

bladder or the bile duct at that time, with temporary obstruction.

Specific agglutinins for the Flexner type of dysentery bacillus were found in the blood of the patient, but none for the Shiga type. This agglutination test was made about 145 days after the last appearance of symptoms and the successful bacteriologic examination of the feces. The persistence of agglutinins for at least 145 days and the absence of continuous positive cultural findings indicate the value of the agglutination test in the detection of carriers or of persistent chronic cases of the Flexner type of dysentery. The recovery of the pathogen only at the time of the appearance of symptoms points not only to the chronicity of the infection, but also to the possibility of an alteration in the resistance of the host.

ISOLATION OF MONILIA PSILOSIS IN TROPICAL SPRUE (PSILOSIS)

REPORT OF CASE THAT ORIGINATED IN KOREA *

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In 1916, Ashford¹ reported finding a monilia in cases of sprue in Porto Rico, distinct from *Monilia albicans*, which Bahr and others had previously reported as occurring in sprue. Ashford called this organism *Monilia psilosis* (Ashford). He considered it the specific cause of sprue when it colonizes in an intestinal tract rendered favorable to it by a glandular insufficiency caused by climatic or other influences and resulting in a lessened outpouring of the digestive juices, with increased bacterial activity producing an increased acidity of the intestinal tract, and so producing conditions favoring the growth of *Monilia psilosis*.²

Other articles by him have since appeared from time to time, giving the results of his further investigations on the etiology and treatment of sprue, dealing with the methods of isolating *Monilia psilosis*, its almost universal presence in sprue at some stage of the disease, and also giving the results of the several hundred complement fixation tests in which suspensions of *Monilia psilosis* were used as antigens on persons with and without evidences of clinical sprue. He also has reported the reactions shown by patients injected with vaccines prepared from this monilia. He obtained in patients with sprue strong allergic reactions, with systemic reactions resembling acute attacks of sprue, whereas with patients who did not show evidences of sprue he did not obtain these reactions.

Dr. Carl Michel,³ of the U. S. Public Health Service, reported in 1917 the results of his work on *Monilia psilosis* in Porto Rico, giving the results of a large series of complement fixation tests and other laboratory investigations which he undertook with Dr. Ashford. In 1918, he⁴ reported the results of the

use of a vaccine made from *Monilia psilosis* in cases of sprue. In 1920, Oliver⁵ reported a case of sprue originating in Porto Rico from which *Monilia psilosis* was isolated.

This organism was isolated from the case of sprue here reported, originating in Korea, where sprue is at present making great inroads among the foreign residents.

Mrs. R. (wife of the writer) went to Korea in October, 1917, and enjoyed good health until after the birth of her first, and only, child in August, 1918. Soon after this she began to complain of heartburn and epigastric distress, which became much more severe after an attack of influenza in November. For some months after this, she rarely had more than a week or ten days of comfort each month. In June, 1919, it was found that the blood pressure was very low (systolic pressure, 85). She was treated for that with subsequent improvement. Soon she was generally comfortable, but in June, 1920, a morning diarrhea began, which had become a daily occurrence by October. She was put on a modified sprue diet in January. In April, 1921, after a very acute attack, she was seen by the other three physicians of the mission, who all had had experience with sprue. The diagnosis was confirmed and she was put on a strict milk diet, with fruits and some vegetables, rice being added later. At first, she did well, but in a month she suffered a relapse, and lost ground constantly, until in September she was advised to return to America for treatment.

After her arrival in America, she was treated along the standard dietetic lines, but failed to make any progress until April, 1922, when she began to improve, and her case is now progressing favorably.

COMMENT

February 16, a specimen of one of the diarrheal stools was cultured on Sabouraud's medium, and three days later an abundant growth of raised, shiny, regular, creamy colonies was noted, standing out well above all the other growth on the plates. These were transplanted to obtain pure cultures, and February 21 these were obtained, showing grossly a raised glistening shiny creamy growth, with sharply defined regular edges and a yeasty odor, faintly suggesting that of soured honey. The cell was a double contoured, round, yeastlike body about the size of a blood cell, though with many variations in size, showing numerous budding forms. All the cells had well-defined vacuoles containing from one to four motile coccoid bodies, these bodies becoming more numerous as the culture aged. The budding forms were gram-positive; the mycelial forms produced later became gram-negative as they aged. The capsule was shown up distinctly with Wright's stain, while Loeffler's methylene blue revealed the granular chromatin material of the cell body. Mycelial growth was freely produced on gelatin and also on ascitic agar under lowered oxygen tension, and, as the colony aged, on other mediums. A gelatin stab produced a very plain inverted pine tree growth, which Ashford regards as very important in identifying this organism. In litmus milk, the surface was rendered more alkaline, while later a faint acid reaction was produced deep in the medium, with a very marked casein digestion. The sugar reactions, which were considered very important in identifying this organism, were these: One per cent. sugar broths were inoculated with the organism, Andrade's indicator being used to detect acidity. Our organism gave marked acid and gas production with glucose; marked acid and very marked gas production with maltose; a small amount of gas and acid with saccharose; no acid

* The laboratory work mentioned here was done in the laboratories of the Crowell Clinic, Charlotte, N. C., at the instance of, and with the advice of, Dr. L. C. Todd of that organization.

1. Ashford, B. K.: Am. J. Trop. Dis. 3: 32, 1915-1916; Monilia Found in Certain Cases of Sprue, J. A. M. A. 64: 810 (March 6) 1915; Studies in Moniliasis of the Digestive Tract in Porto Rico, Am. J. M. Sc. 150: 680, 1915; Etiology of Sprue, ibid. 154: 157 (Aug.) 1917.

