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Amebiasis in Northern Saskatchewan:
Pathological Aspects

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INFECTIONS with *Entamoeba histolytica* occur throughout the world, but disease caused by this parasite is usually associated with residence in the tropics. Nevertheless, invasive amebiasis does occur in temperate and northern regions in isolated cases, but rarely in epidemic form.[1-3] The distribution of infection and the clinical status of amebiasis in Canada, when reviewed in 1946,[4] indicated that apparently indigenous cases of amebic colitis appeared sporadically in various parts of the country; that infection rates in the general population were low, but that high rates did occur in institutionalized groups.

Parasite surveys of aboriginal groups in Canada, the United States and Greenland have shown *E. histolytica* infections to be widespread in Indian tribes and to be present in some Eskimo groups.[5-9] More recently it was demonstrated that Indian bands in the Loon Lake area of Northern Saskatchewan had high infection rates and that there were cases of amebic ulcerative colitis among them.[10] In view of the paucity of information about invasive amebiasis in north temperate regions, some of the pathological findings in five fatal cases of amebiasis from the Loon Lake Reserve are presented.

CASE REPORTS

CASE 1

P.B., a 73-year-old male Indian from the Reserve, was admitted to the University Hospital, Saskatoon, in July 1959, four weeks after he had developed colicky abdominal pain and bloody diarrhea (10 to 12 motions per day). He was dehydrated and had obviously lost considerable weight. Radiological investigation showed that the entire colon was markedly irregular, particularly in the region of the splenic flexure where the mucosal pattern was almost entirely absent, and the appearance of the bowel suggested marked edema of its wall with irregular haustra and possible pseudopolypi. A diagnosis of atypical ulcerative colitis was made. Sigmoidoscopic examination to 15 cm. showed an inflamed mucosa, but no ulceration or bleeding was seen. The erythrocyte sedimentation rate (ESR) was 85 mm. in one hour, and total serum proteins were 5.9 g. per 100 ml.—2.2 g. albumin and 3.7 g. globulin. The antibiotics used were sulfathaladine and neomycin. Four weeks after admission there was no evidence of improvement; he still suffered from recurring lower abdominal cramps and frequent bloody (tomato soup) stools, and had lost 16 more pounds. Sigmoidoscopy at this time again showed no evidence of ulceration, but the walls of the bowel were covered with a mucoid bloody slime. Additional antibiotics were administered including streptomycin, chloramphenicol and chlortetracycline. Cortisone was also used in the treatment. A perforation of the ascending colon occurred and at an emergency operation the entire colon down to the proximal portion of the sigmoid was resected. His condition deteriorated in the following week and he died 10 weeks after the onset of his illness.

Pathological Findings

The specimen consisted of the entire large bowel except for the distal sigmoid colon and rectum, together with a 7.0-cm. length of terminal ileum. The small intestine appeared normal. The gross examination of the colon revealed only very small amounts of intact mucosa. From the ileocecal valve distally there was an abrupt change in the lining of the colon. The mucosa was covered with adherent yellowish-grey material resembling both feces and sloughing tissue. Mucosal folds were preserved but in the cecum there was an irregular polypoid thickening of the mucosa with some induration of the wall. Just distal to the ileocecal valve the wall attained a maximum thickness of 1.5 cm. This thickening was diffuse and extended approximately 2.0 cm. into the ascending colon. In this region also the mucosa was covered by an irregular yellowish-brown slough and most of its surface appeared ulcerated. In those areas where intact mucosa could still be seen it was thickened or had an irregular polypoid form. There was an irregular 3 x 1.5 cm. perforation in the wall of the ascending colon at a point 10.0 cm. distal to the ileocecal valve. The mucosa appeared less ulcerated in the sigmoid colon than elsewhere in the specimen. There was a large ulcer, 4.5 x 2.0 cm., bordering the distal resection line. Its longest measurement was in the transverse axis of the bowel and it had an irregularly rolled edge and a base covered with a slough of yellowish-brown material.

On microscopic examination the small intestine showed a non-specific subacute and chronic in-

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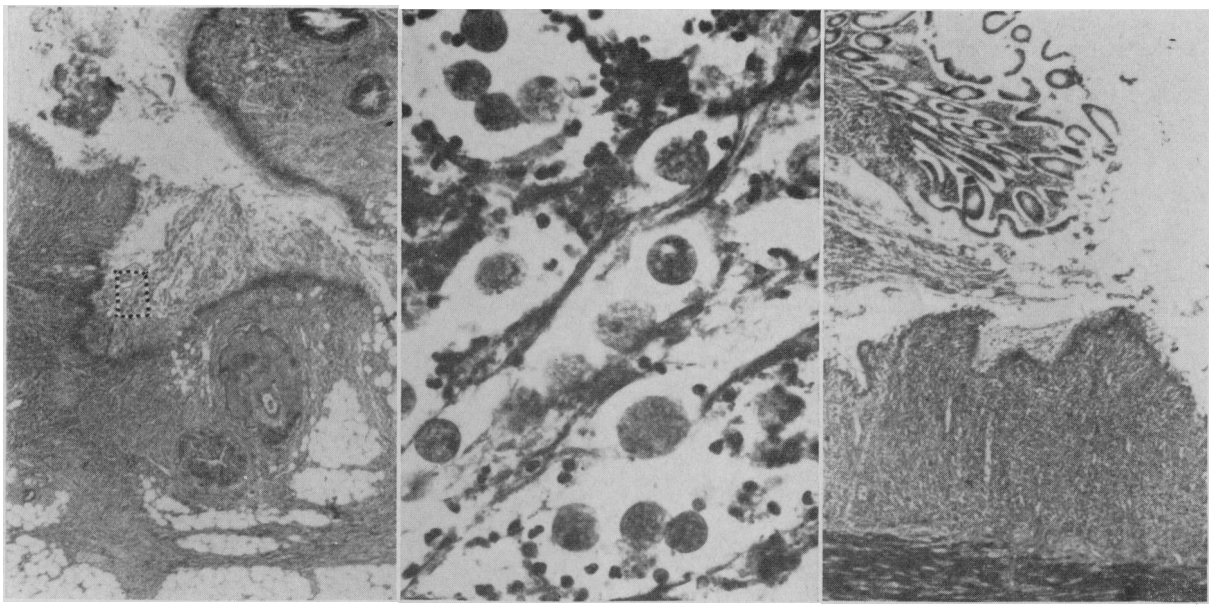

