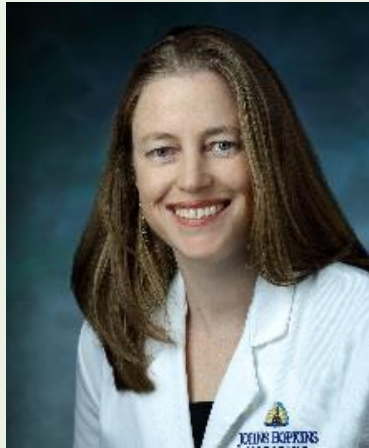


Gut and Immune System

Can We Finally Eat That Peanut?



Corinne Keet, M.D., Ph.D.

Associate Professor of Pediatrics



What is food allergy?

- Food allergy is a specific **immune** response to a food
 - Most commonly caused by IgE antibodies to foods
 - Requires prior sensitization to that food
- There is no FDA approved treatment for food allergy
 - The only accepted management is avoidance of the food and use of self-injectable epinephrine for reactions.
- Food allergy in general, and peanut allergy in particular, appears to be increasing
- Eczema (AKA atopic dermatitis) is a strong risk factor for food allergy



180° on peanut allergy prevention: official guidelines

2000: For high risk infants, it may be reasonable to **delay peanut until 3 years of age**.

2008: There is **no evidence** for delaying allergenic foods, including peanut.

2017: High risk infants should introduce age-appropriate peanut-containing food **as early as 4 to 6 months of age to reduce the risk of peanut allergy**.

Hypoallergenic infant formulas. Pediatrics 2000

Greer et al. Effects of early nutritional interventions on the development of atopic disease in infants and children. Pediatrics 2008

Togias et al. Addendum guidelines for the prevention of peanut allergy in the United States. JACI 2017

American Academy of Pediatrics Committee on Nutrition 2000

Infants at high risk for developing allergy, identified by a strong (biparental; parent, and sibling) family history of allergy may benefit from exclusive breastfeeding or a hypoallergenic formula or possibly a partial hydrolysate formula. Conclusive studies are not yet available to permit definitive recommendations. However, the following recommendations seem reasonable at this time:

- Breastfeeding mothers should continue breast feeding for the first year of life or longer. Solid foods should not be introduced into the diet of high-risk infants until 6 months of age, with dairy products delayed until 1 year, eggs until 2 years, and peanuts, nuts, and fish until 3 years of age.

Hypoallergenic infant formulas. Pediatrics Aug 2000, 106 (2) 346-349;

Historical Context



4,000-year-old baby feeder

19th Century "banjo bottle"

The wet nurse, 1802, Marguerite Gérard

<http://www.bbc.com/news/magazine-25629934>

What is he up to now?



He's bubbling over with health and mischief thanks to

"LACTOGEN"

Since he was put on Lactogen, there's no holding him. Lactogen, in giving him every scrap of nourishment he needs, in a way he can so easily digest, gives him boundless vitality, bubbling health. Lactogen is cow's milk—pasture fresh, rich and pure—to this extra cream and milk sugar is added, and the whole is put through processes which break up the fat globules into minute particles for easy digestion. The finished Lactogen is almost identical with Mother's Milk, but slightly richer in those proteins which build muscle and dense bone. Put your Baby on to Lactogen.

"I feel I must write to thank you for all that Lactogen has done for my baby. He was 7½ lbs. at birth, but lost weight so rapidly that we never thought he would live. No food we tried seemed to suit him. At three months old he only weighed just over 8 lbs. Then my Doctor decided to try Lactogen; the first week baby gained 1 lb. and since then he has never looked back, and at the age of 10 months he weighs 21 lbs. naked. His skin is perfect and his eyes so bright everyone remarks how beautiful he is and how firm his limbs are." Nov. 1931.



Mother! Send for Free Lactogen Sample and Booklet

To The LACTOGEN BABY BUREAU
(Dept. R.P.168), St. George's House,
Eastcheap, London, E.C.3

Please send me a sample tin of Lactogen and a copy of your booklet "Early Days."

Name.....

Address.....

My baby is..... months old.
I expect baby about.....

Wise advice is given in such a simple way in "Early Days." For Baby's sake send now.

PER 2/9 TIN

from all Chemists



By 1946, the proportion of newborns exclusively breastfed at hospital discharge was only 38%

Ads from the 1940s from Nestle and Carnation



Now it's easy!