2. Ashford, B. K.: Personal communication to the author.

3. Michel, Carl: Toxins and Serological Reactions in Sprue, Am. J. M. Sc. 154: 177 (Aug.) 1917.

4. Michel, Carl: Use of the Monilia Vaccine in Treatment of Sprue, J. Infect. Dis. 20: 53 (Jan.) 1918.

5. Oliver, W. W.: Cultural Studies on a Case of Sprue, J. A. M. A. 74: 27 (Jan. 3) 1920.

or gas with lactose, and neither acid nor gas with mannite.

A vaccine made from this organism, prepared according to the technic described by Dr. Michel,⁶ caused a very marked allergic reaction, producing in the patient a large red area about 6 cm. in diameter around the point of injection, accompanied by a systemic reaction resembling an acute relapsé of sprue. When injected into a normal person over a period of sixty days, according to the method described by Michel, it caused no local reaction except a small reddened area, perhaps 2 cm. in diameter, and produced no systemic reactions whatever.

Since this organism seemed to correspond in all respects to *Monilia psilosis* (Ashford), we sent a culture to Dr. Ashford requesting him to test it out and give us his report. This he kindly did, reporting that it was a specimen of true *Monilia psilosis*.

The question then being raised whether *Monilia psilosis* could be found in patients living all their lives in or near Charlotte, N. C., we cultivated specimens from the stools of fourteen patients having chronic diarrhea. The specimens were furnished us by friends practicing in Charlotte. While large numbers of yeast-like organisms were isolated from these specimens and tested out, no *Monilia psilosis* was found. We cultivated a specimen from the stool of the writer and found *Monilia psilosis*. This could be easily expected, since he had been living for four years in the endemic area in a house in which, during the last six years, five cases of sprue had developed, and had been in daily contact with a case of sprue for two years. Several cultures made from the stools of the young son of the patient, with whom we had taken every possible precaution to prevent contact infection, if such exists, were all found to be negative for *Monilia psilosis*, but showed a heavy growth of what appeared to be two species of true yeasts closely allied to bakers' yeast. It is interesting to observe that he has never been fed yeast in any form except in bread, supposedly well baked.

Later, we cultivated a specimen from the stool of a patient who had lived for seven years in Korea, at Songdo (north of Seoul), and who had had amebic dysentery two years previously, at which time I saw her. Since then she had been subject to occasional attacks of diarrhea, but had never had sprue clinically nor any symptoms of it, except for the occasional attacks of diarrhea. In her case there was found no *Monilia psilosis*. So far as I know, no sprue has ever originated at Songdo.

CONCLUSION

An organism which was identified by Dr. Ashford as *Monilia psilosis* was isolated from a case of undoubted and clinically active sprue (or psilosis) originating in Korea. The same organism was also isolated from the stool of the patient's husband, but was not found in the stools of fourteen other persons, all of whom had chronic diarrhea and resided in or near Charlotte, N. C. Also, this organism was not found in the stools of two other persons, residents of Korea, who did not have tropical sprue. One of them did not live in the area where sprue has become so common among the foreign residents.

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OBSERVATIONS ON THE EFFECT OF SODIUM CITRATE ON THE BLOOD

ESPECIALLY CONSIDERING THE p_H FACTOR *

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In a previous communication, one of us¹ drew attention to the possible rôle of the variable p_H of sodium citrate in the causation of untoward results in transfusion by the citrate method. We wish here to emphasize further our position in regard to the relation of the p_H factor to reactions following intravenous injections in general. As indicated in our paper, the proposition of imitating as closely as possible the p_H of the blood by buffering intravenous solutions was by way of suggestion, since it seemed to be a logical procedure. It was distinctly stated then that no claims were made for its efficacy, and none are made now. Such claims can come only from experimental work or from carefully controlled clinical studies.

In the literature of blood transfusion there are numerous attempts to account for the occurrence of more or less severe reactions when careful preliminary tests had indicated complete compatibility of the bloods of donor and recipient. It is scarcely necessary to review here the evidence for the existence of subgroups not discovered in the course of ordinary compatibility tests, or the probable occurrence at times of anaphylactoid reactions from the injection of the more or less foreign proteins of another individual's blood. It is sufficient merely to mention such possibilities to indicate our conviction that not all of these reactions are from the same cause. Our interest has been aroused by the frequent observation that they occur more often when transfusion is performed with citrated blood than when unmodified blood is used.

Several questions at once present themselves. Is sodium citrate toxic in itself? If so, why are not most cases in which it is used affected in this way? Why do some clinicians report a higher proportion of cases with these unexplained reactions than others using the same method? Do various samples of commercial citrate differ among themselves in their tendency to cause this action? In case citrate is not toxic per se, does it produce, in its reactions with the transfused blood, substances that are toxic or cause other unfavorable changes in the blood? That chemical reactions do take place with the blood is, of course, apparent. The very purpose in using citrate is to render calcium unavailable for the formation of thrombin, probably by tying it up in some undissociable form; but the exact reaction involved in this and its end-products have not, to our knowledge, been well studied. The question arises whether these end-products differ at times, owing to varying physical or chemical conditions affecting the reaction. Likewise, may there not be unintended side-reactions, produced by some samples of citrate acting on other salts, the proteins, or even the formed elements of the blood?

6. Michel, Carl: Preparation of the Monilia Antigen, in Tice: Practice of Medicine, Hagerstown, Md., W. F. Prior Company 4: 183-184, 1922; ibid. 4: 188 1922.

* From the Department of Laboratories, Highland Hospital.
1. Mellon, R. R.; Slagle, E. A., and Acree, S. F.: The Practical Application of Buffers, J. A. M. A. 78: 1026 (April 8) 1922.