MILK ALLERGY: A SURVEY OF ITS INCIDENCE; EXPERIMENTS WITH A MASKED INGESTION TEST*†

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WHEREAS most authorities list milk among the three leading foods to act as excitants, there is a marked difference in opinion as to the frequency and importance of ingestant hypersensitiveness in general. If the views of Rowe, Rinkel and Randolph[1,2,3] are correct, most cases are overlooked. They place particular emphasis on chronic or "masked, smoldering" responses arising from the oft-repeated ingestion of corn, wheat, milk, and other frequently ingested foodstuffs.[4] They include among its symptoms not only the classical and borderline expressions of atopy but such atypical states as fatigue, drowsiness, chilliness, and aching or drawing sensations in the muscles.

Everyone agrees that the results of cutaneous tests may be highly misleading in food allergy. For this reason, other diagnostic approaches have been tried, such as food diaries, elimination diets, provocative diets,[5,6,7] and ingestion tests with or without associated studies of blood cytology.[8] Many physicians still feel that nothing replaces a carefully taken history. So controversial is the whole subject that the author thought it worth while to explore two of its phases: first, its incidence, by means of a poll of physicians most likely to encounter it; and second, its diagnosis, as gauged by a specially designed ingestion procedure which called for masking of the suspected food and for placebo feedings. It was expected that these precautions would minimize the influence of psychologic, physiologic, and other extraneous factors on the diagnosis. The investigation was focused on corn and milk, the present report covering the latter.

MATERIALS AND METHODS

Questionnaire.—Inquiry was made concerning: (1) the specialty of the physician, (2) the approximate number of new patients acquired during the past 5 years, (3) the number of these patients considered allergic to milk by clinical standards, and (4) the number reactive by cutaneous test.

Intracutaneous Tests.—By using several dilutions of allergen in volumes of 0.02 c.c., it was usually possible to determine the approximate dose which was required to provoke a maximal wheal-and-flare reaction in the 20 members of our experimental group. The solutions were standardized according to their content of precipitable nitrogen (phosphotungstic acid being the precipitant), 0.1 mg. representing 10,000 "protein" nitrogen units. Most of the 20 individuals examined by this test were also studied with lactalbumin, which was routinely prepared by our laboratory, and with casein and highly purified crystalline β-lactoglobulin supplied kindly by Thomas L. McMeekin,[9] Head, Protein Division, Eastern Regional Research Laboratory of the U. S. Department of Agriculture,

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Philadelphia, Pa. An occasional patient was also studied with his α-casein and β-casein fractions. It was hoped that the derivatives might prove more reliable diagnostic aids than had whole milk.

Ingestion Procedure.—Fresh, certified but unpasteurized milk, freed of its cream, was administered in a volume adjusted to the anticipated susceptibility of each patient. Every attempt was made to prevent the subject from learning on which occasion milk was involved. The placebo consisted of one of three commercial antacids, Amphojel, Basaljel, or Titralac (see footnotes, Table II), mixed with water on one occasion and with milk on another. The consumer was asked to close his eyes and his notrils until after the meal had been brought into the room and swallowed. An independent technician decided which feeding was to include milk and prepared both meals in an adjacent room without informing the patient or the physician of their identity. Cutaneous tests with milk were not done on days of placebo testing.

The tests were conducted according to the prerequisites of Randolph in several particulars, viz., milk was rigorously excluded from the diet for at least 4 days preceding each test and was advocated as part of the daily intake for at least 4 days prior to this exclusion period. The patient sat quietly in the fasting state for one-half hour after reaching the office; all suggestive manifestations were recorded in detail, not only for the ingestive period but for the 48 hours preceding and following it. The patient avoided or recorded the use of drugs as well as of any exposure to other allergens which might complicate the postingestive period. Occasionally, when it was impossible to arrange a second visit, the placebo feeding was presented first and later in the morning the masked milk was offered.

Finally, comparisons were set up between the diagnosis as arrived at through ingestion studies, history taking, intracutaneous test, and a reinterpretation of the ingestion result by the criteria of Randolph and others.

