It was found that the ultrafilterable calcium fraction of a squamous cell carcinoma was sharply reduced on both an absolute and relative basis. The conclusion was reached that the base-binding capacity of an organic fraction which binds calcium is altered in cancer. It is reasonable to expect that this calcium binding complex, which changes in cancer to limit calcium uptake, is located like that demonstrated by Heilbrunn in the cell cortex. The work of Heilbrunn and his associates, covering a number of years, are summarized in his book (*9*).

Further supportive but indirect evidence for the localization of the calcium change in cancer in the cell surface can be found in the work of Coman (*7*), who has found that normal cells are more readily separated by micromanipulation when in calcium-free medium than when in balanced salt solution. Further, he has demonstrated that cancer cells are more readily separated than are normal cells, and the suggestion was made that the decreased adhesiveness of cancer cells results from a local calcium deficiency which facilitates separation of these cells from one another.

Thus, the evidence presented, while undoubtedly weak, makes it possible to correlate the various changes described in a single hypothesis. It seems quite likely that an organic calcium-binding complex of the cell cortex plays an integral part in the growth regulatory mechanism of cells and that at the time of cessation of growth this calcium-binding complex, presumably a protein, is altered or reoriented in such a way as to increase calcium-binding capacity. Thus, a mechanism is offered which at least in a general way synchronizes the changes that occur with age. On the other hand, when the calcium-binding system alters in such a manner as to decrease calcium binding, growth does not cease, age changes do not occur, and, in effect, the state of affairs exists that is associated with cancer. This hypothesis is also compatible with Coman's concept of the invasiveness of cancer.

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Coproantibody Excretion During Enteric Infections[1]

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The immune mechanism responsible for initiation of recovery from infections confined essentially to the lumen and mucosa of the intestinal tract, viz., cholera, bacillary dysentery, and certain *Salmonella* infections, is suggested by the recent work of Burrows and co-workers (*1*), who showed that antibody is excreted in the feces by both infected and immunized animals and immunized human volunteers, and that immunity to experimental infection is associated with its presence. They showed that the appearance of coproantibody precedes that of serum antibody, reaches peak titer and declines while serum antibody is still rising, and completely disappears despite the persistence of serum antibody. They suggested that the independent behavior of serum and fecal antibody might be explained on the assumption that the latter represents intracellular antibody, possibly transported to the lumen of the bowel by lymphocytes. However this may be, the late appearance and persistence of serum antibody strictly limits its diagnostic utility, but the behavior of coproantibody suggests that it might be useful both in the rapid diagnosis of specific acute enteric infection and in providing a clue to the possible etiology of chronic diarrheal disease such as chronic ulcerative colitis.

TABLE 1

Coproantibody Excretion From Patients Suffering From a Variety of Enteric Infections

Clinical diagnosis	No. cases	Pathogens isolated	Copro-antibody present
Acute bacillary dysentery	20	*S. sonnei* from 6; *S. flexneri* from 5; none from 9	20*
Chronic bacillary dysentery	18	*S. sonnei* from 3; *S. flexneri* from 5; none from 10	18†
Acute diarrhea	14	Various *Salmonella* from 10; none from 4	14†
Chronic diarrhea	35	Para A from 9; Para B from 3; none from 23	32‡
Chronic ulcerative colitis	5	*S. flexneri* from 1; *S. sonnei* from 2; none from 2	5§

* Eleven, 1:640 or above; 8, 1:320; 1, 1:160 (maximum titers obtained).

† Coproantibody titer of 1:160 or above obtained against homologous organism, or against one or more species of enteric pathogens, on several occasions from each patient.

‡ Three failed to show coproantibody at any time during the observation period.

§ Usually obtained in highest titer during episode of exacerbation of disease.

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[2] The authors are indebted to William Burrows for making available copies of translations from the Russian (*4*) furnished him by the Translation Unit of the U. S. Public Health Service.

Although we were unaware of previous reports of the presence of fecal antibody in dysenteric stools at the time this work was initiated, it was of some interest to find that Davies (*2*) earlier had demonstrated antibody in dysenteric stools and suggested use of serological examination of feces for rapid diagnosis of acute bacillary dysentery. More recently, Soviet investigators (*4*) have utilized fecal antibody titration in early diagnosis of bacillary dysentery.

The present report is concerned with some observations on the presence of antibody in fecal specimens from patients with a variety of enteric infections. The method of preparation of fecal specimens was essentially that used by Burrows (*1*). Agglutinin titration was carried out in the usual manner. Examinations were made at frequent intervals during active infection and convalescence and, in some instances, over a period of several months. Serum and fecal agglutinin titrations were carried out simultaneously with stool cultures.