Fig. 1.—Case 1. Amebic ulceration of colon penetrating full thickness of bowel wall to pericolic fat. (Original magnification, × 45.) Fig. 2.—Magnified area (rectangle) of Fig. 1 to show trophozoites of *E. histolytica* in base of ulcer. (Original magnification, × 600.) Fig. 3.—Case 1. Amebic ulcer margin in section of colon illustrating characteristic submucosal excavation. (Original magnification × 45.)

flammatory reaction in the serosa and outer muscular layers. In the large bowel there was a very marked subacute and chronic inflammatory process which had resulted in the erosion of a large proportion of the mucosa. Ulcerated areas had become confluent and extended to the muscularis, their bases being formed of loose areolar granulation tissue infiltrated by large numbers of inflammatory cells. In many zones the muscularis appeared relatively spared by the inflammatory infiltrate, with only a few eosinophils and lymphocytes penetrating its substance, but in other zones ulceration had extended deeply through it and penetration into the subserosal fibro-fatty tissue had occurred (Figs. 1 and 2). Where intact mucosa was still found, most notably in the cecum and the sigmoid colon, the ulcers were seen to have overhanging edges beneath which there was marked suppurative excavation of the sub-mucosa (Fig. 3). In these regions large numbers of amebae were identified.

The primary ulcerative process appeared to be complicated by a marked, super-added, suppurative inflammation. There was extensive necrosis of tissue through all layers of the colonic wall, with the formation of pools of necrotic debris and pus and infiltration by many polymorphonuclear leukocytes. These changes extended to the subserosal fat, and here also there was diffuse infiltration of polymorphs as well as a chronic inflammatory reaction both beneath and on the serosal surfaces. An extensive perforation was obvious.

CASE 2

M.M., a 64-year-old Indian woman from the Reserve, was admitted to the University Hospital, Saskatoon, in June 1964, 51 weeks after the onset of diarrhea. She had been treated by a visiting nurse and as her condition became worse—with bloody stools, anorexia and marked weight loss—by a physician, whose advice to go to hospital for treatment was rejected. Eventually she did enter a local hospital (two weeks before her death) and received sulfonamides and chloramphenicol. Vomiting and diffuse abdominal pain had developed four days before her admission to the University Hospital, by which time she had become seriously ill. A barium enema showed a markedly abnormal colon with irregular margins and considerable thickening and apparent rigidity of the walls. Sigmoidoscopic examination, extended to the rectosigmoid junction, showed an extensive area of ulceration covered by a thick yellowish slough. The slough was adherent and when removed revealed multiple deeply ulcerated bleeding areas which were extensive and of various sizes and shapes. A biopsy was taken from the margin of an ulcer. Stool examinations were positive for *E. histolytica* trophozoites. The ESR was 20 mm. in one hour. Total serum proteins were 4.1 g. per 100 ml. with 1.6 g. albumin and 2.5 g. globulin. Treatment was started with emetine hydrochloride, diiodohydroxyquinoline (Diodoquin) and oxytetracycline (Terramycin). The patient's condition deteriorated rapidly and she died six days after admission. Unfortunately, permission for an autopsy was refused.

Pathological Findings

The biopsy material was a piece of normal mucous membrane shading off into an eroded area with remnants of glands and debris. Trophozoites of *E. histolytica* were numerous in the eroded areas and in the neighbouring mucous membrane. There

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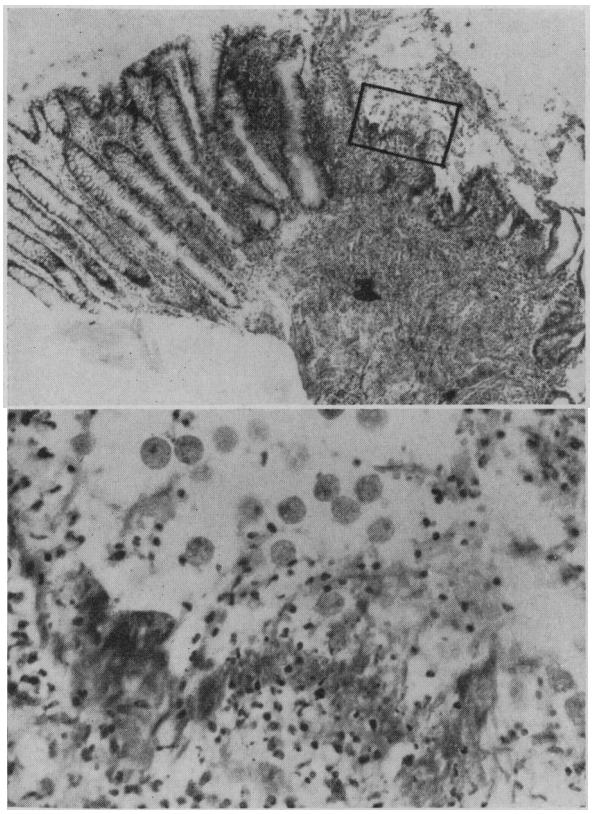

