigenous infection has also been achieved.

Nombre del artículo: Surveillance of Poliomyelitis in the United States, 1958-61 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1915173/pdf/pubhealthre-porig00096-0009.pdf Autor principal/año: PSU, 1962 P7, Tabla 5. About 20-30% of the paralyzed patients in 1958-61 were vaccinated.

Nombre del artículo: From Emergence to Eradication: The Epidemiology of Poliomyelitis Deconstructed https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2991634/pdf/kwq320.pdf PMID: 20978089

Autor principal/año: Revista:
Neal Nathanson, 2010 American Journal of Epidemiology

P 8.

Prior to the introduction of poliovirus vaccines, each state reported some cases of poliomyelitis every year. However, beginning with the introduction of OPV around 1961, the number of states reporting cases of polio due to wild polioviruses gradually dropped, reaching zero in 1973.

371 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 633:

Most industrialized countries, including many Western European countries, have recommended schedules in the past that relied exclusively on OPV for the prevention of poliomyelitis. More recently, encouraged by progress of the GPEI and by the desire to reduce or eliminate the burden of VAPP, many of the high- and middle-income countries are reevaluating their vaccination policy options. As of 2011, a total of 56 countries and reporting entities rely exclusively on IPV...

Título del libro: Deadly Choices https://www.amazon.com/Deadly-Choices-Anti-Vaccine-Movement-Threatens/dp/0465029620 Autor principal/año: Paul A. Offit, 2011 Publicador: Basic Books P 127: Because international travel is common, and because most people who are contagious aren't sick, it is likely that poliovirus walks into the United States every year.

373	Nombre del artículo: The Israeli public health response to wild poliovirus importation		PMID: 26213249
	Autor principal/año: Ehud Kaliner, 2015	Revista: Lancet Infectious Diseases	

P 4:

Finally, the Ministry of Health accepted the emergency response team's recommendation to reduce the risk for re-emergence of wild poliovirus type 1 by vaccinating, from 2014 onwards, all children born after July 1, 2013, with a dose of bOPV at age 6 months and a second dose at age 18 months, in addition to the routine IPV-only schedule.

374

Título del libro:

Patenting The Sun: Polio and the Salk Vaccine

https://www.amazon.com/Patenting-Sun-Polio-Salk-Vaccine/dp/0688094945

Autor principal/año: Publicador:

Jane S. Smith, 1990 William Morrow & Co

P 359-367.

375

Título del libro:

Patenting The Sun: Polio and the Salk Vaccine

https://www.amazon.com/Patenting-Sun-Polio-Salk-Vaccine/dp/0688094945

Autor principal/año: Publicador:

Jane S. Smith, 1990 William Morrow & Co

P 360.

376

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1430:

As a result of this much-publicized "Cutter incident" [...] administrative authority for the regulation of biologicals was transferred by Congress to the Division of Biologics Standards (DBS), a newly created division within the NIH.

377

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1311

However, there was no specific federal involvement in immunization activities until 1955, when the IPV vaccine was licensed. Through the Polio Vaccination Assistance Act, Congress appropriated funds in 1955 and 1956 to the Communicable Disease Center (now the CDC) to help states and local communities buy and administer vaccine.

378

Título del libro:

Patenting The Sun: Polio and the Salk Vaccine

https://www.amazon.com/Patenting-Sun-Polio-Salk-Vaccine/dp/0688094945

Autor principal/año: Publicador:

Jane S. Smith, 1990 William Morrow & Co

P 354

The failure of the Department of Health, Education and Welfare to make any plans for allocating the limited supplies of polio vaccine or to discuss any measures for paying for the vaccinations of those unable to afford them, seems to have been not an oversight but an ideological decision... [Secretary Hobby] apparently saw the polio vaccine program as a routine matter of manufacture and commerce, best handled by the private sector.

379

Título del libro:

Patenting The Sun: Polio and the Salk Vaccine https://www.amazon.com/Patenting-Sun-Polio-Salk-

Vaccine/dp/0688094945

Autor principal/año: Publicador:

Jane S. Smith, 1990 William Morrow & Co

P 369

Spurred by the kinds of problems that brought on the Cutter incident, the federal government has since assumed a much more active role in regulating the production of biomedical products...

380

Título del libro:

Patenting The Sun: Polio and the Salk Vaccine https://www.amazon.com/Patenting-Sun-Polio-Salk-

Vaccine/dp/0688094945

Publicador:

Autor principal/año: Jane S. Smith, 1990

William Morrow & Co

P 368:

The laboratory of Biologics Control... was reorganized in the wake of the tragic problems with polio vaccine. On July 15, 1955 it was named Bureau of Biologics, with the promise of a greatly expanded staff and newly enlarged facilities for vaccine testing... By 1956 over one hundred people worked in the polio division, testing vaccines.

381-400

381

Título del libro:

Patenting The Sun: Polio and the Salk Vaccine https://www.amazon.com/Patenting-Sun-Polio-Salk-

Vaccine/dp/0688094945

Publicador:

Autor principal/año: Jane S. Smith, 1990

William Morrow & Co

P 369:

For the epidemiologists of the Communicable Disease Center, the Cutter incident was the crisis that made their reputation... One of Surgeon General Scheele's first acts after the early reports of problems with Cutter vaccine was to establish a program of national surveillance, with all states reporting cases of poliomyelitis directly to the CDC in Atlanta.

