magnetic disturbances have been extensive and they are very valuable. The magnetic charts of the Soviet Union are, I am given to understand, much more detailed in relation to the Western Arctic and Siberia than are any U. S. charts of northern areas.

These magnetic observations are of great help to navigators of the air and sea in those areas which are more than often fogbound and so cloud covered as to restrict astronomical navigation.

But the greatest aids to the detailed exploration of the northern areas are the heavy tractor and the "cat trains" which have ploughed their way through swamps and tundra and over highlands and plateaus. We in this country have heard a great deal about the Alaska Highway and the Burma Road. Within the Soviet Union there are several "Alaskan Highways" and many hundreds of miles of "Burma Road" which winds over terrain equally as difficult as anything to be found in China or Burma.

It is, as a matter of fact, over such roads which lead to Kunming and Chungking that the Russians have delivered to the Chinese so much of the ground-warfare supplies that have been used by the Chinese in their successful resistance against the Japanese.

Great web-ways of tractor roads over Russia have opened great and rich food-producing areas in Central and in Northern districts and have played no small part in the glorious successes of the Soviet Army.

In the far north tractors have provided the means for transport throughout a great part of the year, but they operate most successfully during the depth of winter when the ground and the swamps and the rivers are solidly frozen over.

Such transportation has opened up vast fields for occupation and this in turn has led to much exploration in the Soviet Union in respect to soil chemistry and the development of a quick-growing variety of grain-producing plants. Wheat, oats and barley suitable for growing in the short Arctic summer season have been developed on the agricultural farms for research in the Soviet Union. And in respect to these findings, the Soviet scientists have given liberally to others in many parts of the world. The rich harvests produced in northern Canada are, in a great measure, due to the research and results of Soviet scientific exploration.

The development of such grain-producing, short-season varieties of plants is a matter of great importance to the United States if, for instance, the development of Alaska is undertaken. There are millions of acres in Alaska which are as suitable for development as the millions of acres in similar latitude and climatic conditions in the Soviet Union. The difference is, mainly, that there is no population in Alaska to take advantage of these areas.

There are others at this meeting who will tell you of the civic and cultural explorations within the Soviet Union, but I believe that only those of us who were privileged to see the beginning of that splendid and healthy development and who were in a position to realize the magnitude of the task can appreciate fully the tremendous progress that has been made in the Soviet Union between the years of 1923 and 1943.

How far such developments will effect the friendly cooperation of the two great countries, the U. S. A. and the U.S.S.R., is a matter for mutual consideration. It is my belief that such friendliness and cooperation can and should be boundless.

The magnitude of the cooperation might depend largely on the development the United States is prepared to make in her northern areas. But whatever the efforts of the United States may be, it can be taken for granted that through the field of exploration, followed by healthy, energetic exploitation, the U.S.S.R. will shortly, as world time is measured, be able to stand side by side with the United States in no disproportionate stature. And it will not be long, as world time is measured, before the U.S.S.R., with her multitudinous population and tremendous resources, will stand towering above the United States in material and economic magnitude. This is a matter for pleasant contemplation, provided we encourage and maintain the cooperation that is greatly to be desired.

SOME MODERN CONCEPTIONS OF AMEBIASIS
II

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PATHOLOGY AND SYMPTOMOLOGY

It is not the purpose of this paper to provide a clinical description of amebiasis but rather to analyze some of the fundamental evidence on host-parasite inter-relationship in amebiasis which may assist the clinician in visualizing his problems. A clear picture of the levels at which the amebic lesions occur, their numbers and the depths of penetration of the amebae constitutes the essential fundamental background for a clinical appreciation of the disease. Thus, a mucous

diarrhea, with amebic trophozoites in the stool, but without macroscopic blood suggests early, rather extensive superficial invasion of the bowel wall or a mild relapse, while a fulminating dysentery indicates deep invasion in at least one focus, usual in the rectal area.