Fig. 4.—Case 2. Biopsy specimen of margin of amebic rectal ulcer. (Original magnification × 65.) Fig. 5.—Magnified area (rectangle) of Fig. 4 to show trophozoites of *E. histolytica* in biopsy specimen of ulcer margin. (Original magnification × 400.)

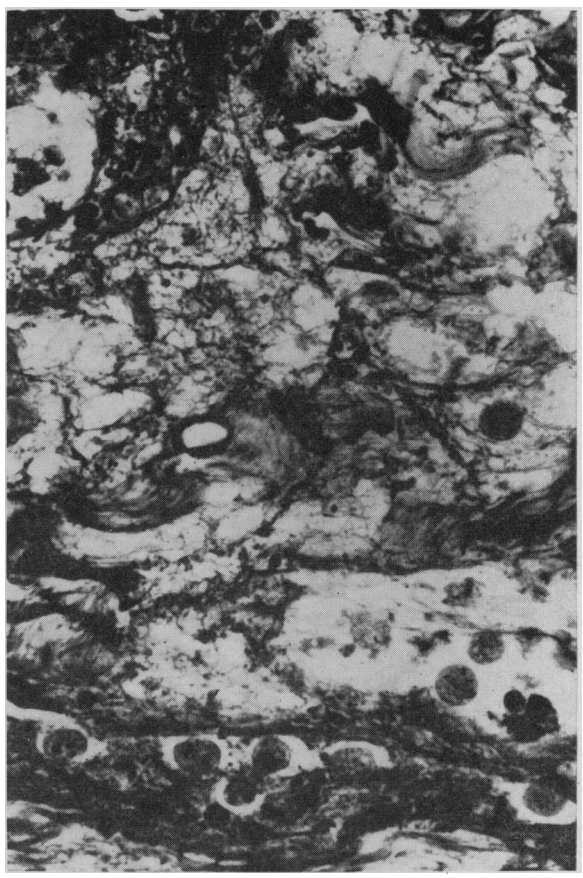

Fig. 6.—Case 3. Foci of trophozoites of *E. histolytica* in submucosal coat of autolyzed ileum. (× 400.)

was little evidence of tissue reaction, and the amebae were commonly present in the tissues in clusters. The mucous membrane overlay an abnormal submucosa characterized by fibrous reaction and dense inflammatory infiltration (Figs. 4 and 5).

CASE 3

W.C., an 83-year-old male Indian from the Reserve, was admitted to the University Hospital in September 1964, two weeks after he had developed diarrhea with bloody watery stools. He was in shock (blood pressure was 85/45 mm. Hg) and had a markedly distended abdomen and edema of both ankles. The radiological findings were consistent with an acute inflammatory process with some degree of obstruction of the small bowel, perhaps secondary to amebic colitis.

The patient's condition deteriorated rapidly and he died the day after admission. The autopsy was delayed until 36 hours after death.

Pathological Findings

Ileum.—The bowel wall was edematous but the mucosa appeared to be intact. There were fairly intense inflammatory changes with polymorphonuclear leukocytes throughout. Amebic trophozoites were scattered through the submucosa (Fig. 6). Autolytic changes were marked and obscured structural details.

Colon and rectum.—The bowel wall was edematous; the mucosa was dark reddish-brown with scattered small and medium-sized darker hemorrhagic areas. There was widespread distribution of discrete and confluent ragged areas of ulceration. The ulcers had shaggy undermined edges. Intervening mucosa was not ulcerated, but lacked colonic haustrations and appeared smooth.

Microscopic study revealed marked edema of all bowel layers with infiltration by eosinophils, lymphocytes and plasma cells. The ulcers involved mainly the mucosa and submucosa, and their bases were made up of necrotic debris resting on an edematous submucosa. Amebic trophozoites were scattered throughout the submucosa and deeper layers (Figs. 7, 8, 9 and 10). Autolytic changes were pronounced.

CASE 4

B.C., a 1-year-old Indian girl from the Reserve, was admitted to the University Hospital in December 1965, five days after she had developed fever and diarrhea, with a temperature of 104.3° F. Three days before, treatment with penicillin, tetracycline and streptomycin was started at a local hospital where she had developed listlessness and a stiff neck and had refused fluids. On admission, a chest