382

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1311:

Through the Polio Vaccination Assistance Act, Congress appropriated funds in 1955 and 1956 to the Communicable Disease Center (now the CDC) to help states and local communities buy and administer vaccine.

383

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 1311:

When the grant program began in 1963, the only vaccines available were diphtheria and tetanus toxoids and whole-cell pertussis (DTP), polio, and smallpox. Since that time, funding has been expanded to cover vaccines routinely recommended for children.

384

Nombre del artículo:

Safety Testing of Poliomyelitis Vaccine

PMID:

13432758

Autor principal/año: Revista:
Paul Meier, 1957 Science

P 4

Many of the technical reports and publications which have appeared both before and after the Cutter incident have been vague about those facts which might open the status of the program to criticism. For example, the public statement proceeding the field trial did not mention the finding of live virus... Perhaps the most disturbing element of the entire program has been the disparity between the risks that were known to be involved and the repeated assurances of safety.

385 Nombre del artículo:

Safety Testing of Poliomyelitis Vaccine

PMID: 13432758

Autor principal/año: Revista: Paul Meier, 1957 Science

P 4

To the query, "what is the estimated calculated risk of inducing poliomyelitis infection by the inoculation of vaccine under present safety standards?" the foundation reply is "None, No risk"

Archivo:

386

Nombre del artículo:

The Present Status of Polio Vaccines

https://drive.google.com/open?id=13MEzjI

rvcvuzbltwTqBhGiOm8nZln2I4

Autor principal/año: Revista:

Herbert Ratner, 1960 Illinois Medical Journal

p 9

How is it that today you hear from the members of this panel that the Salk vaccine situation is confused; yet, what everybody knows from reading the newspapers, and has been known since the vaccine was introduced, is that the situation as far as the Salk vaccine is concerned was and is marvelous?

...the best way to push forward a new program is to decide on what you think the best decision is and not question it thereafter, and further, not to raise questions before the public or expose the public to open discussion of the issue.

387

Título del libro:

The Cutter Incident: How America's First Polio Vaccine Led to the Growing Vaccine Crisis

https://www.amazon.com/Cutter-Incident-Americas-Vaccine-Growing/dp/0300126050

Autor principal/año: Publicador:

Paul A. Offit, 2005 Yale University Press

P 101-102.

388

Título del libro:

The Cutter Incident: How America's First Polio Vaccine Led to the Growing Vaccine Crisis

https://www.amazon.com/Cutter-Incident-Americas-Vaccine-Growing/dp/0300126050

Autor principal/año: Publicador:

Paul A. Offit, 2005 Yale University Press

P 102:

Quietly and with little attention from the public or the media, Wyeth recalled one lot of its vaccine.

389

Título del libro:

The Cutter Incident: How America's First Polio Vaccine Led to the Growing Vaccine Crisis

https://www.amazon.com/Cutter-Incident-Americas-Vaccine-Growing/dp/0300126050

Autor principal/año: Publicador:

Paul A. Offit, 2005 Yale University Press

P 102:

The Wyeth Problem [report] was sent to the director of the Communicable Diseases Center, the director of the National Institutes of Health, the Surgeon General of the United States, and the director of the Laboratory of Biologics Control. It was never released to the media, never shown to polio researchers, never shown to the National Foundation, never shown to polio vaccine advisers, never distributed to health care professionals, never published in medical journals, and never made available to defense attorneys in subsequent lawsuits against Cutter Laboratories. As a result, only a handful of people knew about the problem with Wyeth's vaccine.

390

Título del libro:

The Cutter Incident: How America's First Polio Vaccine Led to the Growing Vaccine Crisis

https://www.amazon.com/Cutter-Incident-Americas-Vaccine-Growing/dp/0300126050

Autor principal/año: Publicador:

Paul A. Offit, 2005 Yale University Press

P 103:

Nathanson surmised that the government never publicly disclosed the Wyeth problem because it wanted to maintain the public's trust in the polio vaccine program. If people thought that the problem was limited to one company's incompetence, the solution was simply to eliminate that company's vaccine. But if the problem was industrywide, people would be afraid to use any polio vaccine. "As long as the problem was with one manufacturer and a couple of lots of vaccine," Nathanson recalled, "it would be viewed as an aberration due to sloppy manufacturing or testing procedures and not an intrinsic problem. Once it was extended to a second manufacturer, it would be seen as intrinsic to the product."