Perhaps the most commonly overlooked syndrome which should suggest the possibility of amebiasis, especially in tropical countries, is that of appendicitis. Amebic lesions in the cecum, appendix or adjacent levels of the ileum or ascending colon may give rise to dull throbbing or intense knife-like pain in the lower right quadrant of the abdomen or by reference the pain may suggest gall bladder disease or peptic ulcer. Patients having infection at this focus may consistently pass stools which are formed or constipation may alternate with diarrhea. In New Orleans 10 per cent. of appendicitis cases in the surgical service of Dr. Alton Ochsner in Charity Hospital were found to have amebic involvement.[69] In the Santo Tomas Hospital in Panama the frequency has been one third of appendicitis cases coming to operation. Early recognition by the clinician of the frequency of amebiasis of the cecal area usually allows management of the case by the internist and prevents unnecessary surgical intervention, since anti-amebic therapy in these cases will probably eventually be required.

Asyndromic amebiasis[70] may cause general colonic disturbance, nervous symptoms or fatigue. In such patients one or more well-established amebic ulcers have usually developed, most commonly in the cecal area.

In chronic amebiasis the amebic lesion is usually secondarily infected with bacteria, which provokes an infiltration of neutrophilic leukocytes. Moreover, in this type of amebiasis a moderate leukocytosis is frequently observed in the circulating blood, so that the blood picture disguises the diagnosis of amebiasis.

Amebic invasion of the liver is probably much more common than the records of acute hepatic amebiasis indicate. Amebae which enter the mesenteric venules in the submucous coat of the large bowel are swiftly carried to the liver, to be filtered out in the portal capillaries. In the great majority of cases the amebae do not colonize in the liver parenchyma but soon die. The cause of this amebostatic action is unknown, but it is plausible that the same unknown substance in liver extract which has been found experimentally to control the infection in the bowel operates even to a greater degree in the liver itself. If the suggestion may be carried one step farther, it is possible that a quantitative reduction in the production of this as yet unknown fraction of liver extract allows the amebae to multiply, with resultant amebic hepatitis or liver abscess.

[69] A. Ochsner, *Surgery*, 1: 633–636, 1937.

[70] J. S. D'Antoni, *New International Clinics*, Ser. 5, 1: 101–109, 1943.

Diagnosis

While an internist who has had years of experience in the study of dysenteries can frequently make an accurate diagnosis of fulminating amebic or bacillary dysentery on the macroscopic appearance of the freshly passed stool, this method does not provide a safe basis for diagnosing amebiasis in its broader aspects. In practice it is necessary to recover *Endamoeba histolytica* itself either in its trophozoite or cystic stage, and to differentiate it from other protozoa of the digestive tract as well as from macrophages and *Blastocystis*.

Visualization of the organism can be accomplished from microscopic films prepared from formed, semiformed or liquid stools, from purgative or enema specimens, from proctoscopic material or after *in vitro* culture of the ameba. None of these is 100 per cent. efficient.

In the laboratories of the Department of Tropical Medicine of Tulane University the following routine method of examination for *Endamoeba histolytica* has been in operation for several years. First of all, microscopic films of the freshly passed stool are prepared. These consist of (1) a direct film, one side unstained, one side stained with D'Antoni's iodine; (2) a supplementary hematoxylin-stained direct film; (3) a film resulting from concentration of cysts by the zinc sulfate centrifugal flotation technique. Three stools, passed on alternate days or preferably every third day, are examined in this way. Both by practical tests and by calculation it has been found that 85 to 90 per cent. of positive cases are diagnosed by these combined techniques on the three stool samples, whereas a single direct fecal film accounts for only 20 to 25 per cent. of *E. histolytica* positives. In individual cases with a history of chronic colitis proctoscopic examination, purgation with Glauber salts or phospho-soda, or high physiologic salt enemas are carried out.

While cultures of the specimen on *E. histolytica* culture media are satisfactory for the demonstration of the organism recovered from liquid or semi-liquid stools, cysts of this organism at times fail to excyst in the culture medium, thus providing false evidence of a negative.

In areas or population groups of high endemicity, in which there is not only a high incidence of infection in the population but also a large number of amebae per individual, evidence of infection is readily obtained from stool examination. In areas of low endemicity, in which the incidence is low and the average number of amebae per individual is small,

the problem of diagnosis is difficult or at least tedious. In the United States very high incidence occurs in certain population groups, as in rural areas of the Southern Appalachians and in children's asylums in New Orleans. In other areas, particularly in the north, the incidence may be as low as 1 per cent., although in most regions it varies between 5 and 10 per cent. The ease or difficulty experienced in the diagnosis of *Endamoeba histolytica* in any particular locality will depend not only on the skill of the diagnostician and the methods which he utilizes but also on the wealth or dearth of the amebae in the patient's feces.