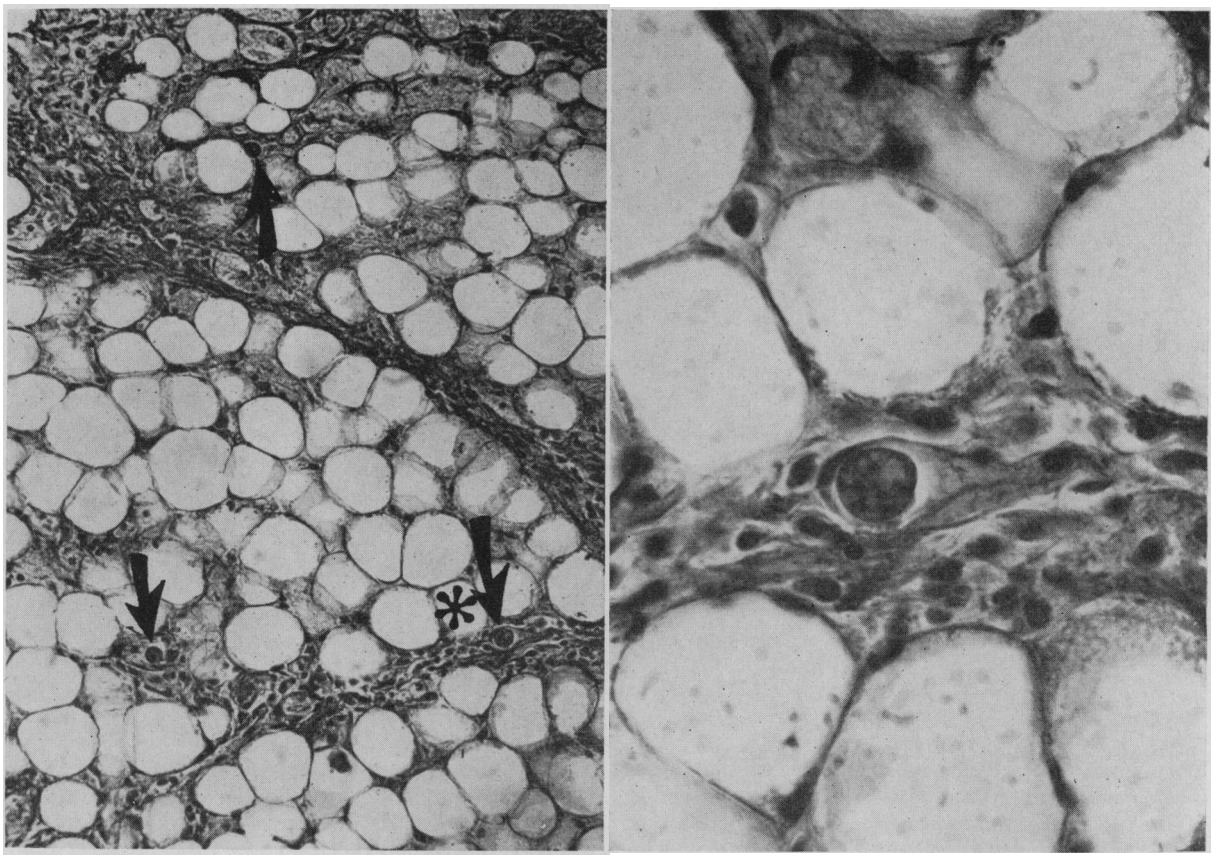

Fig. 7.—Case 3. Trophozoites of *E. histolytica* (arrows) scattered in the mesentery of colon lying within lymphatic channels. (Original magnification, × 145.) Fig. 8.—Enlarged view of *E. histolytica* trophozoite shown by asterisk in Fig. 7. (Original magnification, × 600.)

radiograph showed prominence of the left heart border and right hilum. Investigation could not determine a cause for her meningismus; agglutination tests were negative for typhoid, paratyphoid and brucellosis. Stool and blood cultures were normal. The white blood cell count was 27,750 per c.mm. Despite continued treatment with tetracycline, daily temperatures as high as 102° F. were recorded. The lower border of the liver became palpable two and one-half fingerbreadths below the right costal margin. The abdomen was distended, but no definite tenderness was present. A later chest radiograph showed a dramatic change from the previous film; the heart was displaced upward and to the left and there was marked elevation of the right hemidiaphragm, anteriorly and medially. This appeared to be pushed upward by a large abdominal mass which impinged on and overlapped the medial border of the stomach and depressed the transverse colon and right colonic flexure. The left border of the mass extended above the level of the posterior part of the left hemidiaphragm to the region of the heart.

Because an amebic abscess of the liver was suspected, treatment with emetine and chloroquine was started. Under general anesthesia, a liver scan showed a 6-cm. defect situated in the upper third anteriorly. The entire liver was markedly enlarged. Immediately afterwards, through closed drainage, about 500 ml. of a murky fluid with white flakes and debris was aspirated. This contained rare vegetative amebae as well as numerous polymorphonuclear leukocytes, much cellular debris and crystalline material. Following the liver aspiration there was a short-lived dramatic improvement in the general condition of the patient, but next day respirations became laboured and there was evidence of pericardial and pleural effusions. The patient became grossly edematous and death rapidly supervened.

