

## ORIGINAL ARTICLES

### STUDIES ON THE ALLERGENICITY OF CORN PRODUCTS

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**H**YPERSENSITIVITY to corn (maize) is a well-defined clinical entity, but there is no general agreement as to its incidence in allergic persons. Published estimates of its occurrence in patients with food allergy vary from 0.16 per cent to 30 per cent.

Likewise, there is no agreement as to whether sugars derived from the hydrolysis of corn have allergenic properties. Ratner and Gruehl,<sup>1</sup> using the technique of guinea pig anaphylaxis, found no evidence of antigenicity in samples of dextrimaltose mixtures, corn syrup, or crystalline sugars derived from corn. They also showed that while the malt extracts and barley malt used in the preparation of certain forms of dextrimaltose preparations are highly anaphylactogenic, there was no evidence that antigenic amounts of these substances were present in the final product.

On the other hand, Rinkel, Randolph, and Zeller,<sup>2</sup> and Randolph and Yeager<sup>3</sup> found evidence, by clinical trial, of allergy to corn and sugars and starches derived from corn in approximately 25 per cent of patients with food allergy, and they rank corn second only to wheat as a food allergen. These observations have been questioned by Loveless<sup>4</sup> and Bernton<sup>5</sup> who, using a masked ingestion test, were unable to confirm these findings.

Since various types of corn sugars are used widely in infant feeding as carbohydrate modifiers of all types of milk formulas, especially during the period when gastrointestinal disturbance (colic) is common, there has

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been raised the question of whether the sugars could be a factor (in addition to milk) in the production of these symptoms on an allergic basis. As an extension of the work of Ratner and Gruehl,<sup>1</sup> we decided to test four such sugars for possible antigenicity, using more sensitive immunologic techniques, that is, the passive transfer reaction and the Schultz-Dale test.

The sugars studied were as follows:

1. A maltodextrin preparation formed by the acid hydrolysis of cornstarch (dextrose equivalent 24).
2. A commercial edible grade of dextrose, also prepared by the acid hydrolysis of cornstarch.
3. Sucrose, derived from cane sugar, used as a control.
4. A dextrimaltose preparation prepared by the enzymatic action of barley malt on cornstarch (dextrose equivalent 36).
5. A corn syrup prepared by the acid hydrolysis of cornstarch (dextrose equivalent 38).

These sugars are designated by number throughout the experimental work.

#### PASSIVE TRANSFER TESTS

Serum was obtained from two known corn-sensitive persons. Neither was sensitive to barley, and the sera of both gave consistently positive reactions to whole corn extract by passive transfer test. These full-strength sera were prepared in dilutions of 1:2, 1:5, 1:10, 1:100, and 1:1,000, and all were used in preparing suitable testing sites on a nonallergic recipient.

Six separate sets of sites were prepared, beginning with the full-strength serum and continuing down to the 1:1,000 dilution. The first set was tested with whole corn extract (1,000 PNU per cubic centimeter) both to prove the presence of corn reagin and to quantitate its strength by the dilution technique. Each of the other five sets of sites was tested with a 10 per cent aqueous solution of one of the five sugars described. A positive passive transfer reaction was considered to be present when a 2 plus reaction (a wheal measuring 0.5 to 1.0 cm. in diameter) was obtained and the control was negative.

A total of nine passive transfer studies were performed. In each instance the serum showed a positive response to testing with whole corn extract as far as the 1:10 or 1:100 dilutions, while all controls were negative. Sugar No. 4 gave a positive reaction in four of the nine passive transfer tests in dilutions of 1:2 or 1:5. Sugar No. 5 gave three positive tests in nine trials, while the other three sugars, including the sucrose control, gave no significant responses.

A 25 per cent concentration of the sugars was used in two additional passive transfer tests but gave positive reactions not only in all the test sites but in the control areas as well. These were deemed to be irritant rather than allergic reactions.

SCHULTZ-DALE STUDIES

Virgin female guinea pigs, weighing approximately 300 grams each, were sensitized with a fresh corn extract potentiated by the use of Freund's adjuvant. These animals were derived from stock which had been on a diet free of corn and barley for more than four generations. The guinea pigs were

G.P. SENSITIZED 10-18-57 WITH FRESH CORN,  
FREUND'S ADJUVANT

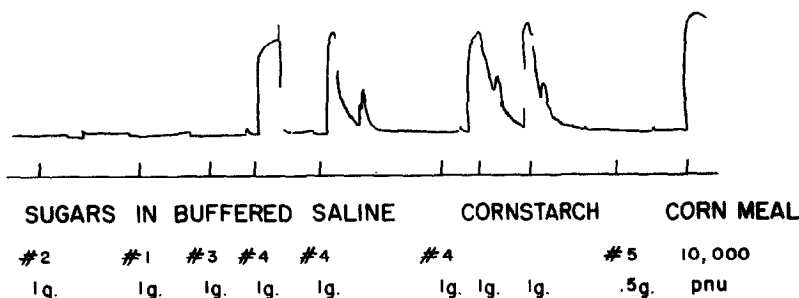


Fig. 1.