391	An abbreviated description of the SV-40 affair appears in - Nombre del artículo: Monkeys, viruses, and vaccines https://www.thelancet.com/action/showPdf?pii=S0140-6736%2804%2916746-9			
	Autor principal/año: Tom Curtis, 2004	Revista: Lancet		
	P 1.			
	A more in-depth description appears here - Nombre del artículo: The Virus and the Vaccine Sitio web: The Atlantic https://www.theatlantic.com/magazine/archive/2000/02/the-virus-and-the-vaccine/377999/ Archivo: https://archive/2000/02/the-virus-and-the-vaccine/377999/			Fecha: Feb 2000
				ve.is/xxoiH
	In addition, Paul Offit also confirms the main points - Título del libro: Deadly Choices https://www.amazon.com/Deadly-Choices-Anti-Vaccine-Movement-Threatens/dp/0465029620			

Autor principal/año: Paul A. Offit, 2011	Publicador: Basic Books
P 17.	

392 Nombre del artículo:

Transmission Of Poliomyelitis Virus

PMID: 14889394

Autor principal/año: Albert B. Sabin, 1951 Revista: Journal of Pediatrics

P 7:

...one of the most striking facts in the epidemiology of poliomyelitis is the regularity with which most members of a family either succumb within a few days of one another when there are multiple frank cases, or are found to be simultaneous carriers of the virus. While there are a number of possible explanations for this, all of which may apply at different times, the consumption of a common article of food or drink, contaminated before or after it reaches the home, is as plausible and possible as any other.

393 Nombre del artículo:

Poliomyelitis Problems

PMID: 14796117

Autor principal/año:

Revista:

Archibald L. Hoyne, 1951

Medical clinics of North America

Foods, including milk and water, have all been acquitted as vectors.

394 Nombre del artículo:

Review: Science and the Law: The Case of DDT

Reviewed Work: DDT: Scientists, Citizens, and Public Policy. by Thomas R. Dunlap

https://www.jstor.org/stable/2701809

Autor principal/año: Revista:

Reviews in American History John H. Perkins, 1982

DDT was sufficiently cheap and effective to open up new possibilities for insecticide use that has previously been technically and economically impossible.

395

Nombre del artículo:

Present Position of DDT in the Control of Insects of Medical Importance

Autor principal/año:

Revista:

Fred C. Bishopp, 1946

American Journal of Public Health

DDT is a nerve poison, as indicated by the early appearance of muscular tremors and other symptoms.

396

Nombre del artículo:

Present Position of DDT in the Control of Insects of Medical Importance

Autor principal/año: Revista:

Fred C. Bishopp, 1946

American Journal of Public Health

P 2:

DDT must not be allowed to get into foods or to be ingested accidentally.

397

Nombre del artículo:

Present Position of DDT in the Control of Insects of Medical Importance

Autor principal/año:	Revista:
Fred C. Bishopp, 1946	American Journal of Public Health

P 2:

One of the outstanding characteristics of DDT is its persistence. In fact, this is perhaps the major element in making it superior to many other insecticides. This persistence, however, makes it necessary to use care when applying it on crops or products intended for food or feed.

398 No

Nombre del artículo:

Possible Hazards From The Use of DDT https://ajph.aphapublications.org/doi/pdf/10.2 105/AJPH.39.7.925

Archivo:

https://drive.google.com/open?id=1n3Ni yviMKqjEFbZ9PzowYd0R-2L6DA6t

Autor principal/año: Revista:

Editorial (unsigned), 1949 American Journal of Public Health

P 2:

In April it urged 5 that "this insecticide not be applied to animals producing milk for human consumption. In the light of current information the Bureau also advises that safer materials be used for insect control in places where the milk might be contaminated, such as dairy barns, milk rooms, rooms containing dairy feed, or in similar situations on the farm. Nor should DDT be used for fly control in milk-processing plants.

399

Nombre del artículo:

Public Health Aspects Of The New Insecticides

Autor principal/año: Revista:

Morton S. Biskind, 1953 American Journal of Digestive Diseases

P 1:

DDT is a delayed-action poison. Due to the fact that it accumulates in the body tissues, especially in females, the repeated inhalation or ingestion of DDT constitutes a distinct health hazard. The deleterious effects are manifested principally in the liver, spleen, kidneys and spinal cord... DDT is excreted in the milk of cows and of nursing mothers after exposure to DDT sprays and after consuming food contaminated with this poison. Children and infants especially are much more susceptible to poisoning than adults.

400

Nombre del documento:

Health Hazards Of Electric Vaporizing Devices For Insecticides

Autor principal/año:

AMA Council On Pharmacy And

Chemistry, 1952

Archivo:

https://drive.google.com/open?id=1Um6gN AsFgcM-TDf5Po7IAT0c6BSKtwK7

P 1:

...it is not reasonable to expect that human beings can avoid injury if they are exposed year after year to a toxic agent in atmospheric concentrations that kill insects in a few hours... the resultant injury may be cumulative or delayed, or simulate a chronic disease of other origin, thereby making identification and statistical comparison difficult or impossible.

401-420

401

Nombre de la página:

Select Committee to Investigate the Use of Chemicals in Food and Cosmetics (1950-52)

Sitio web:

Archives.GOV

 $\underline{https://www.archives.gov/legislative/guide/house/chapter-22-select-food-and-cosmetics.html}$

The committee was authorized to inquire into the extent and the effect of the use of chemicals, synthetics, pesticides, and insecticides in the production and preparation of food products and to determine the effects of such use on the public and upon agricultural stability.