FINDINGS

Incidence of Hypersensitivity.—Table I indicates that 142 physicians belonging to the American Academy of Pediatrics or the American Academy of Allergy responded to the questionnaire by estimating that 4,260 of their patients showed cutaneous allergy toward milk. Since they were attending nearly 180,000 individuals, this meant an incidence of 2.3 per cent. When the figures for this population were added to those of another 49 pediatricians who do not perform cutaneous tests to diagnose food allergy, it was learned that the incidence of milk hypersensitiveness according to clinical standards amounted to only 1.5 per cent. Nearly 250,000 patients were under consideration. The questionnaires had been sent almost exclusively to physicians in the vicinity of Greater New York City with the idea that suitable material for ingestion tests might be uncovered. Figures are not included for Randolph, Rinkel, Rowe, or their followers. The result would have been considerably altered had this been the case, for these men arrive at incidences 5 to 10 times higher by the use of food diary, ingestion, and elimination procedures in combination with atypical symptoms.

TABLE I. INCIDENCE OF ALLERGY FOR MILK

NUMBER OF PHYSICIANS	NUMBER OF PATIENTS IN SURVEY	NUMBER ALLERGIC	INCIDENCE (%)
	As Judged by Cutaneous Test		
142*	179,434	4,260	2.3
	As Judged by Clinical Standards		
191†	244,719	3,691	1.5

*Internist allergists, 32; pediatric allergists, 8; pediatricians, 29; allergists, 69; dermatologists, 3; otolaryngologist, 1.

†Above group plus 49 pediatricians who did not do skin tests.

Ingestion Studies.—Table II presents in some detail the salient points of the history and the results of feeding and intracutaneous tests for 8 subjects in our experimental group. The data for these 6 adults and 2 boys have been arranged according to their histories for allergy toward milk. Each individual will now be briefly discussed.

CASE 1.—There could be no doubt as to the susceptibility of the woman, WE1, for her diagnosis was unequivocal by any standard. She gave a story of repeated asthmatic responses promptly after the ingestion of the smallest traces of milk. A sore mouth and urticaria were also very prone to occur some hours later. When a scratch test was done with whole milk a few days before she was referred to us, the wheezing was so severe that 2 injections of epinephrine had to be administered.

Our ingestion result was equally convincing. After having been entirely well for 12 days, she took water mixed with Basaljel with no reaction except slight belching and nausea which we attributed to the character of the placebo. She was symptom-free in 15 minutes and remained so for another one-half hour, at which time 1½ oz. of milk were served mixed with flavored Basaljel. Eructation occurred as before but was now associated with wheezing. After one-half hour, another 3 oz. of milk were taken. Asthma of moderate severity ensued within 15 minutes. By the time her observation period was over it had subsided somewhat, but it persisted in mild form through the rest of the day.

Five days later, the experiment was repeated with peppermint-flavored Amphojel as the placebo as a substitute for Basaljel. It was mixed with 90 c.c. of tap water. No symptoms developed during the one-half hour following this placebo feeding. One and one-half ounces of milk containing the flavored placebo material were then offered, with the production of definite asthma in 15 minutes. The attack remained at its moderately severe level after another feeding of 3 oz. in 30 minutes and a third meal of 9 oz. in 60 minutes. The final specimen elicited nausea and vomiting as well as a pruritic erythema of neck and chest. We later learned that she developed generalized urticaria that evening.

CASE 2.—The young man, GIA, in Group 1, stated that one-half a tumblerful of milk would cause nausea and abdominal cramps after 4 hours, and that 1 or 2 glasses led to diarrhea. His history was complicated by the impression that various vegetable gums, pork, lamb, citrus fruits, raw vegetables, and fatty foods often provoked similar upsets. Extracts containing as few as 10 protein units of milk or its fractions gave rise to significant cutaneous responses, placing him in the +++ class. Whereas our placebo ingestion test with 2 tablets of Titralac in 8 ounces of water was well tolerated, a similar volume of milk with Titralac taken on another morning caused mild indigestion and distention after 2 hours.

It was taken for granted that both these cases would have yielded results comparable to those described for our ingestion experiments had the subjects been aware that milk was involved. They have, therefore, been rated as positive for milk allergy according to the Randolph criteria as well as by the other diagnostic approaches. The correlation between the several methods can be readily seen in Table III. It refers to the 8 members of the ingestion covered by Table II.