G.P. SENSITIZED 10-18-57 WITH FRESH CORN,  
FREUND'S ADJUVANT

KILLED 2-6-58, UTERINE END

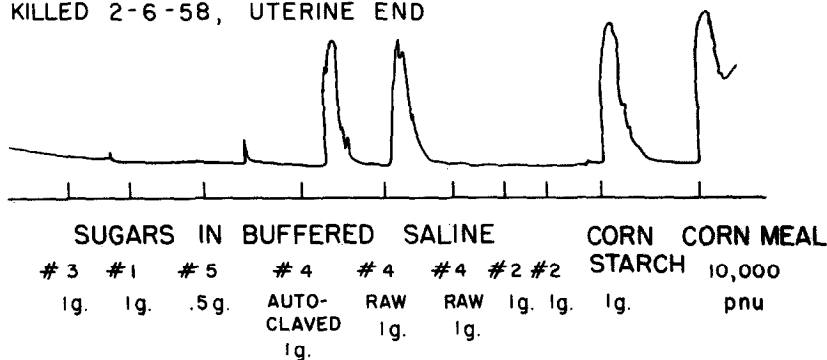


Fig. 2.

Figs. 1 to 6.—Demonstration of a fraction of corn antigen in one sugar derived from cornstarch. Kymograms of the reactions of the uterine horns of sensitized guinea pigs following stimulation with the designated materials in the Schultz-Dale bath. (All guinea pigs were sensitized to fresh whole corn extract potentiated with Freund's adjuvant.)

Figs. 1 and 2 show a contraction of the uterine horn to sugar No. 4, raw or autoclaved. When sugar No. 4 no longer reacts, corn meal still causes a reaction, demonstrating that the antigenic property of sugar No. 4 is only a fraction of the whole corn antigen. (The cornstarch response is a known nonspecific reaction.)

sacrificed after two months, and strips of the uterine musculature were tested in the Schultz-Dale muscle bath as follows:

*Group I.*—The uterine horns were first shocked with corn meal (10,000 PNU) until contractions were no longer obtained, and then they were tested to the various sugars. Sample tracings are shown in Figs. 5 and 6. In none

of these tests did any of the sugars produce any response after exhaustive shocking with corn meal, but these horns were still able to respond to either cornstarch or histamine.

*Group II.*—In this group the uterine horns were challenged with the various sugars in random order before being challenged with corn meal extract. Figs. 1, 2, 3, and 4 indicate the varied responses obtained. In approximately one-half (eleven) of the horns tested, sugar No. 4 gave a definite positive reaction, as shown in tracings 1 and 2. In the other twelve tests no reactions could be obtained to any of the sugars, as shown in tracings 3 and 4. Autoclaving of sugar No. 4 had no apparent effect on its ability

G.P. SENSITIZED 10-18-57 WITH FRESH CORN,  
FREUND'S ADJUVANT

KILLED 12-20-57, OVARIAN END

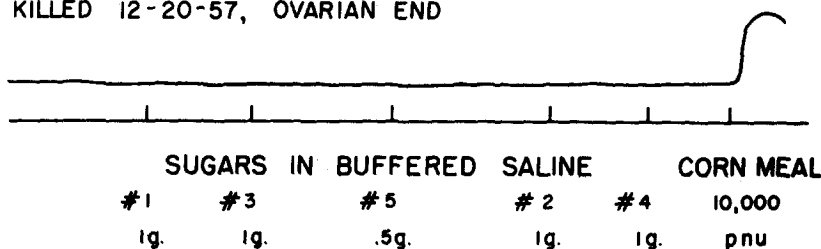


Fig. 3.

G.P. SENSITIZED 10-18-57 WITH FRESH CORN,  
FREUND'S ADJUVANT

KILLED 12-18-57, UTERINE END

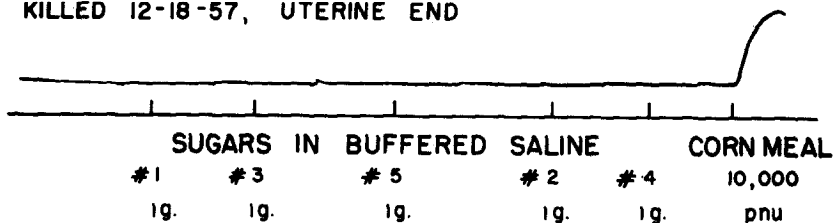


Fig. 4.