402

Nombre del documento:

A Legislative History of the Pesticide Residues Amendment of 1954 and the Delaney Clause of the Food Additives Amendment of 1958 https://www.ncbi.nlm.nih.gov/books/NBK218051/

Autor principal/año:

http://archive.is/pPZ1p

Archivo:

Bruce S. Wilson, 1987

P 2-3:

On June 30, 1952, the House Select Committee to Investigate the Use of Chemicals in Foods and Cosmetics (Delaney Committee) culminated its two-year investigation into the "nature, extent and effect of the use of chemicals" in food and food production. The committee recommended that the House pass legislation to control the flow of chemical substances into the nation's food supply.

403

Nombre del documento:

Public Law 518 STATUTE-68

Autor principal/año:

Archivo:

US, 1954

https://drive.google.com/open?id=1TbDH-ACNLOpuwTlyWdRcrIpeS75xuLfT

P 1-2.

404

Nombre del documento:

Health Hazards Of Electric Vaporizing Devices For Insecticides

Autor principal/año:

Archivo:

AMA Council On Pharmacy And Chemistry, 1952

https://drive.google.com/open?id=1Um6gN AsFgcM-TDf5Po7IAT0c6BSKtwK7

P 2-3:

Federal regulatory agencies, particularly the Insecticide Division, United States Department of Agriculture, have challenged the promotion and use of these dispensers in homes and small capacity areas... Several states and municipalities have recognized the urgency of this problem at the state and local level and are considering ordinances and other types of appropriate regulations.

405

Nombre del documento:

Health Hazards Of Electric Vaporizing Devices For Insecticides

Autor principal/año:

Archivo:

AMA Council On Pharmacy And Chemistry, 1952

https://drive.google.com/open?id=1Um6gN AsFgcM-TDf5Po7IAT0c6BSKtwK7

P 1-2:

This atmospheric level of lindane coupled with its comparatively greater freedom from long-term toxic effects may have partially influenced the change from DDT which has occurred in the use of the automatic, thermostatically controlled type of insecticide generators. The principal reason behind this change, however, was the increasing incidence of insect resistance which is being encountered with the use of DDT. Resistance

factors may have also contributed to selection of lindane as the impregnate in insecticide fumigating strips which in continental Europe are being proposed for home and commercial use.

406 Nombre del artículo:

The epidemiology of poliomyelitis: enigmas surrounding its appearance, epidemicity, and disappearance

PMID: 400274

Autor principal/año: Neal Nathanson, 1979 Revista:

American Journal of Epidemiology

As a disappearing disease, interest in poliomyelitis has waned during the 25 years since the introduction of inactivated poliovirus vaccine (IPV).

407

Nombre del artículo:

Some Observations on Poliomyelitis Lameness Surveys

PMID: 6740075

Autor principal/año:

Revista:

Roger H. Bernier, 1984

Reviews of Infectious Diseases

408

Nombre del artículo:

Some Observations on Poliomyelitis Lameness Surveys

PMID: 6740075

Autor principal/año:

Revista: Roger H. Bernier, 1984

Reviews of Infectious Diseases

P 2-3, Tabla 1.

Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

In the last three decades, a series of lameness surveys were conducted in many developing countries that reported between 5 and 10 lameness cases per 1,000 children in the age group studied, suggesting that approximately 1 in 100 to 1 in 200 children acquire paralytic disease attributable to poliovirus.

409

Nombre del artículo:

The Epidemiology of Polio in Israel - An Historical Perspective

Autor principal/año:

Revista:

Tiberio A. Swartz, 2008 Israel Center for Disease Control (ICDC), Ministry of Health

Israel data appear on page 45, Table 4.3.

410

Nombre del artículo:

Differential Diagnosis of Acute Flaccid Paralysis and Its Role in

PMID: 11218380

Poliomyelitis Surveillance

Autor principal/año:

Revista:

Arthur Marx, 2000 Epidemiologic Reviews

P 7:

lower socioeconomic status... have been shown to increase the risk of acquiring paralytic manifestations,...

411 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 573-574

...polio was a worldwide disease with an incidence in the tropics that was as high as that in the developed world, but it was unrecognized due to the concentration of cases in infants younger than 2-years-old.

Nombre del artículo: Some Observations on Poliomyelitis Lameness Surveys Autor principal/año: Roger H. Bernier, 1984 Reviews of Infectious Diseases

P 2.