Pathological Findings

The postmortem examination revealed the following gross pertinent features:

Large intestine.—This contained a small amount of pale brown, soft feces. There were two small ulcerations with hyperemic rims in the transverse colon measuring 0.4 and 0.6 cm. in diameter. The mucosal surface of the sigmoid colon was slightly hyperemic. On microscopic study the cecum was found to be slightly hyperemic and the mucosa was partially autolyzed. The ascending colon revealed some distension of the submucosal vessels and sloughing of the surface epithelium of the mucosa. There was a small ulcer in the transverse colon (Fig. 11). The base of the ulcer consisted of

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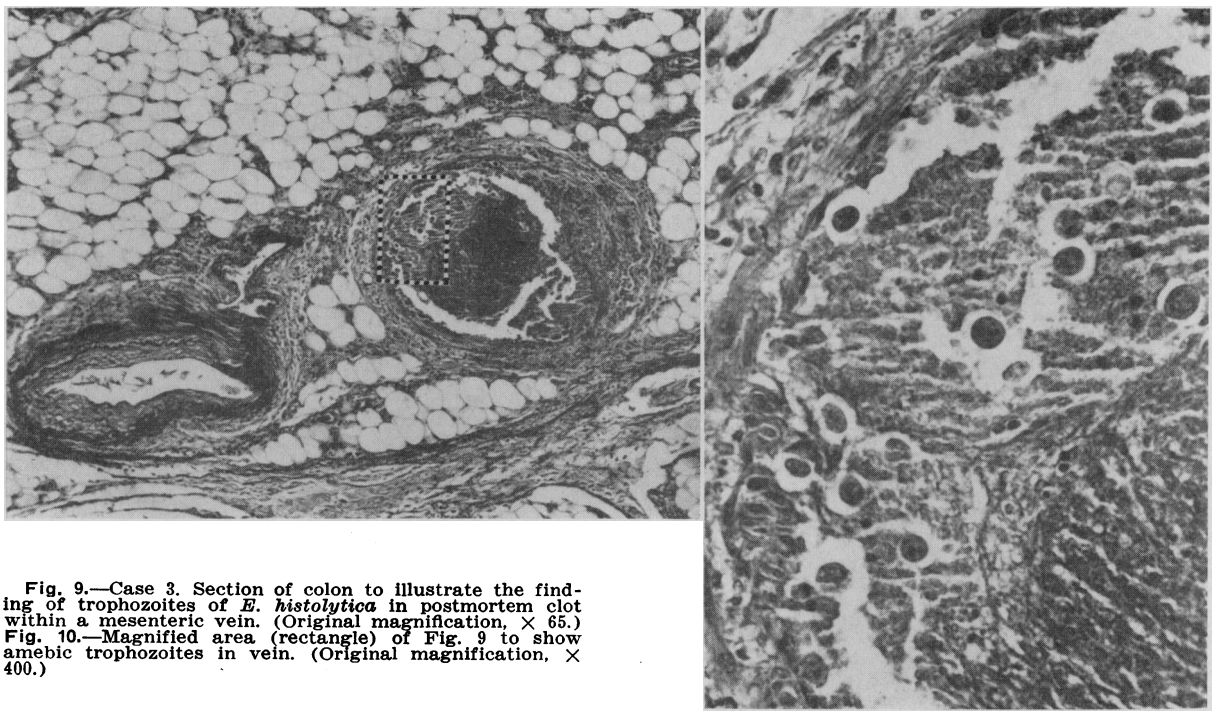

Fig. 9.—Case 3. Section of colon to illustrate the finding of trophozoites of *E. histolytica* in postmortem clot within a mesenteric vein. (Original magnification, × 65.)
Fig. 10.—Magnified area (rectangle) of Fig. 9 to show amebic trophozoites in vein. (Original magnification, × 400.)

loose granulation tissue with marked capillary distension and some fibrinopurulent exudate. The edge of the ulcer was undermined and the regenerating lining epithelium showed some mitotic figures. The ulcer was limited to the submucosa and failed to reveal any amebae. The descending and sigmoid colon as well as the rectum did not appear to be abnormal.

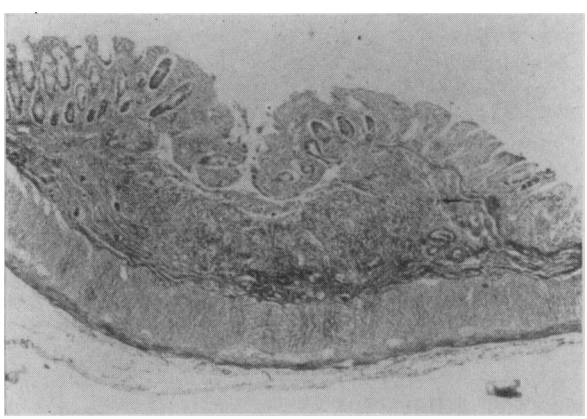

Fig. 11.—Case 4. Small amebic ulcer of colon showing thickened submucosa beneath the undermined mucosal margins, to form characteristic flask-shaped ulcer. (Original magnification, × 45.)

Liver.—The inferior aspect of the liver was smooth, moist and glistening, except for the left side where the entire surface was bulging (Fig. 12). The dome of the liver was tightly adherent to the diaphragm, which in turn was firmly adherent to the pericardium. On sectioning the liver, a large amount of dark reddish-grey turbid watery fluid escaped, exposing a huge abscess cavity measuring 11.5 x 9.5 cm., which occupied almost the entire left lobe with only a thin rim of dark brown liver tissue. The wall of the abscess consisted of pinkish-yellow, friable, necrotic tissue measuring 1.5 cm. in thickness. There was no recognizable liver tissue between the abscess and the diaphragm, to which the pericardium was adherent. There was no definite perforation or communication between the abscess and the pericardial cavity. The right lobe appeared to be dark brown with an accentuated lobular architecture. The liver weighed 600 g. after the abscess was drained.