Figs. 3 and 4 show no contraction when the uterine horn is stimulated by any of the sugars. This was true in half the animals tested.<sup>12</sup>

to produce a contraction in the sensitized muscle. It will be noted in Figs. 1 and 2 that after sugar No. 4 failed to produce any additional response in the uterine horn, a positive response could still be obtained to corn meal, cornstarch, and histamine. It should also be noted that cornstarch caused a reaction in every instance in which it was used, even after the muscle strip had been made nonreactive to corn meal. It has been shown that cornstarch gives a nonspecific reaction in any uterine horn, regardless of the presence or absence of sensitization to corn.

# INTERPRETATION OF RESULTS

The passive transfer reaction, considered by many to be a more sensitive immunologic test than gross anaphylaxis of the Schultz-Dale test, gave definite positive reactions to sugars No. 4 and No. 5 in nearly one-half the tests performed, while no reaction was obtained to the other sugars. This would indicate that sugars No. 4 and No. 5 contain sufficient amounts of corn antigen to be irregularly identified by the passive transfer technique. It is possible, however, that we are dealing with an irritant factor which might be eliminated with further dilution of the testing materials, as was suggested by the results obtained with 25 per cent concentrations of the sugars.

G.P. SENSITIZED 10-18-57 WITH FRESH CORN, FREUND'S ADJUVANT

KILLED 12-20-57, OVARIAN END

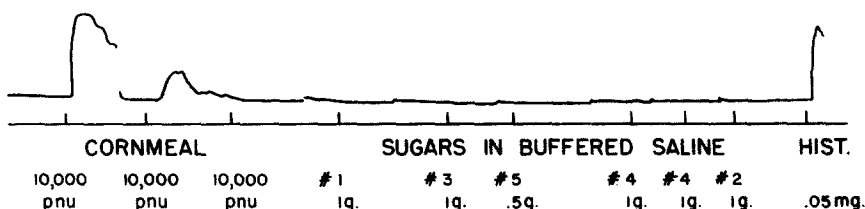


Fig. 5.

G.P. SENSITIZED 10-18-57 WITH FRESH CORN,

FREUND'S ADJUVANT

KILLED 2-6-58, UTERINE ENDS

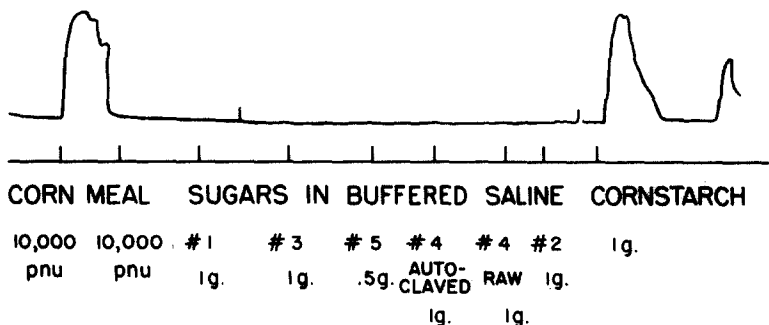


Fig. 6.

Figs. 5 and 6 demonstrate the exhaustion of whole corn antibody by stimulation with corn meal, so that sugar No. 4 does not react when it follows corn meal. Fig. 6 confirms the nonspecific nature of the cornstarch reaction occurring after the muscle has been depleted of corn antibody.

In the Schultz-Dale muscle bath, sugar No. 4 produced muscle contractions in several instances but never depleted corn antibody, since corn meal always produced a reaction after sugar No. 4 had failed. This is taken to indicate that the amount of corn antigen in sugar No. 4 is small and cannot

properly exhaust the uterine strip, which will still respond to large doses of the antigen (law of multiple proportions), or possibly that sugar No. 4 contains only one or a few of the antigens present in corn extract.

#### SUMMARY AND CONCLUSIONS

1. Five sugars of the type used in infant feeding have been tested for the presence of corn antigen by the passive transfer and Schultz-Dale techniques. Sugar No. 1 is a maltodextrin preparation, and sugar No. 2 is dextrose, both prepared by acid hydrolysis of cornstarch. Sugar No. 3, used as a control, is sucrose (cane sugar). Sugar No. 4 is a dextrimaltose prepared by the enzymatic action of barley malt on cornstarch, while sugar No. 5 is a commercial corn syrup prepared by the acid hydrolysis of cornstarch.

2. By the passive transfer and Schultz-Dale techniques, sugars No. 1, No. 2, and No. 3 have no demonstrable antigenic activity.

3. By passive transfer, sugars No. 4 and No. 5 show inconstant evidence of the presence of corn antigen.

4. By the Schultz-Dale technique, sugar No. 4 produced positive responses in approximately one-half the animals tested. These positive reactions may be due to the presence of small amounts of whole corn extract or to the presence of one or more antigens in the extract.

5. From the data presented, there is suggestive evidence that detectable amounts of corn antigen or antigens may be present in certain sugars used in infant feedings. No evidence is presented to indicate that these amounts are sufficient to be important; rather, it is suggested that additional work, both experimental and clinical, is indicated to clarify the role of corn as a possible allergen in infant feeding.

#### REFERENCES

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