413 Nombre del artículo:

From malaria control to eradication: The WHO perspective https://onlinelibrary.wiley.com/doi/epdf/10.1111/j.1365-3156.2009.02287.x

Autor principal/año: Revista:

Kamini Mendis, 2009 Tropical Medicine and International Health

P 2

When the potent tools DDT and chloroquine became available, WHO launched the Global Malaria Eradication Programme in 1955, which led to a campaign to interrupt transmission in all endemic areas outside tropical Africa where the intensities of transmission were low to moderate (WHO 1956). As a result of this campaign, 37 of the 143 countries that were endemic in 1950 were free from malaria by 1978, including 27 in Europe and the Americas

According to this article, the global fight against malaria began as early as the late 1940s -

PMID: 12364370

PMID:

19497083

Nombre del artículo:

Evolutionary and Historical Aspects of the Burden of Malaria https://www.ncbi.nlm.nih.gov/pmc/articles/PMC126857/

Autor principal/año: Revista:

Richard Carter, 2002 Clinical Microbiology Reviews

P 21

In the late 1940s and early 1950s, national malaria control campaigns were established in almost all of the affected countries of the region, from the Middle East, through the Indian subcontinent and Southeast Asia, to the islands of the Western Pacific, including those of Indonesia and the Philippines. Under the broad direction and encouragement of the newly formed World Health Organization, and employing the residual insecticide DDT to spray homes, spectacular reductions in malaria incidence and malaria-related mortality were achieved, especially in India and Ceylon...

414 Nombre del artículo:

Paris Green in the Eradication of Anopheles Gambiae: Brazil 1940, Egypt 1945

Autor principal/año: Revista:

Fred L. Soper, 1966 Journal of the American Mosquito Control Association

P 1:

Egypt eradication came in 1945, three years after the invasion occurred. The basic method used in each country was a straightforward chemical attack with Paris Green.

P 6.

In Egypt, as in Brazil, gambiae proved to be highly susceptible to Paris Green larviciding.

Green that was used to eradicate the vector.

The last gambiae in Egypt was found on February 19, 1945, just seven months after routine application of Paris Green began.

Nombre del artículo:
Eradication of Anopheles gambiae from Brazil: lessons for malaria control in Africa?

Autor principal/año:
Gerry F Killeen, 2002

Revista:
Lancet Infectious Diseases

P 6:
The Rockefeller team was summoned and adapted the methods developed in Brazil to the ecological situation in Egypt. Although DDT had become available, its use was limited to residual spraying of railway carriages, aeroplanes, and boats. While domestic pyrethrum

A Survey Of Neutralizing Antibodies To Poliomyelitis Virus In Cairo,
Egypt

Autor principal/año:
John R. Paul, 1952

Revista:
American Journal of Epidemiology

P 1-2.

spraying was used to quell epidemic malaria transmission, it was larviciding with Paris

416 PMID: Nombre del artículo: Epidemiology Of Poliomyelitis And Allied 14064722 Diseases--1963 Archivo: https://www.ncbi.nlm.nih.gov/pmc/articles/P https://drive.google.com/open?id=1fV_w0 MC2604573/pdf/vjbm00599-0011.pdf 3BSORQKex-hR7DkGZH44EXUwpTv Autor principal/año: Revista: Dorothy M. Horstmann, 1963 Yale Journal of Biology and Medicine For, although virtual control of paralytic poliomyelitis has been achieved in large geographical areas, in others (particularly tropical and sub-tropical ones) the disease is only now beginning to appear for the first time in epidemic form.

In 2009 scientists warn against using DDT to eradicate malaria
Nombre del artículo:
Should DDT Be Used to Combat Malaria?

Sitio web:
Scientific American
https://www.scientificamerican.com/article/ddt-use-to-combat-malaria/

Nigeria, India and other African countries continue to use DDT against malaria Nombre del artículo: African countries adopt controversial deadly chemical, DDT, for malaria treatment Sitio web: Fecha: July 17, 2013 Archivo: http://archive.is/5NhNd

Premium Times http://www.premiumtimesng.com/news/141150-african-countries-adopt-controversial-deadly-chemical-ddt-for-malaria-treatment.html

	DDT is found extensively in adipose tissue, breast milk and blood in the bodies of Third World humans in agricultural areas and areas sprayed against malaria. Nombre del artículo: Agricultural Pesticide Use In Developing Countries: Health Effects And Research Needs			PMID: 9142603
	Autor principal/año: Catharina Wesseling, 1997	Revista: International	Journal of Health Service	
	P 18.			
	The use of DDT for the fight again was stopped and re-started seven For example, in 2006, the WHO the use of DDT to combat malaring the seven seven the seven seven the seven seven seven the seven se	eral times. re-approved	Archivo: http://archive.is/bn2o	
	Nombre de la página: WHO gives indoor use of DDT a clean bill of health for controlling malaria			
Sitio web: WHO http://www.who.int/mediacentre/news/releases/2006/pr50/en			s/2006/pr50/en/	
	In 1994, a survey of three African countries - Uganda, Kenya and Tanzania - found use of DDT. Nombre del artículo: Agricultural Pesticide Use In Developing Countries: Health Effects And Research Needs			PMID: 9142603
	Autor principal/año: Revista: Catharina Wesseling, 1997 International Journal of Health Service			
	P 5.			

Nombre del documento: TOXICS AND POVERTY: The Impact of Toxic Substances On the Poor in Developing Countries Archivo: https://drive.google.com/open?id=1B qiPquQKvBUxnCP11icG1FwNmzkj OEpP Autor principal/año: World Bank, 2002

P 46

Overall, WHO food-sampling data indicated that DDT and its derivatives (DDE and DDD) have the highest levels in the food supply directly in countries where DDT is still in use or only recently has been banned; they continue to be found in the food chain in countries where DDT use has been prohibited for many years. Substantial quantities of DDT and its metabolites are found in human blood, fat tissue, and breast milk in surveys around the world.