On microscopic examination the wall of the abscess appeared to consist of three morphologically

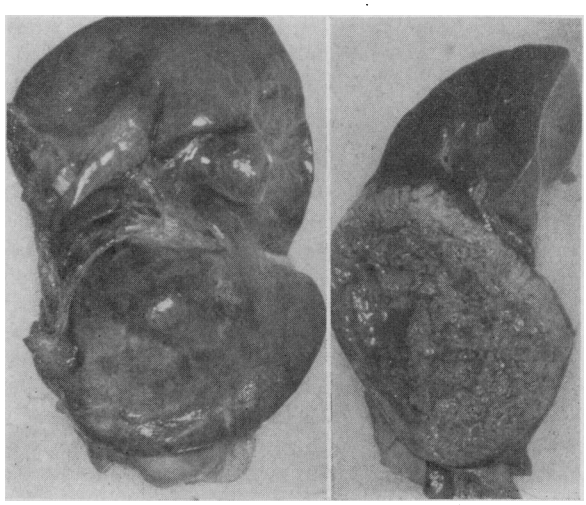

Fig. 12.—Case 4. Gross specimen of liver with amebic liver abscess to illustrate bulging capsular surface over abscess and necrotic character of abscess when sectioned.

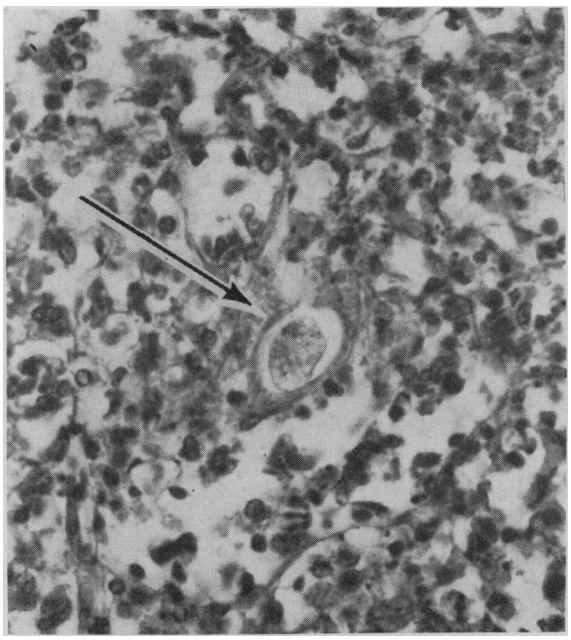

Fig. 13.—Case 4. Margin of liver abscess showing an *E. histolytica* trophozoite in disintegrating tissue. (× 600.)

distinguishable layers. The innermost was a histolytic necrotic zone which had only the vague architecture of connective tissue and no viable cells recognizable among abundant amorphous eosinophilic cellular debris. Next to this layer was a zone of prominent polymorphonuclear cell infiltration intermingled with areas of necrosis. There was a thin outer layer of viable liver cells, some of which were partially necrotic while others were separated by a heavy infiltration of chronic and acute inflammatory cells with some fibrosis. In some sections there was an additional outermost layer characterized by congestion with necrosis of the liver parenchyma without cellular infiltration, where the normal architecture was still recognizable. Only a few of the liver cells around the portal triads were viable in their outermost layer. A few trophozoites of *E. histolytica* were seen (Fig. 13).

CASE 5

C.P., a 24-year-old Indian woman from the Reserve, was admitted to the University Hospital 227 days after minimal bilateral pulmonary tuberculosis had been diagnosed and 107 days after a diagnosis of amebic dysentery had been confirmed. She had been treated elsewhere with paromomycin, an amebicidal drug that has limited effects on amebae in the tissues; shortly after that she entered the Saskatoon Sanatorium where the diagnosis of tuberculosis was confirmed and treatment with isoniazid, PAS and streptomycin was started. She was four months pregnant at this time. Six weeks after admission to the sanatorium she developed abdominal cramps and diarrhea, the latter becoming bloody and very frequent. In March 1966 she was admitted to the University Hospital where stool examination revealed trophozoites of *E. histolytica*. Treatment was started with diiodohydroxyquinoline, but following premature spontaneous delivery of a 7-month-old fetus and further treatment with emetine hydrochloride, the patient's condition deteriorated and she died 13 days after admission to hospital.

Pathological Findings

The large bowel revealed multiple ulcers varying in depth and size. They were most numerous in the sigmoid colon, the splenic flexure of the transverse colon and in the cecum. At the latter site the intervening mucosa was markedly edematous and congested. The ulcers ranged from 1.5 to 1.0 cm. in diameter. Some were sharply outlined, others undermined the surrounding mucosa. Areas of serosal discolouration in the cecum and the sigmoid colon were the sites of deep ulcers, the bases of which seemed to lie in the subserosa. In the ascending and the transverse colon as well as in the descending colon, the mucosa was rather pale and moderately edematous. Here, the few ulcers present were rather shallow. In the rectum the mucosa was markedly ulcerated and the intervening portions were edematous and congested.

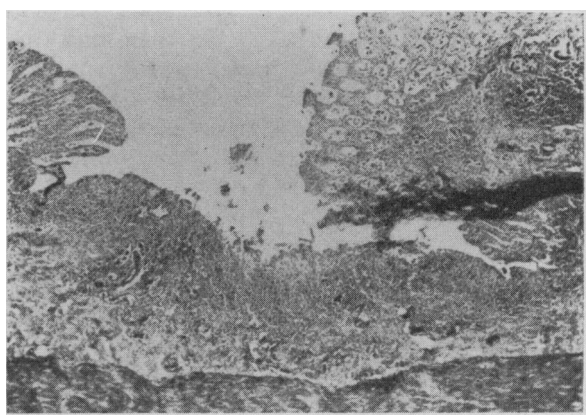

Fig. 14.—Case 5. Ulcer of colon with mucosa overhanging undermined edges. (Original magnification, × 45).