TABLE II

PATIENT	HISTORY OF RESPONSE TO MILK INGESTION	RESULTS OF INGESTION EXPERIMENTS WITH MILK: VOLUME IN MEAL	RESULTS OF INGESTION EXPERIMENTS WITH MILK: CLINICAL RESULT	RESULTS OF INGESTION TESTS WITH PLACEBO: PLACEBO	RESULTS OF INGESTION TESTS WITH PLACEBO: CLINICAL RESULT	RESPONSE TO INTRACUTANEOUS TEST WITH 0.02 C.C. OF EXTRACT: SKIMMED MILK (STRENGTH IN PTA-NITROGEN UNITS PER C.C.)	RESPONSE TO INTRACUTANEOUS TEST WITH 0.02 C.C. OF EXTRACT: LACTALBUMIN (STRENGTH IN PTA-NITROGEN UNITS PER C.C.)	RESPONSE TO INTRACUTANEOUS TEST WITH 0.02 C.C. OF EXTRACT: BETA-LACTOGLOBULIN (STRENGTH IN PTA-NITROGEN UNITS PER C.C.)	RESPONSE TO INTRACUTANEOUS TEST WITH 0.02 C.C. OF EXTRACT: CASEIN (STRENGTH IN PTA-NITROGEN UNITS PER C.C.)
Group I: History Definitely Indicative of Milk Allergy									
1. WEI	Asthma +++ in 10 min. Stomatitis, hives 12 hr. after even traces of milk	135 c.c. + Basaljel* 375 c.c. + Amphojel†	Nausea ++ in ¼ hr. Asthma ++ in ¼ hr. for 8 hrs. Nausea, vomiting ++ in ¼ hr. Erythema neck, chest in ¼ hr. Asthma ++ in ¼ hr. Hives in 12 hrs. +++	90 c.c. water with Basaljel	Nausea ++ for ¼ hr. in ¼ hr.	(Scratch test= slight + with systemic in 10 min.)			
2. GIA	Nausea, vomiting, colic 4 hrs. after milk, 8 oz., or lamb, pork, vegetable gums, citrous fruits, raw vegetables, fats	240 c.c. + Titralac‡	Mild indigestion and abdominal distention in 2 hrs. for 24 hrs.	240 c.c. water + 2 tablets Titralac	Negative	5 u/c.c.=++ 10u/c.c. = +++ salt = +±	10 = +++±	10 = ++±	10 = ++±
3. III	Nausea, abdominal colic, 10 min. after milk; fluid retention, marked edema, poor vision, memory, and thinking in several hours. Occasional hives	50 c.c. by stomach tube (with suggestion water only was being given)	Negative	Water by stomach tube with suggestion of milk	Positive	1000 = + 100,000 = ++	10,000 = ±	10,000 = 0	20,000 = ±

4. BA	One glass of milk causes abdominal cramps and coughing in 10 min.	200 c.c. + Basaljel	Momentary near-syncope in 20 min.	90 c.c. water + Basaljel	Chilly for 1½ hr. Drowsy in 45 min.	10,000 = +++	10,000 = 0	10,000 = 0	20,000 = 0
Group II: Presumptive History for Milk Allergy									
1. BLU aet 15	Asthma + after glass milk. Tolerates 2 tsp. milk, ice cream, butter, cheese. Grass, ragweed, danders also allergenic	600 c.c. during 1½ hr. + Basaljel	Asthma + in 12 hrs. for 3 hrs.	200 c.c. water + Basaljel (preceding milk test on same morning)	Negative for ½ hr. observed before milk given	10,000 = ++ salt = 0 100,000 = ++	10,000 = 0	10,000 = ±	20,000 = ±
2. RU	Tolerates 1 glass per week but 3 per week causes itchy rash dorsum both feet	250 c.c. + Basaljel	Headache +++, nausea +, drowsy + in 45 min. Itchy rash dorsum one foot in 7 days	150 c.c. water + Basaljel	Pre-existing headache + became ++ in 45 min. after ingestion	1000 = + 10,000 = +++	10,000 = 0	10,000 = 0	20,000 = 0
Group III: History Negative for Milk Allergy									
1. HA	Sense of fullness if drinks quart milk; otherwise tolerates it well	250 c.c. + Basaljel	"Restless, dizzy" for 36 hrs. but ate only 1 sandwich, orange juice, broth.	Not tested		10,000 = + 100,000 = ++± salt = 0	10,000 = 0	10,000 = 0	20,000 = 0
2. ZI aet 10	Infantile eczema + asthma from milk + other foods. Tolerates unlimited evaporated milk	250 c.c. + Basaljel	Negative	Not tested		1000 = ++± salt = 0	1000 = ++	1000 = +	1000 = +

*Basaljel (Wyeth, Inc.), an aluminum carbonate gel, flavored with vanilla (synthetic).