420	Nombre del artículo: Agricultural Pesticide Use In Developing Countries: Health Effects And Research Needs		PMID: 9142603
	Autor principal/año: Catharina Wesseling, 1997	Revista: International Journal of Health Service	
	P 4: According to the review of the WHOLJNEP Working Group, developing countries consume only between 20 and 25 percent of the world pesticide production. However, the review noted that the fastest growing markets are located in developing regions such as		

Africa, South and Central America, Asia, and the Eastern Mediterranean Region and that pesticide use in developing countries would double between 1983 and 1993.

421-440

Autor principal/año:
Arthur Marx, 2000

P 11:
Exposure (often agricultural or industrial) to chemicals such as lead, arsenic... may cause peripheral motor neuropathy... Arsenic-containing compounds such as melarsoprol are still being used in developing countries for the treatment of African trypanosomiasis (sleeping sickness) and may cause Guillain-Barre syndrome-like AFP.

Agricultural Pesticide Use In Developing Countries: Health Effects And Research Needs Autor principal/año: Catharina Wesseling, 1997 Revista: International Journal of Health Service P 1: Over 60 percent of the economically active population in the Third World depends on agriculture. Agricultural workers are exposed to many risk factors such as biological, physical, and chemical agents, and trauma, but the use of toxic pesticides is likely to be one of the most relevant occupational hazards for agricultural workers in the Third World.

423	Nombre del artículo: Pesticides, health and environment	Fecha: Mar 26, 2007	
	Sitio web: Pakissan http://www.pakissan.com/english/news/newsDetail.php?ne http://www.pakissan.com/english/news/newsDetail.php?ne wsid=13465	Archivo: http://archive.is/yZN6D	
	Some of the classical members of following groups are used in Pakistan: Chlorinated Hydrocarbon Pesticide: (1) Aldrin, (2) BHC (lindane/gammexane), (3) Chlordane, (4) DDT, (5) Dieldrin, (6) Endrin, (7) Heptachlor, (8) Thiodane.		
	Nombre del artículo: How Pakistan's farmers are cleaning up cotton	Fecha: Jun 27, 2011	
	Sitio web: The Telegraph https://www.telegraph.co.uk/journalists/sally- williams/8592326/How-Pakistans-farmers-are-cleaning- up-cotton.html	Archivo: http://archive.is/uZN0W	
	Then there is the black market. Here farmers can buy illegal seeds and the sort of highly toxic mix where incorrect application results in more than dead bollworms. DDT (dichlorodiphenyltrichloroethane), for example, belongs to one of the most hazardous groups of chemicals called persistent organic pollutants		
	Nombre del artículo: Persistence Of DDT Pesticides In Residues Of Tobacco Crop		

https://fuuast.edu.pk/biology%20journal/images/pdfs/2ndis sueallpaperpdf/PERSISTENCE%20OF%20DDT%20PES TICIDES%20IN%20RESIDUES%20OF%20TOBACCO %20CROP.pdf

Autor/año:

Nusrtat Hassan, 2011

It is suggested that since people in Pakistan, Particularly in northern parts, use homemade tobacco preparations for chewing purposes, therefore DDT spray even in nursery stages are not recommended due to its toxic nature

424 Nombre del artículo:

Differential Diagnosis of Acute Flaccid Paralysis and Its Role in

PMID: 11218380

Poliomyelitis Surveillance

Revista:

Autor principal/año: Arthur Marx, 2000

Epidemiologic Reviews

P 11:

Exposure (often agricultural or industrial) to chemicals such as lead, arsenic... may cause peripheral motor neuropathy... Arsenic-containing compounds such as melarsoprol are still being used in developing countries for the treatment of African trypanosomiasis (sleeping sickness) and may cause Guillain-Barre syndrome-like AFP.

425 Nombre del artículo:

Pesticide use in developing countries

PMID: 11246121

Autor principal/año: Revista: Donald J. Ecobichon, 2001 Toxicology

In agriculture, the tendency is to use 'older', nonpatented, least expensive, more acutely toxic and environmentally persistent agents that can be manufactured in country or formulated from active ingredients imported from regional sources having chemicals synthesizing capabilities. Many of these chemicals have been banned or their use severely restricted in 'western' nations but are freely available on the world market.

426 Nombre del artículo:

Agricultural Pesticide Use In Developing Countries: Health Effects

PMID:

And Research Needs

9142603

Autor principal/año:

Catharina Wesseling, 1997

International Journal of Health Service

P 6:

Inadequate agricultural practices, ignorance of the dangers inherent in pesticides, illiteracy, poor legislation, and lack of enforcement are generally the rule in Third World countries, and greatly increase the risks for workers and the general population in these countries.

427

Nombre del artículo: Agricultural Pesticide Use In Developing Countries: Health Effects PMID:

And Research Needs

9142603

Autor principal/año: Catharina Wesseling, 1997

International Journal of Health Service

P 2, 4-5, 14.