Gerber's NEW Meats for Baby so good . . . so time-saving . . . so economical!

They're **ARMOUR** Quality Beef! Veal! Liver!

In these new meats produced and brought to you by Gerber's and Armour, you can see the high quality—you can taste it too! For these meats for your baby have true-meat color, plus the lean-meat goodness for which Armour is famous. And you can get this quality at real savings in time, work and money.

Spend 3 minutes instead of 35 preparing tasty veal for baby. *Just heat!* No tiresome scraping! You'll save from 10 to 20 minutes of your precious time with strained beef or liver.

All with important high-quality proteins. So, ask your doctor how early in the first year you can add Gerber's Meats to baby's Gerber-good menus of Fruits, Vegetables and Desserts.

All this . . . and savings, too! Several servings in each can. Gerber's Strained Meats for tiny babies and Junior Meats for older tots come in one size can at one moderate price. Far less expensive than home-prepared baby meats.



Accepted by the Council on Foods and Nutrition of the American Medical Association



Gerber's
BABY FOODS
FREMONT, MICH. OAKLAND, CAL.

1949 ad

BRINGING UP BABIES

A FAMILY DOCTOR'S PRACTICAL
APPROACH TO CHILD CARE

BY WALTER W. SACKETT, JR., M.D.

1962



64. At 2-3 Days, Cereal is given to babies under my care at twelve noon and at twelve midnight, again because this is the handiest time for nurses in the hospital to get out on the floor and teach

66. At 10 Days, Strained Vegetables are added to the noon meal.

67. At 14 Days, Strained Meats are offered either at noon, along with the vegetables, or at 6:00 P.M. with the cereal feeding. There is

68. At 17 Days, Soups and Meat Combinations, such as lamb and rice or beef and vegetables, are introduced, and we realize now that baby is eating regular little meals. He may have meat and vegetable

72. At 5 Weeks, Eggs are introduced, and this addition provokes a great deal of controversial comment. Some authorities insist that

74. At 9 Weeks, Bacon and Eggs, Just Like Dad! In not-so-strange

By the mid-1960s the typical age at introduction of solids had decreased from 6-7 months to 4-6 weeks

Backlash against these practices

- Starting in the 1930s, researchers tied infant formula to higher risk of eczema
- In the following decades weak evidence accumulated for protective effect of breast feeding
- In the 1980s, hydrolyzed infant formulas were developed
 - Some evidence that these formulas might reduce the risk of eczema transiently
- Few studies that combined use of hydrolyzed formulas with delayed introduction of solid foods
 - No studies about delayed introduction of peanut alone

Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy

George Du Toit, FRCPCH,^a Yitzhak Katz, MD, PhD,^b Peter Sasieni, PhD,^c David Mesher, MSc,^c Soheila J. Maleki, PhD,^d Helen R. Fisher, BSc,^a Adam T. Fox, FRCPCH,^a Victor Turcanu, MD, PhD,^a Tal Amir,^e Galia Zadik-Mnuhin, MD,^f Adi Cohen, MD,^f Irit Livne, MD,^g and Gideon Lack, FRCPCH^a *London, United Kingdom, Tel Aviv, Haifa, and Jerusalem, Israel, and New Orleans, La*



Peanut allergy prevalence among Jewish children:

Israel: 0.17%

UK: 1.85%

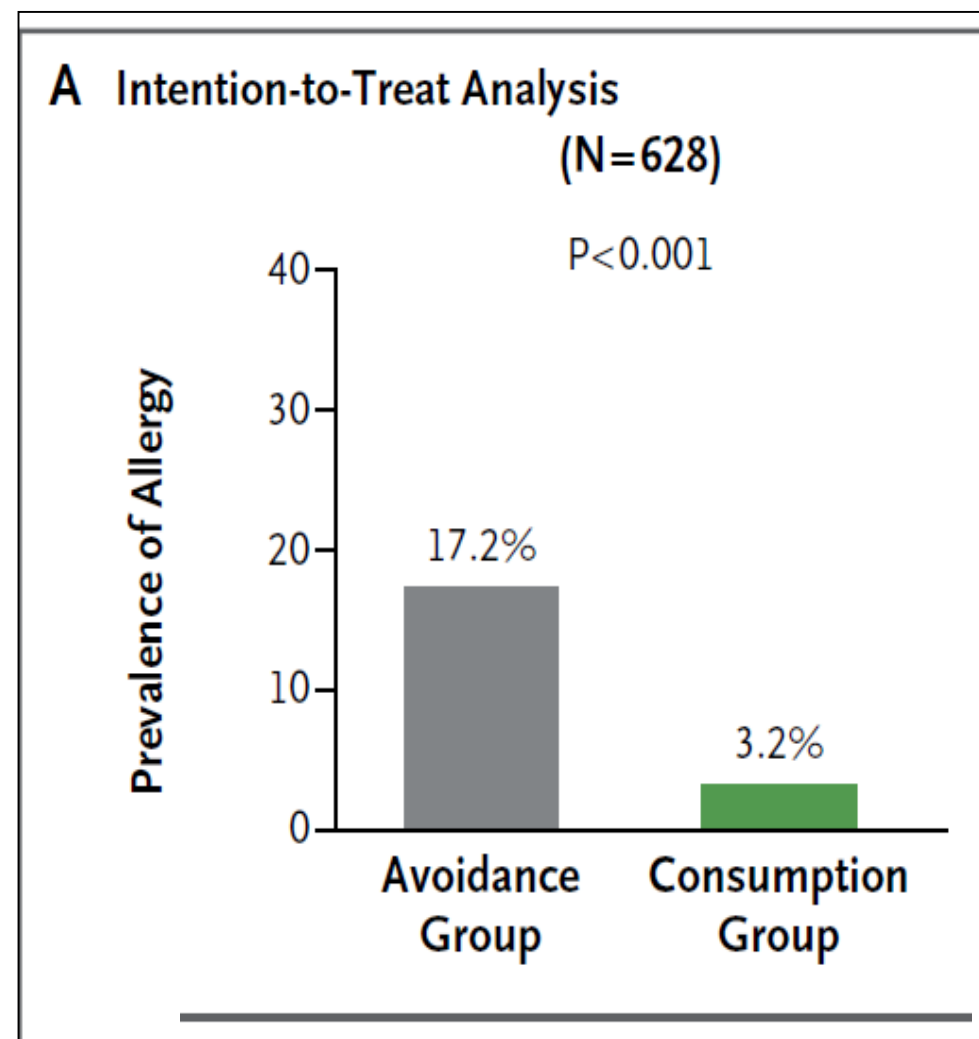
Almost 10 times as much peanut allergy

Peanut consumption in infants:
median 7.1g in Israel vs 0g in UK
per month

Du Toit JACI 2008

LEAP study

- 640 infants aged 4-11 months with severe eczema, egg allergy, or both
- About 11% excluded because they had a large SPT at baseline
- Randomized to 2 groups – peanut avoidance or regular peanut consumption
- Final outcome determined by a peanut food challenge at 5 years



82% Reduction Overall

Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases–sponsored expert panel

Alkis Togias, MD,^a Susan F. Cooper, MSc,^a Maria L. Acebal, JD,^b Amal Assa'ad, MD,^c James R. Baker, Jr, MD,^d Lisa A. Beck, MD,^e Julie Block,^f Carol Byrd-Bredbenner, PhD, RD, FAND,^g Edmond S. Chan, MD, FRCPC,^h Lawrence F. Eichenfield, MD,ⁱ David M. Fleischer, MD,^j George J. Fuchs III, MD,^k Glenn T. Furuta, MD,^l Matthew J. Greenhawt, MD, MBA, MSc,^j Ruchi S. Gupta, MD, MPH,^m Michele Habich, DNP, APN/CNS, CPN,ⁿ Stacie M. Jones, MD,^o Kari Keaton,^p Antonella Muraro, MD, PhD,^q Marshall Plaut, MD,^a Lanny J. Rosenwasser, MD,^r Daniel Rotrosen, MD,^a Hugh A. Sampson, MD,^s Lynda C. Schneider, MD,^t Scott H. Sicherer, MD,^u Robert Sidbury, MD, MPH,^v Jonathan Spergel, MD, PhD,^w David R. Stukus, MD,^x Carina Venter, PhD, RD,^y and Joshua A. Boyce, MD^z

Bethesda, Md; McLean, Va; Cincinnati and Columbus, Ohio; Ann Arbor, Mich; San Rafael and San Diego, Calif; New Brunswick, NJ; Vancouver, British Columbia, Canada; Aurora, Colo; Lexington, Ky; Chicago and Winfield, Ill; Little Rock, Ark; Rockville, Md; Padua, Italy; Kansas City, Mo; New York, NY; Boston, Mass; Seattle, Wash; and Philadelphia, Pa