†Amphojel (Wyeth, Inc.), an aluminum hydroxide gel for hyperacidity; a mild local astringent free of alkalis; represents 4 per cent of *aluminum oxide, peppermint flavored.*

‡Titralac (Schenley Laboratories); one tablet contains 0.15 Gm. glycine and 0.35 Gm. calcium carbonate. Titration curve similar to that of fresh milk.

CASE 3.—HI was a housewife who gave a history of prompt nausea, cramps, and diarrhea after drinking milk. She also felt that she retained fluids, became slightly edematous all over, gained pounds of weight and had pressure in her head as well as vertigo, faulty memory, and impaired vision some hours after ingesting this food. That these manifestations were related to the "suggestion" of milk rather than to its allergens was shown by Dr. Harold Wolff and his associates who describe their experiments in another article of this issue. Their feedings were administered through a stomach tube, with "reversed" suggestions for the placebo and the milk. Diagnostic methods which fail to appraise the psychologic factor would have failed miserably in this case. The history and the cutaneous indications were equally misleading, as shown in Table III.

TABLE III. MILK ALLERGY AS DIAGNOSED BY HISTORY IN COMPARISON WITH MASKED INGESTION TEST, RANDOLPH CRITERIA, AND INTRACUTANEOUS TEST

PATIENT	HISTORY	MASKED INGESTION	RANDOLPH CRITERIA	INTRACUTANEOUS TESTS	
				WHOLE MILK	FRACTIONS
		Group 1: History Positive			
WEI	+ (definite)	+ (definite)	+	++	
GIA	+ (probable)	+ (slight)	+	+++	++±
HI	+ (definite)	0	+	+	0
BA	+ (definite)	0	+	++	0
		Group 2: History Suggestive			
BLU	+ (probable)	+ (possible)	+	+	0
RU	+ (probable)	+ (possible)	+	++	0
		Group 3: History Negative			
HA	0 (definite)	0 (probably)	+	+	0
ZI	0 (probably)	0 (definitely)	0	++±	+
Consistent with history		6	7	6	2
Inconsistent with history		2	1	2	5

It seems likely that the fourth member of Group 1, BA, was also neurotic, for her story that acute abdominal pains and coughing would promptly result from the ingestion of a glass of milk did not materialize when she was given 200 c.c. of milk mixed with Basaljel, without being aware of the milk content. Aside from a momentary spell of weakness, bordering on syncope, there were no developments. During her control experiment 6 days earlier, BA had complained of persistent cold feet in spite of a warm room, and of drowsiness 45 minutes after the feeding. Although Randolph and others would interpret these symptoms as allergic, the patient had taken nothing but Basaljel in water, and the same placebo was later used in her milk feeding without eliciting either of these complaints. If our conclusion is correct, that this patient was not susceptible to ingested milk, then her intracutaneous response was misleading in the case of whole milk but reliable with the fractions, as Table III indicates.

Thus, whereas all 4 members of Group 1 gave positive histories for milk allergy, only 2 of them could be confirmed by ingestion test. They would all have been deemed positive by Randolph and Rinkel, due to the lack of control feedings and the wide latitude of acceptable symptoms. Intracutaneous findings were misleading for 2 cases in the instance of whole milk, whereas the fractions appeared to be reliable in the 3 individuals tested.

Similar investigations pursued with Group 2 were less instructive because their histories as well as their ingestion results were difficult to interpret.

CASE 1.—The 15-year-old boy, BLU, explained that he tolerated 2 tsp. of milk used in his coffee, also ice cream and cream cheese, but that a glass of milk precipitated an attack of asthma in 6 or 7 hours. The placebo feeding of water and Basaljel evoked no symptoms.

Since he was not enthusiastic about returning, he was given during the same morning a total of 600 c.c. of masked milk in 3 one-half-hour servings. There were no consequences until 12 hours later when a mild, 3-hour attack of asthma developed. In spite of his complicated history of pollen asthma, nonseasonal nasal allergy, and positive cutaneous responses to several varieties of animal dander, we listed his ingestion result as "possibly" positive. The Randolph criteria led to the same conclusion. Cutaneous reactions were observed for whole milk but not to its derivatives.