Table 1 summarizes the results. The grouping of patients was based on the clinical diagnosis, isolation of enteric pathogen, and presence of fecal agglutinins for the particular infectious agents indicated. Although positive cultures were obtained from only 47.8 per cent of the patients included in the table, it is of some interest that fecal agglutinins were found in 96.7 per cent of the cases. Thus, of 20 cases of acute bacillary dysentery and 18 of chronic bacillary dysentery, all showed fecal agglutinins of significantly high titer; likewise, of 14 cases of acute diarrhea and 35 of chronic diarrhea, most of the fecal specimens contained high-titer agglutinins. Three in the latter series failed to show coproantibody at any time patient during the period of examination. Acute diarrhea of *Salmonella* origin followed the fecal antibody pattern of acute bacillary dysentery. In chronic *Salmonella* infections it was possible to obtain high-titer fecal agglutinins on one or more occasions during the period of observation. In chronic ulcerative colitis it was found that relatively high-titer fecal agglutinins for at least one species of *Shigella* were present during episodes of exacerbation of symptoms.

It is of some interest that, in those instances in which positive cultures were obtained, fecal agglutinins were found in highest titer during the period in which presumably the greatest numbers of the causative organism were excreted, *i.e.* during greatest activity of the infection, but disappeared after recovery was established. Although it is not clear as to the origin of fecal antibodies in these infections, it is significant from a diagnostic point of view, and presumably for initiation of recovery, that antibody is excreted during the active phase of the infection or, in the case of chronic infections, during periods of clinical activity of the disease. The diagnostic utility of these observations is obvious, for in instances in which no etiologic agent can be found, the presence of fecal agglutinins appears to indicate, indirectly at least, the probable causative organism. The finding of fecal agglutinins for various species of *Shigella* from patients suffering from chronic ulcerative colitis is interesting with respect to Felsen's (*3*) views on the relation of bacillary dysentery to chronic ulcerative colitis. More important from the point of view of the patient is the role coproantibody plays in initiating recovery; that it is not completely effective in some

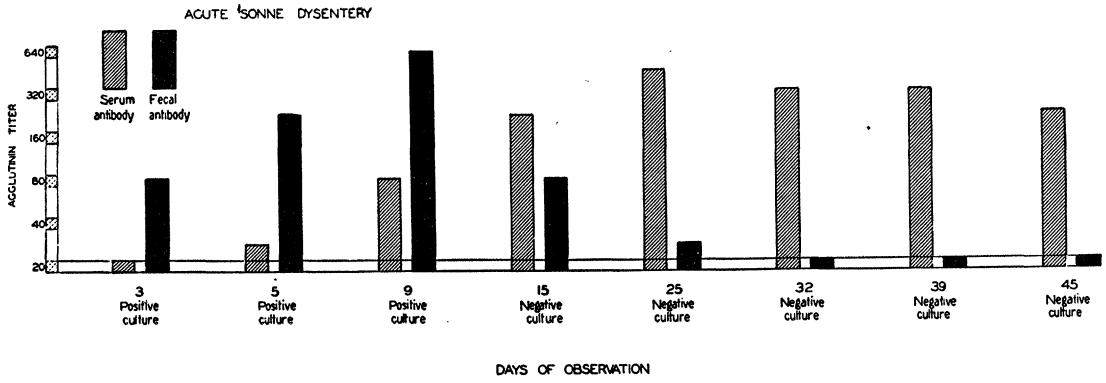

FIG. 1. Summary of serum and fecal agglutinin response in acute bacillary dysentery.

during the observation period. Five cases of chronic ulcerative colitis were studied; fecal agglutinins were demonstrable in high titer in all cases during one or more episodes of exacerbation of the disease.

Fig. 1 illustrates the typical serum and fecal agglutinin response observed in acute bacillary dysentery. Fecal agglutinins were demonstrable as early as the 3rd day of disease, rose to high titer by the 9th day, and disappeared soon after stool cultures became negative and after recovery definitely was established. On the other hand, circulating antibody did not appear to significant titer until about the time recovery was initiated, but then rose to high titer and remained at a high level during the period of observation.

In cases of chronic bacillary dysentery significant fecal agglutinin titers were obtained on several occasions from each instances is indicated by finding fecal agglutinins to high titer in chronic forms of enteric infection. Under such conditions however, the demonstration of coproantibody parallels evidence of clinical activity of the disease, even though the infectious agent is not recovered.

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