TABLE I. Summary of addendum guidelines 1, 2, and 3

Addendum guideline	Infant criteria	Recommendations	Earliest age of peanut introduction
1	Severe eczema, egg allergy, or both	Strongly consider evaluation by sIgE measurement and/or SPT and, if necessary, an OFC. Based on test results, introduce peanut-containing foods.	4-6 months
2	Mild-to-moderate eczema	Introduce peanut-containing foods	Around 6 months
3	No eczema or any food allergy	Introduce peanut-containing foods	Age appropriate and in accordance with family preferences and cultural practices

What about other foods?

- Now about 6 studies done of egg introduction:
 - Mixed results about efficacy
 - Very high rates of allergic reactions to egg powder used in several studies
 - Extensively cooked egg (“baked egg”) better tolerated
- No studies of tree nuts, fish, shellfish
- Milk data is difficult to interpret

What went wrong?

- We gave broad-sweeping recommendations based on low quality evidence
 - Caveats were ignored
- We reasoned from faulty mechanistic theories
- We gave into the pressure to “do something”
- We underestimated the possibility of harm

Questions that keep me up at night

- What might be the unintended consequences of our new guidelines?
 - Will more screening lead to more false positive diagnoses of peanut allergy and other food allergies?
 - Will screening overwhelm the available medical resources?
 - Will people really introduce peanut earlier?
- In terms of the new treatments that are now in phase III trials:
 - What are the long term outcomes of treatment?
 - What exactly are we treating?
 - In the long term, will these treatments lead to more reactions or fewer?
 - Are there easier ways to reduce anxiety and increase freedom?

Extra slides



Cutaneous exposure through inflamed skin leads to allergy, while oral exposure leads to tolerance.

George du Toit, Teresa Tsakok, Simon Lack, Gideon Lack

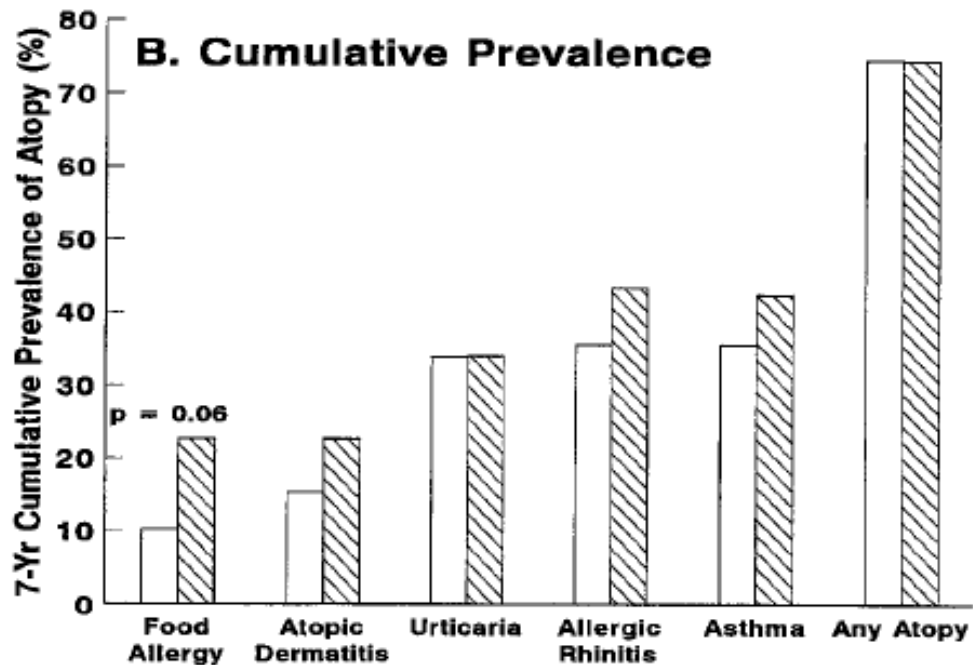
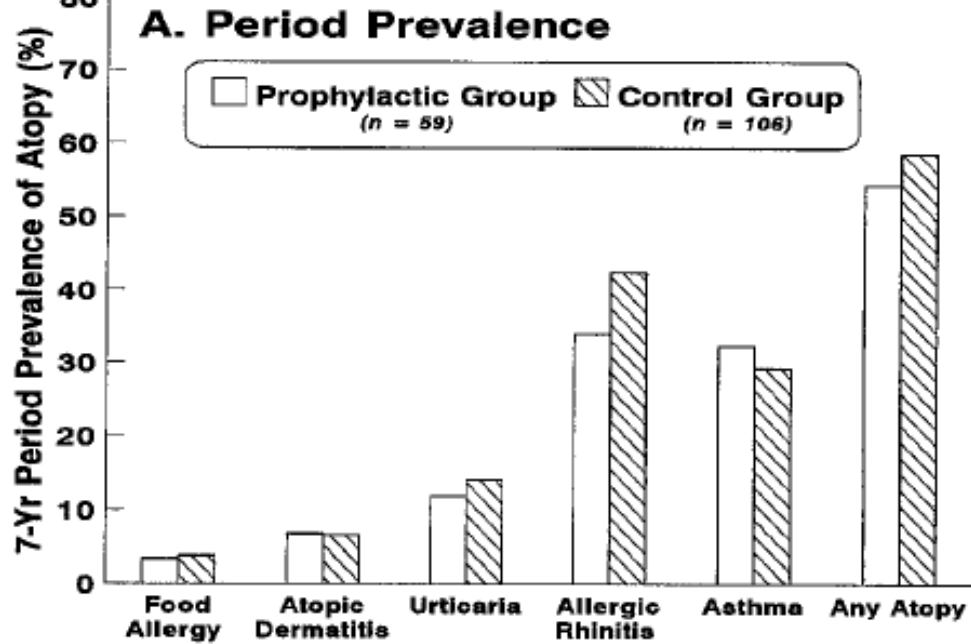
Prevention of food allergy