CASE 2.—The other member of Group 2 was Ru, a woman who was certain she could take 1 glass of milk without consequences but that 3 glasses during a week's time would lead by the eighth day to an itchy eruption on the dorsum of each foot. On the morning of her placebo feeding of water and Basaljel, a pre-existing mild headache was made somewhat worse. On another morning the drinking of 250 c.c. of milk mixed with the same placebo was productive of mild nausea, drowsiness, and marked cephalalgia after 45 minutes. When seen 7 days later she had a freshly erupted patch of atopic dermatitis on one foot. We somewhat hesitatingly attributed this to the milk ingestion test, in spite of the long "incubation period." According to the Randolph standards the results of both the milk and the control meal were indicative of allergy. It was unfortunate that additional studies could not be arranged to appraise the possible roles of the placebo, extraneous allergens, and psychologic factors. Table III shows that her cutaneous reactivity toward whole milk was ++ whereas there was no observable susceptibility to its fractions.

The data were more valid, particularly with reference to history and ingestion study, in the cases of the 2 members of Group 3 (Tables II and III).

CASE 1.—The adult male, HA, had been concerned over his positive cutaneous response to milk, although he had never experienced any difficulty from milk, except when he consumed an entire quart and felt temporarily distended! It came as somewhat of a surprise, therefore, when he telephoned, 2 days after our milk ingestion test with 8 oz., that he had been dizzy and restless for the ensuing 36 hours. On further inquiry, it was discovered that his eagerness to comply with our instructions to avoid all possible complications was so great that he ate nothing more than 1 sandwich, some orange juice, and broth during that period. It seemed logical to attribute his complaints to deficiency in nourishment. Hence, although the result is listed as positive by Randolph criteria, it was considered negative by our own. Slight responses were obtained with whole milk but none to fractions during intracutaneous tests. It is our hope to be able to do additional ingestion studies on this man.

CASE 2.—With the boy, ZI, the ingestion of 250 c.c. of milk was without effect. Although he had been permitted unlimited amounts of evaporated milk, his parents had withheld ordinary milk because it had provoked both asthma and eczema during his infancy. In spite of this negative ingestion response, as judged by both our own and the Randolph standards, the boy reacted almost markedly to intracutaneous injections of both whole and fractionated milk.

Summarizing these comparisons among the several diagnostic methods, it will be seen at the foot of Table III that our ingestion results were in agreement with the history in 6 of the 8 trials. The Randolph interpretation yielded 7 conclusions in keeping with the history. The intracutaneous test paralleled the history in 6 cases when whole milk was involved, but in only 2 of the 7 individuals tested with derivatives.

More crucial comparisons could be made, however, if the ingestion results were taken as the true index to the diagnosis. Table IV is a rearrangement of the same data on this basis. It will be seen that one-half the 8 cases were positive by ingestion, the remainder negative. Our results were confirmed by the Randolph standards in 5 instances, by the history in 6, and by cutaneous

studies with whole milk in 4. Thus, the history stood next to the ingestion result in reliability whereas the skin test was last. Although the fractions afforded essentially the same proportion of correct answers as did whole milk (4 out of 7), this was dependent on their tendency to give negative responses. Whole milk, on the contrary, proved active in all members of the group. That this difference was not due to degradation of the fractions during their preparation was indicated by the positive responses of Gia to concentrations as low as 10 protein units per c.c. Even higher dilutions of these derivative allergens gave unequivocal reactions in an infant to be discussed below.

TABLE IV. MILK ALLERGY AS DIAGNOSED BY INGESTION TEST IN COMPARISON WITH DIAGNOSIS BY HISTORY, INTRACUTANEOUS TEST, AND RANDOLPH CRITERIA

PATIENT	INGESTION TEST	HISTORY	INTRACUTANEOUS TEST		RANDOLPH CRITERIA
			WHOLE MILK	FRACTIONS	
WEI	Definite positive (2 tests)	Definite positive	++		Positive
GIA	Positive for slight allergy	Definite positive	+++	+++	Positive
BLU	Probably positive	Probably positive	+	0	Positive
RU	Possibly positive	Probably positive	++	0	Positive
BA	Negative (psychologic)	Definite positive	++	0	Positive
HI	Negative (psychologic)	Definite positive	+	0	Positive
HA	Negative (physiologic)	Negative	+	0	Positive
ZI	Negative	Probably negative	++±	++	Negative
Tests consistent with ingestion results		6	4	4	5
Inconsistent with ingestion results		2	4	3	3