TREATMENT

It would be unsuitable for the writer to deliver a set of dicta on anti-amebic treatment for the practising physician, but there are certain basic observations which are relevant and proper.

Twenty-five years ago ipecac was commonly utilized in the treatment of acute or chronic amebic colitis. It frequently cured the patient who could retain enough of the drug to act on the amebae. Meanwhile emetine hydrochloride had been demonstrated to be very effective in bringing the infection under control and particularly in alleviating symptoms. Stovarsol (acetarsone), originally prepared by Ehrlich, was first utilized by the French for the treatment of syphilis and African sleeping sickness, but by 1920 it was found to be effective in the control of amebiasis. Because of the high percentage of patients taking the drug who developed severe intestinal colic as well as other types of arsenic intolerance, this product has been practically replaced in recent years by less toxic anti-amebic drugs. Carbarsone, another arsonic acid compound originally prepared by Ehrlich, was introduced by Anderson and Reed in 1931[71] as a highly specific drug for the treatment of amebiasis and was described as much better tolerated than stovarsol. Meanwhile, in 1921, Mühlens and Menk[72] advocated the use of chiniofon, an iodo compound which they introduced under the trade name "Yatren." This drug was soon given extensive clinical trial and found to be a very efficient and well-tolerated anti-amebic drug. In 1936 diodoquin, another iodo compound, was released by Searle for clinical trial in the treatment of amebiasis. Its use is gradually being extended as its anti-amebic value and high tolerance are being demonstrated. Vioform, a third iodo compound, has been recommended for the treatment of amebiasis but has never been widely used.

To-day the drugs most commonly prescribed for amebiasis in the United States are emetine hydrochloride, carbarsone, chiniofon and diodoquin. Emetine hydrochloride is the only known eminently satisfactory preparation for the treatment of amebic hepatitis and amebic liver abscess. For amebiasis of the intestinal tract its usefulness consists primarily in controlling acute symptoms, but within limits of safe administration it can not be guaranteed to terminate the infection. For routine treatment of amebic colitis, whether acute, chronic or "carrier type," carbarsone, chiniofon and diodoquin constitute the present-day drugs of choice. For patients with arsenic intolerance one of the iodo preparations should be utilized. Moreover, in experimental amebiasis in the dog the writer and a junior colleague[73] have recently demonstrated that carbarsone has only a 75 per cent. amebicidal efficiency compared with chiniofon. For a short course of treatment chiniofon is most likely to eliminate the infection, but in some persons it provokes a severe watery diarrhea. Diodoquin apparently has no contraindications, but requires a longer period of treatment because of its slower absorption rate into the bowel wall.

An analysis of the present status of chemotherapy in amebiasis indicates that marked progress has been made in the past quarter of a century in the development of a few relatively specific drugs which are rather well tolerated by the patient. Yet in amebic colitis no one of these drugs and occasionally no combination of them provides a guaranteed cure. There is abundant need and opportunity to explore other preparations, including refined products of crude drugs utilized by Oriental and Amerind peoples, as well as new synthetics.

Finally, a suggestion may appropriately be made concerning the nutritional state of the patient in amebiasis. Experimental evidence suggests that during the period of treatment the carbohydrate intake should be reduced and that nutritious, readily digestible animal proteins should be increased. The possible role of vitamins in raising the threshold of resistance to the pathogen has never been given experimental or clinical trial, either in preventing infection or in controlling tissue invasion. This suggests the need for serious intensive study.

CONTROL

Justification of preventive measures in any particular disease is based on two premises: (1) that the disease is clinically important and (2) that it is a public health hazard. In an infection like amebiasis it is easier to dodge the issue than to meet it squarely and to provide machinery for practical control. Yet an honest evaluation of the evidence in amebiasis

[71] H. H. Anderson and A. C. Reed, *Calif. and Western Med.*, 35: 439–443, 1931.