Journal of Allergy and Clinical Immunology, Volume 137, Issue 4, 2016, 998–1010

<http://dx.doi.org/10.1016/j.jaci.2016.02.005>

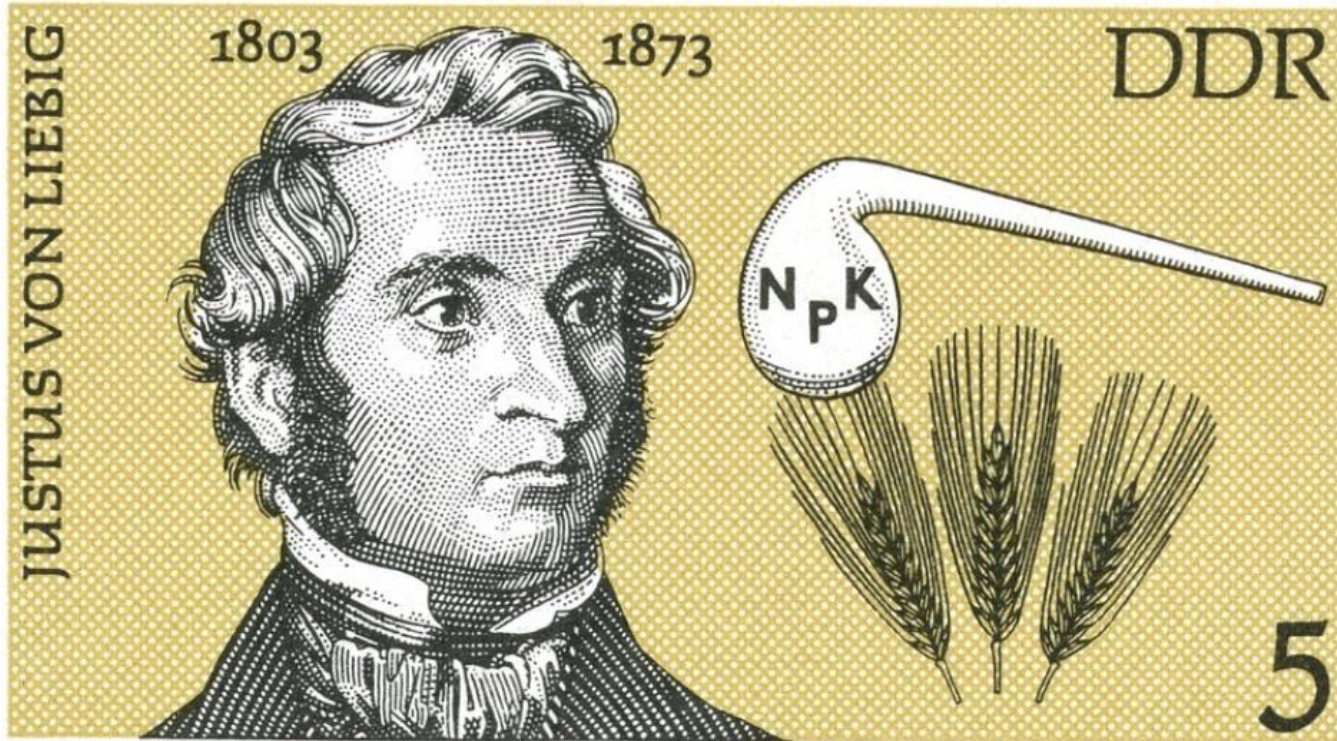
Our current study

- Supported by the NIAID
- Goal of
 - Understanding the risk of reaction at introduction among three risk groups
 - Evaluating different screening tests for peanut allergy in infancy
 - Understanding how parents introduce peanut in real life
- Enrolling infants 4 to 11 months old
 - Siblings and children of those with peanut allergy
 - Those with moderate-to-severe eczema
 - Those with other food allergies



Clinical trial

- 59 intervention and 106 control
- Mothers avoided cow's milk, egg, and peanut during the last trimester of pregnancy and lactation
- Infants avoided cow's milk until age 1 (casein hydrolysate supplementation before age 1)
- Egg until 2
- Peanut and fish until 3

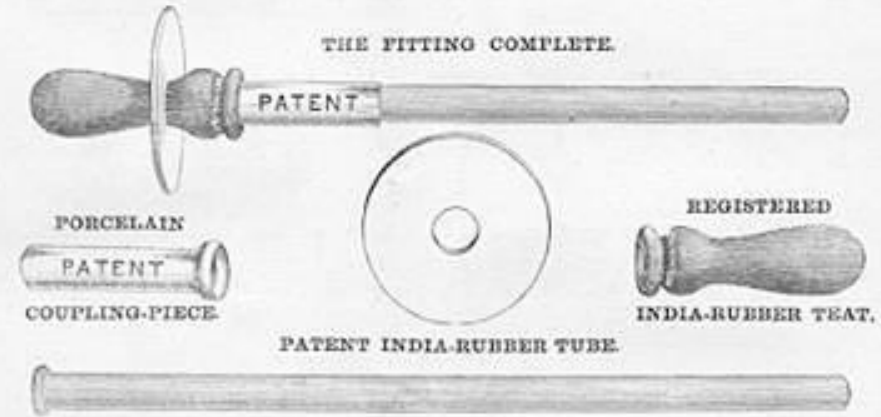


1978

In 1865, chemist Justus von Liebig patented an infant formula made of cow's milk, wheat and malt flour, and potassium bicarbonate

S. MAW, SON & THOMPSON'S Improvement in Feeding Bottles

Patented in England, December 4, 1879;
Patented in the United States, April 27, 1880.



Patent India-rubber Tubes, in $\frac{1}{2}$ gross and 1 gross Boxes—			
9-inch White	<i>per gross</i>	10/6
10 " " Super	"	16/-
9-inch Black	<i>per gross</i>	15/-
10 " " "	"	16/-

Registered India-rubber Teats, in 1 doz. Boxes—
2 Sizes (Small and Medium), *per gross*, White, 8/- & 14/-; Black, 12/- & 21/-
Patent Coupling-pieces, in 3 doz. Boxes *per gross* 8/-

S. MAW, SON & THOMPSON beg to inform the Trade that in future all their Feeding Bottles, except Sixpenny, will be fitted with the above **PATENTED IMPROVEMENT**, unless ordered to the contrary.

The improvement consists in the introduction of the New Registered Teat, and in the construction of the Coupling-piece, the latter **passing over the exterior** of the India-rubber Tube, by which arrangement injurious contraction is avoided, and the cleaning of the Tube facilitated, a Tube Brush being easily passed through without the removal of the Coupling-piece.