428

Nombre del artículo:

Pesticide use in developing countries

PMID:

11246121

	Autor principal/año: Donald J. Ecobichon, 2001	Revista: Toxicology	
	P 3:		
Examination of recent literature reveals that the largest proportion of human acute toxic			
	data related to pesticide intoxications comes from developing nations.		

429	Nombre del documento: Eradication Of Poliomyelitis http://apps.who.int/gb/archive/pdf_files/WHA57/A57_8-en.pdf		
	Autor/año: WHO, 2004	Archivo: https://drive.google.com/open?id=1zQQ DktBDr1bAexQD4Wear	Ov0K5OGFKGaF

430	Nombre del artículo: Paralytic poliomyelitis: seasoned strategies, disappearing disease		PMID: 7910329
	Autor principal/año: Harry F. Hull, 1994	Revista: Lancet	
	P 1: Current eradication strategies recommended by the Worl national mass campaigns administering oral polio vaccin age, enhanced surveillance to detect cases of acute flaccillaboratories for viral diagnosis, and targeted immunization poliovirus transmission is likely to persist.		under 5 years of ting a network of

431	Nombre del documento: The Time To Eradicate Polio Is Now	
	Autor/año: CDC, 2014	Archivo: https://drive.google.com/open?id=16bIfvF2FotFsAxAsR5x0NmkfEwntow8b

-	,		
432	Nombre del documento: Eradication Of Poliomyelitis http://apps.who.int/gb/archive/pa	df_files/WHA57/A57_8-en.pdf	
	Autor/año: WHO, 2004	Archivo: https://drive.google.com/open?id=1zQOv0K5OGFKGaF DktBDr1bAexQD4Wear	
	P 1: In 1988 wild-type poliovirus paralyzing more than 350,000 cl	was endemic in over 125 countries and on five continents, nildren each year.	
	Nombre del documento: The Time To Eradicate Polio Is Now		
	Autor/año: CDC, 2014	Archivo: https://drive.google.com/open?id=16bIfvF2FotFsAxAsR5x0NmkfEwntow8b	
	P 1: Polio cases worldwide 1988 = 3	50,000	
	Nombre del documento: Polio Eradication		
	Autor/año: UNICEF, 2001	Archivo:	

more.

https://drive.google.com/open?id=1DmySyWXHgy0kj6 YfZ83XK0bdkTY4Wg75 P 1: Polio cases have declined by 99 per cent since the launch of the polio eradication initiative in 1988, from 350,000 to less than 3,500 in 2000. Nombre del artículo: PMID: The global polio eradication initiative: Lessons learned and prospects 22486981 for success Autor principal/año: Revista: Bruce Aylward, 2011 Vaccine At the time of the 1988 WHA resolution on polio, more than 125 countries were still considered to have transmission of indigenous wild polioviruses (WPVs), and each year,

more than 350,000 children were paralyzed by the disease.

433 Nombre del artículo: PMID: Paralytic poliomyelitis: seasoned strategies, disappearing disease 7910329 Autor principal/año: Revista: Harry F. Hull, 1994 Lancet P 14: In 1992, the officially reported figure was 15,406 cases (figure 3) an 8% increase from the 14,199 reported the previous year but a 52% fall from the 32,419 reported in 1988. In its defense, the World Health Organization claimed that the number of reported cases was much lower than its actual rate -15932011 Nombre del artículo: Polio Eradication Initiative In India: Deconstructing The GPEI Autor principal/año: Revista: C. Sathyamala, 2005 International Journal of Health Services P 18: In 1988, when the WHO launched the global eradication program, the total number of paralytic poliomyelitis cases reported worldwide was 32,419. However, the WHO increased the figure 10-fold to justify the claim that paralytic poliomyelitis was a major problem of public health importance. Thus, post facto, the number of polio cases worldwide artificially rose from about 35,000 to 350,000 for 1988. The WHO's argument was that the reported cases were an underestimate and that they were at least ten times

434	Título del libro: Paralyzed with Fear https://www.amazon.com/Paralysed-Fear-Story-Gareth-Williams/dp/1137299754	
	Autor principal/año: Gareth Williams, 2013	Publicador: Palgrave Macmillan
	P 85. Before vaccination took hold, the poliovirus caused virtually all cases of 'acute flaccid paralysis', the clinical hallmark of polio.	

43	Differential Diagnosis of Acute Flaccid Paralysis and Its Role in	PMID: 11218380
	Poliomyelitis Surveillance	

Autor principal/año: Revista:
Arthur Marx, 2000 Reviews

P 1

Acute flaccid paralysis (AFP) is a clinical syndrome characterized by rapid onset of weakness, including (less frequently) =weakness of the muscles of respiration and swallowing, progressing to maximum severity within several days to weeks.

436 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 503. Tabla 28-2.

437 Nombre del artículo:

PMID:

Differential Diagnosis of Acute Flaccid Paralysis and Its Role in Poliomyelitis Surveillance

11218380

Autor principal/año: Arthur Marx, 2000 Revista: Epidemiologic Reviews

P 3-5.