[72] P. Mühlens and W. Menk, *Münsch, med. Wochenschr.*, 68: 802, 1921.

[73] E. C. Faust and J. E. Tobie. Unpublished experiments.

definitely indicates its actual or potential danger to individuals and communities which harbor the etiologic agent.

The problem of control is somewhat simplified by remembering that reservoir hosts play no important part in the propagation of amebiasis, so that man may thank himself for the infection. Moreover, the individual who is least likely to manifest symptoms, namely, the so-called "carrier case" who is passing cysts in his stools, is the primary offender. Exposure occurs through entry of viable infection-stage cysts of *Endamoeba histolytica* as a contamination into the mouth. Infection may occur from a single massive dose of cysts, or from repeated lighter doses taken into the mouth in food or water. While the epidemiologic evidence is not conclusive, it is apparent that the safeguarding of food and drink from contamination should do much to protect the population. The public must be made aware that dirty food handlers should not be tolerated. By sanitary regulations these individuals should be examined for amebic infection and, if found positive, should be treated until they are negative. Filth flies should not be allowed to breed; they are not only a menace in this infection but in practically all other diseases primarily involving the gastro-intestinal tract. Thorough sanitary campaigns should be carried out in eleemosynary institutions to clean out these hotbeds of infection. An awakening of the public consciousness regarding the potential dangers of amebiasis constitutes an additional essential part of the control program. Meanwhile the practicing physician, by his respectful attitude towards amebiasis in his own patients, whether they manifest symptoms or are apparently symptomless, can do much to further this end.

Conclusions

The material which has been presented in this paper is not intended for immediate practical application by the clinician but as a basis for reorientation and re-evaluation of the problem of amebiasis. Some of the remarks are personal reflections of the writer which have never previously been expressed except in informal conferences. It is believed, however, that the subject justifies this type of presentation. It is the writer's sincere hope that some little stimulus will have been provided which will aid the physician and the epidemiologist in elucidating the several obscure aspects of the problem of amebiasis, so that in the future practical means may be found for its control.

It has been a very real honor to be the 1943 recipient of the Alvarenga Prize of the Philadelphia College of Physicians and a privilege to address this distinguished body.

OBITUARY

L. CHARLES RAIFORD

PROFESSOR L. CHARLES RAIFORD died on January 8 at the age of seventy-one years after a very short illness. He is survived by a daughter, Mrs. Mark Hagerman, of Towanda, Pa., and a grandson, Mark, Jr.

Professor Raiford was born on August 2, 1872, in Southampton County, Va. He received the Ph.B. degree at Brown University in 1900, the M.A. in 1904 and the Ph.D. at the University of Chicago in 1909. He was on the teaching staff at the Mississippi Agricultural College, the University of Chicago, Clemson College, the University of Wyoming and the Oklahoma A. and M. College before going to the University of Iowa in 1918, where he served as professor of organic chemistry up to the time of his death. He was also head of the division of organic chemistry until 1942 when he reached the age of seventy years. During this period he directed the research of over a hundred graduate students for advanced degrees. These are scattered all over the United States in teaching and industrial positions.

Professor Raiford was a fellow of the American Association for the Advancement of Science, a member of the American Institute of Chemists, the American Chemical Society, the American Association of University Professors, the Oklahoma Academy of Science, the Iowa Academy of Science, Sigma Xi, Phi Beta Kappa, Phi Lambda Upsilon, Alpha Chi Sigma, Phi Delta Chi, the Research and Triangle Clubs. In the American Chemical Society, he served as national chairman of the organic division in 1937. In the local section of that organization, he served as chairman and secretary and was elected councilor nine times, a very notable record which indicated his popularity and standing in the profession.

Professor Raiford was active in these societies and always willing to do any service, no matter how much work was involved. He was president of Phi Beta Kappa in 1922–23 and was local secretary of that organization when a national directory was prepared, to which undertaking he contributed by gathering the necessary data for the members of the Iowa chapter. He represented the department of chemistry on the library board for many years, and the excellent maintenance of the chemistry library was due in great measure to his efforts. He served as president of the Research Club.

In 1942, when he reached his seventieth birthday, a testimonial dinner was given in his honor at the Alpha Chi Sigma chemical fraternity at which addresses were