Microscopic examination confirmed the apparently extensive ulcerative process. Generally, the ulcers were large but smaller lesions were quite common. Their bases lay in the submucosa or inner muscular coat; in several instances, however, the ulcers had penetrated the entire colonic wall. Necrotic debris and degenerating mucopurulent exudate in variable amounts covered the ulcer craters. Some ulcers had sloping margins with the bordering mucosa creeping down the edges; other ulcers, particularly the smaller ones, showed undermining with the surface epithelium overhanging the lateral extensions of the ulcer bed (Fig. 14). These ulcers appeared flask-shaped, although the mouth at the mucosal surface was quite large. Beneath the ulcer base, especially in the shallow lesions, there was abundant pro-

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liferated granulation tissue densely infiltrated by large mononuclear cells, plasma cells, lymphocytes and fibroendothelial elements. Large masses of granulation tissue were also present in the submucosa beneath the areas of retained mucosa interspersed between the ulcers. Edema of varying degree about the ulcers was most noticeable in the adjacent submucosa and inner muscularis. Polymorphonuclear leukocytes were strikingly absent in the granulation tissue and around the lesions. Attempts at re-epithelialization were feeble and rarely seen.

Vegetative forms of *Entamoeba histolytica* could not be identified.

DISCUSSION

The diagnosis of amebic colitis depends upon the demonstration of the presence of *Entamoeba histolytica* trophozoites. These are most readily found and identified in the dysenteric stools of patients, provided proper diagnostic criteria and techniques are utilized. Alternatively, they may be seen in biopsy or aspirated material from ulcers visualized at sigmoidoscopy. Recent serological studies with more effective antigens are producing promising results,[11] and are particularly helpful in the diagnosis of amebic liver abscess. Clinically, the most constant finding in amebic ulcerative colitis is diarrhea and the presence of mucus and blood in the stool. If the disease has persisted for some time, there will invariably be an associated weight loss. The occurrence of other signs and symptoms, such as abdominal pain with or without tenderness, tenesmus and fever, will depend on the nature, distribution and extent of bowel lesions, and also on the degree of secondary bacterial invasion of the ulcers. Radiological findings may be helpful but are not specific for this disease.

Because amebic colitis is not frequently recognized in Canada, the possibility of its occurrence may be overlooked. Obviously this happened with one patient (Case 1) in whom the diagnosis was made only after pathological examination of the tissues following colectomy. An added difficulty in this patient was the absence of lesions in the rectum and lower sigmoid, which rendered sigmoidoscopy valueless. It is of interest to note that Musgrave[12] described 50 cases of fatal intestinal amebiasis in which diarrhea was either absent or of such minor significance that it was overlooked. In 36 of his cases there was no lesion in the lower colon and rectum.

In the four cases of amebic dysentery presented here, amebic trophozoites were demonstrated, either in the feces or in tissues collected at biopsy or post mortem. In all, the amebic infection was considered to be a major contributor to the cause of death. Patients with amebic colitis who receive adequate chemotherapy early enough do not, as a rule, die from this disease. For a variety of reasons, the treatment received by four of the patients under discussion could not be described as adequate. In one (Case 1) the diagnosis was overlooked and chemotherapy was started too late. In another (Case 2) hospitalization was refused until two weeks before death and the disease was not diagnosed until sigmoidoscopy and the subsequent examination of biopsy material several days before death; a third (Case 3) died within 24 hours of admission to hospital; the diagnosis of amebic dysentery was considered but was confirmed only at autopsy, when amebae were seen in tissue sections. Another patient (Case 5) received inadequate treatment when amebic dysentery was first diagnosed, and when the disease recurred while the patient was in the sanatorium she received only symptomatic treatment; after her admission to the University Hospital, emetine treatment was withheld for fear of inducing a miscarriage, and only after the spontaneous premature delivery 10 days before death was emetine given for four consecutive days. In this patient no amebae were seen in the characteristic and extensive ulcerations of the large bowel revealed at autopsy, and it would appear that the short four-day course of emetine was effective in eliminating the amebic infection.

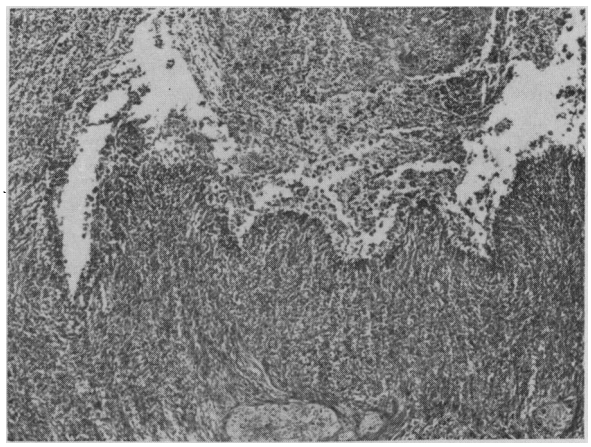

Fig. 15.—Case 1. Amebic ulcer illustrating necrotic ulceration penetrating into the major muscular coat of the colon. (Original magnification, × 65.)