Intracutaneous Studies in 12 Other Subjects.—A brief report will be made on 12 individuals who were investigated by history and cutaneous tests but not by ingestion procedures, largely because a goodly proportion of them were infants who might have been thrown into acute exacerbations of asthma or eczema by this test in its present crude form. There were 6 cases of atopic eczema or dermatitis in the group, 4 of acute gastrointestinal disturbance (1 also had bronchial asthma), and 2 who were not allergic to milk. Using the history as the second-best index to sensitiveness, we assorted them into 4 classes as shown in Table V. Each was then subdivided according to the reactivity noted during intracutaneous tests with whole milk. With the 3 exceptions designated, the figures given in Table V also apply to the fractions of milk. No clear-cut pattern could be found for either type of allergen, there being negative cutaneous findings in patients positive by history and vice versa.

A few lines should be devoted at this point to the unusual case of Un, a Negro boy, aged 1 year, whose marked asthma and eczema had been provoked and controlled repeatedly by the giving or withholding of milk. Intracutaneous test with milk derivatives in concentrations of only 0.01 protein nitrogen unit per c.c. elicited the following responses: lactalbumin, ++++; β-lactoglobulin,

+++; casein, +± alpha and beta caseins were negative in this strength, the latter also failing to provoke any significant reaction in concentrations of 0.1 and 1.0 units. Prausnitz-Kustner tests were positive with 10 unit solutions of lactalbumin and of β-lactoglobulin, but were only questionably so for whole casein. β-casein was active in 10 unit strength and must have accounted for the response finally provoked by whole casein when employed in 1000 unit concentration, for α-casein proved inactive even with 10,000 unit solution. Enough of this infant's serum was on hand to permit one cross test to be done. A serum site no longer reactive to β-lactoglobulin developed a maximum wheal and flare when tested with whole casein, thus indicating that the specificity of the latter differed from that of the globulin fraction.

TABLE V. CORRELATION BETWEEN CLINICAL HISTORY AND INTRACUTANEOUS TESTS FOR MILK ALLERGY

HISTORY FOR MILK ALLERGY	NO. OF CASES	INTRACUTANEOUS SENSITIVITY CLASS*			
		+++	++	+	NEGATIVE
Definite	4	1		1	2
Suggestive	2			2†	
Questionable	4			1‡	3
Negative	2		1	1§	

*For whole milk; also for fractions except where otherwise noted.
†Toward fractions, one patient was +, one patient 0.
‡Casein reaction ++, lactalbumin 0, β-lactoglobulin +.
§No tests done with fractions.

Because casein enjoys the reputation of causing allergy very infrequently, it should be remarked that there were 3 definitely positive reactors among our series of 12 patients; and it can be seen in Table II that there were 2 others among the 7 tested with it in the ingestion group. Unfortunately, no feeding experiments with any milk fractions could be carried out due to the scarcity of the highly purified material.

Diagnostic Significance of Intracutaneous Responses to Whole and to Fractionated Milk.—A few simple comparisons were set up to determine whether fractions might be superior to whole milk in intracutaneous tests. For this purpose 9 cases were selected in which the diagnosis was unequivocal for the presence or the absence of milk allergy as judged by ingestion test and/or history. (Three were positive by ingestion test, 3 by history only; the remainder were negative by one or both criteria.) Cutaneous test provided false negative results in 1 instance with whole milk, in 3 with fractions. The false positive reactions were 3 with whole milk and 2 with its derivatives. Thus each type of allergen gave misleading information in about one-half the trials, milk erring in the direction of false positives, and the fractions tending to provide false negatives. Obviously the trials were too limited to carry statistical weight.