438 Nombre del artículo:

PMID:

Polyneuropathy Following Exposure To Insecticides

14120595

Autor principal/año: Revista:

R. B. Jenkins, 1964 Archives Of Internal Medicine

P 1:

A cause-and-effect relation between exposure to insecticides and subsequent development of polyneuropathy is very difficult to prove even when strongly suspected... Our two patients... might have been considered to be suffering from a sporadic form of the Guillain-Barre' syndrome of cryptogenic origin had not the close association between exposure to insecticide and neurologic manifestations made an etiologic relationship probable.

439 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 601:

Because AFP has many causes, including Guillain-Barre syndrome, transverse myelitis, and infection with nonpolio enteroviruses (see "Differential diagnosis"), laboratory confirmation is critical to establishing the diagnosis of poliomyelitis. The basic approach is to attempt to isolate poliovirus from the stools of patients with AFP and to characterize any poliovirus isolates to determine whether they are vaccine-related or wild.

Nombre del artículo:

PMID:

Paralytic poliomyelitis: seasoned strategies, disappearing disease

7910329

Autor principal/año: Revista: Harry F. Hull, 1994 Lancet

P 1

A syndrome identical to polio is caused by other enteroviruses, notably enterovirus 71, and some atypical cases may be difficult to differentiate clinically from Guillain-Barre syndrome. A definitive diagnosis requires laboratory confirmation, and virus isolation from stools is the most reliable test.

440 Por ejemplo, in Australia -

Nombre del documento:

Poliovirus infection case definition summary

https://www.health.gov.au/internet/main/publishing.nsf/Content/cda-phlncdpolio.htm/\$FILE/polio.pdf

Autor principal/año:

Public Health Laboratory Network (Australia), 2000

Archivo:

https://drive.google.com/open?id=1RCX0f4JIgD Whu4Ypvf55CUPB8b1FJg3f

P 7:

- 4.2 Paralytic Poliomyelitis Potential Case = Acute Flaccid Paralysis: Any case of acute flaccid paralysis (AFP), a syndrome characterised by acute onset of progressive weakness and flaccidity of the extremities without sensory loss, plus/minus weakness of muscles of respiration & swallowing, progressing to maximum severity within 1-10 days.
- 4.3 Paralytic Poliomyelitis Confirmed Case: A case of acute flaccid paralysis with culture of wild-type poliovirus from the throat, blood, faeces or CNS material confirmed by the RRL.

441-447

441 Nombre abreviado:

Plotkin 2013 - Vaccines (6th edition)

P 638, picture 28-12.

442 Nombre del artículo:

Polio programme: let us declare victory and move on

PMID: 22591873

Autor principal/año: Revista:

Neetu Vashisht, 2012 Indian Journal of Medical Ethics

It is sad that, even after meticulous surveillance, this large excess in the incidence of paralysis was not investigated as a possible signal, nor was any effort made to try and study the mechanism for this spurt in non-polio.

443 Nombre del artículo:

Jan 3, 2013 Polio free does not mean paralysis free

Sitio web:

The Hindu

http://www.thehindu.com/opinion/lead/polio-free-does-

not-mean-paralysis-free/article4266043.ece

Archivo: http://archive.is/EGiTb

Fecha:

Unfortunately, the cases of children with non-polio AFP were not being monitored by either the polio eradication programme or the larger state health care system. As a result, there was no clear picture of what was causing the AFP, the kind of diseases these children displayed, or how many of them were seriously affected.

444 Nombre del artículo:

Eradicating poliomyelitis: India's journey from hyperendemic to

PMID: 23760372

polio-free status

Autor principal/año: Revista:

T. Jacob John, 2013 Indian Journal Of Medical Research

Many children got polio in spite of seven or 10 or even 15 doses of tOPV.

Nombre del artículo:
Asymptomatic Wild-Type Poliovirus Infection in India among Children with Previous Oral Poliovirus Vaccination

Autor principal/año:
Nicholas C. Grassly, 2010

Revista:
Journal of Infectious Diseases

P 6, Tabla 2:
Nearly 60% of the children in the study received more than 10 vaccine doses.

Autor principal/año:
Neetu Vashisht, 2012

P 2:
This shows that the non-polio AFP rate increases in proportion to the number of polio vaccines doses received in each area. Nationally, the non-polio AFP rate is now 12 times higher than expected.

Nombre del artículo:
Paralytic consequences of poliomyelitis infection in different parts of the world and in different population groups
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1525657/pdf/amjphnation

PMID:
14885514

Autor principal/año:
Albert B. Sabin, 1951

Revista:
Albert B. Sabin, 1951

P 10:
...the goal of poliomyelitis research is not the elimination of poliomyelitis infection but of the paralysis which is the important consequence of that infection.

Autor principal/año: Neal Nathanson, 1979 PMID: 400274 Revista: American Journal of Epidemiology P 1: Poliomyelitis has undoubtedly received as much attention from epidemiologists as any other viral disease of man. Yet in spite of intensive study over a century, many of the salient epidemiologic features of this infection must still be considered enigmas. Even some of the accepted dogmas about poliomyelitis can be debated as perhaps erroneous.