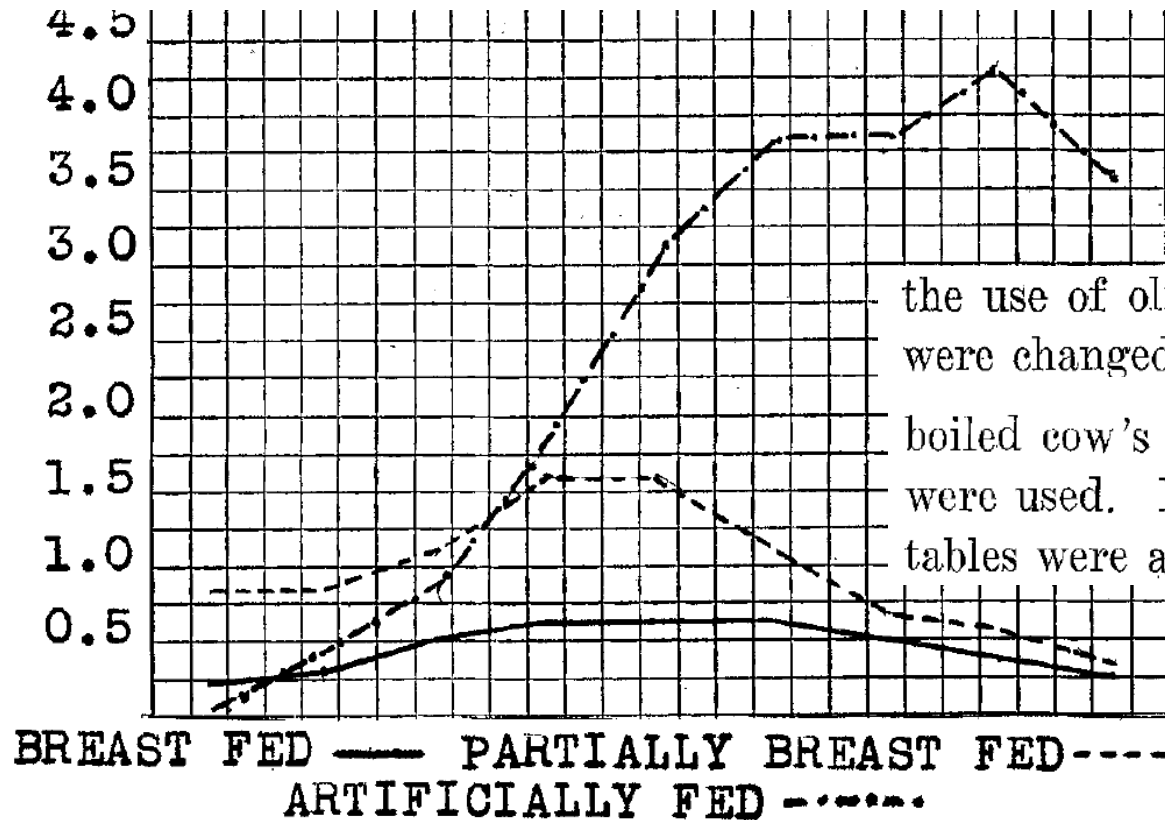
In the fitting up of ordinary Feeding Bottles, the Shield fixes the Teat upon the Union Joint, preventing its easy removal, and making it difficult to replace the Teat in its airtight position, without which the action of a Feeding Bottle is perfect. The New Registered Teat is so formed as to receive the shield and retain it in position without connection with the Coupling-piece, the Teat thus being easily removed and replaced without damage.

S. MAW, SON & THOMPSON, LONDON.

THE INFLUENCE OF BREAST AND ARTIFICIAL FEEDING ON INFANTILE ECZEMA

CLIFFORD G. GRULEE, M.D., AND HEYWORTH N. SANFORD, M.D.
CHICAGO, ILL.

1 **T**HERE is probably no subject in pediatrics that has received so much attention in the last few years as that of infantile eczema.



the use of olive oil only for cleansing purposes. None of the feedings were changed in any way. In the artificially fed infants, 1.5 ounces of boiled cow's milk and 0.1 ounce of cane sugar per pound body weight were used. In all infants cod liver oil, orange juice, cereals, and vegetables were added to the diet.

Chart 1.—Monthly incidence of infantile eczema.

1960s-2000

- Concern about early introduction of solids and decreased breast feeding led to more research in the 1960s and 1970s about the role of breast feeding in allergies.
- With the development of broken down cow's milk formulas in the 1980s-1990s, more research into effect of infant diet on development of eczema and food allergy.
- Some relatively weak evidence for breastfeeding or hypoallergenic formula to prevent eczema or food allergy.
 - There were no studies of delayed peanut only.
 - Some of the data was fabricated (see retraction in the BMJ from RK Chandra)