SUMMARY AND DISCUSSION

Judged by a poll of 191 physicians, the incidence of allergy to milk is low, amounting to only 1.5 per cent when diagnosed by clinical standards and to 2.3 per cent by cutaneous tests. The questionnaires were sent to pediatricians and allergists, specialists whose encounter with this disorder should be maximal. By inference, the occurrence of this malady must be rare among the general

population. Such a statement stands in striking contrast to the opinions of Randolph, Rinkel, and Rowe who regard milk and food allergens as highly important excitants. One reason for this is that they include signs and symptoms which generally are not accepted as allergic by most physicians. Among these are fatigue, drowsiness, headache, chilly sensations, and pains or "drawing" of the muscles. The writer certainly gained the impression that allergy for milk is unusual when trying to locate subjects suitable for ingestion studies during the past 1½ years, only 20 being procured. It should be stated, however, that no effort to determine the true incidence of milk hypersensitiveness will be rewarding until more scientific means of diagnosis have been found than those in current use.

The present investigation was an exploratory excursion into a primitive area of allergy, combined with an attempt to devise a more satisfactory approach. Eight patients, selected on the basis of their histories for the existence or absence of allergy toward milk, were given milk in masked form in conjunction with control, or placebo, feedings. The conditions surrounding the test were those prescribed by Rinkel and Randolph. As in the case of 12 other subjects, they were also studied by intracutaneous tests with whole milk and its individual proteins. Comparisons were then drawn among the various diagnostic methods. When the ingestion result or a clear-cut history was used as the yardstick, the intracutaneous method appeared to produce a number of false positive responses. Its fractions, on the other hand, tended to err in the opposite direction.

Reinterpretation of our ingestion results according to the Randolph criteria brought positive findings for 3 individuals whose manifestations were judged by us to be psychogenic or physiologic rather than allergic. The placebo feedings given 2 of these subjects had clarified the diagnosis. In spite of our effort to screen out such subjects through history taking, 1 of our 8 ingestion cases was clearly, and another was presumably, neurotic—"allergic" to the idea but not to the allergens of milk! This situation is not surprising in view of the association of milk with reproductive functions and of its role in infant-mother relationships. At any rate, diagnostic methods which fail to take this possibility into account, whether they be ingestion tests, elimination or provocative diets, or based on food diaries, will introduce false positive findings. The risk is particularly great if one accepts as allergic such commonly neurotic complaints as headache, fatigue, chilliness, and muscle discomfort. Placebo ingestion studies would seem indispensable.

Although the results presented herewith are preliminary both in nature and in number, it is hoped they will stimulate others to seek more objective means for the diagnosis of ingestant allergy. For example, even with our ingestion method, the use of flavoring and of antacids to simulate milk was not found ideal. Probably plain, powdered milk in capsules would be superior, providing desiccation can be achieved without degradation. Purified milk proteins should also be tested by the oral route, but as yet it is not practical to prepare them in amounts sufficient for the test. Our laboratory is hoping to accomplish this by use of the electrophoresis-convection apparatus of Kirkwood. It should then be feasible to reproduce the studies[10] done with cottonseed extract, where the

thresholds of susceptibility were expressed in chemical units for the skin, conjunctiva, serum, and for the oral route. There also is an urgent need to investigate the validity of Randolph's claim that headache, fatigue, and other manifestations not generally considered typical of allergy do belong in this category and are being widely misdiagnosed.

Finally, a word of caution seems in order. It would seem unwise, in view of our crude knowledge, to alarm the layman by publicizing the "dangers" attached to such common foods as milk and cereals, to say nothing of their derivatives, the sugars, starches, and oils, before confirmation by objective methods is possible. So much lay concern has been developed along this line, however, that several recent hearings were held before the United States Food and Drug Administration concerning the need to label salad dressings, bread, etc., as to their content of allergens.

CONCLUSIONS

1. A poll of 191 specialists in pediatrics or allergy revealed that 1.5 per cent of 245,000 patients were allergic to milk by clinical standards, whereas 2.3 per cent of 180,000 individuals responded to intracutaneous test.

2. An ingestion procedure was devised which called for masking of the allergen and for control feedings with placebo meals.

3. Applied to 8 patients, this approach gave promise of being superior to other diagnostic techniques in current use. Its chief asset is the exclusion of psychogenic influences from the results.

4. Intracutaneous tests with milk erred in the direction of giving false positive results, whereas protein fractions derived from milk tended toward false negative ones.

5. The need is cited for re-evaluation of the symptomatology of allergy, particularly as regards the claims of Randolph, Rinkel, and Rowe, and for the development of scientific methods of diagnosis in food allergy.

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