The infant with liver abscess (Case 4) presented with a high spiking fever and subsequently developed an enlarged and tender liver with a leukocyte count of 27,000 per c.mm. These findings are characteristic of amebic liver abscess, and the diagnosis was confirmed by demonstrating amebae in abscess fluid and later in liver tissue. A factor contributing to the delay in diagnosis may have been the location of the abscess in the left lobe of the liver, thus render-

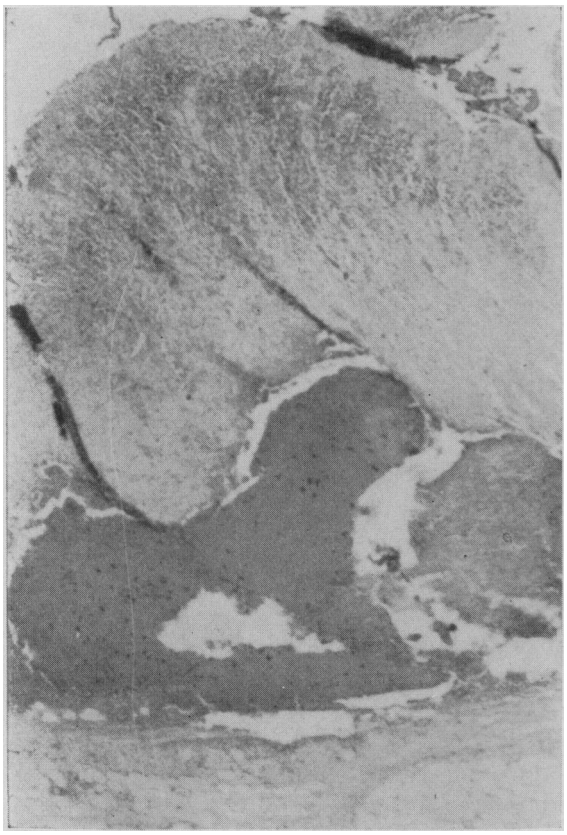

Fig. 16.—Case 3. Amebic ulceration of colon illustrating hemorrhage within the muscle layers. (× 45.)

ing more difficult the recognition of early liver enlargement. This was unfortunate, as in the majority of such cases the abscess does localize in the right lobe.

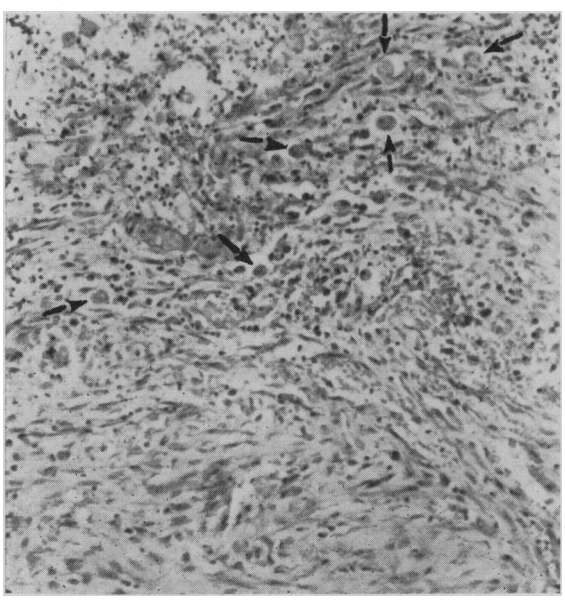

Fig. 17.—Case 1. Submucosal base of amebic ulcer of colon illustrating fibroproliferative reaction adjoining an area of amebic invasion (arrows).

Apart from serology and the microscopic demonstration of amebae, laboratory tests are not particularly helpful in establishing the diagnosis of amebic colitis or liver abscess. Leukocyte counts are of value in liver abscess, when they are almost always increased. In amebic dysentery the leukocyte count may be normal or elevated, probably depending on the degree of secondary bacterial involvement. The ESR is usually elevated in advanced cases, but may be normal. Of the four cases where the information was obtained, all showed low serum proteins and reversed albumin/globulin ratios. This can be interpreted as a reflection of a poor nutritional status, which in turn may have been a factor in the rapid and fatal progression of the disease in these cases.

Pathology

These five cases offer an instructive review of the variety of lesions to be seen in amebic ulcerative colitis. Thus we see the classic flask-shaped ulcer with its broad base in the sub-

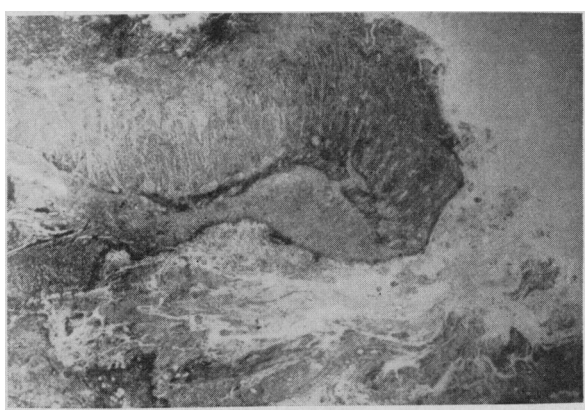

Fig. 18.—Case 1. Amebic ulcer of colon penetrating deep into pericolic tissues and illustrating the sloughing necrosis which has undermined the mesentery outside the muscular coats. (Original magnification, × 15.)

mucosa and the narrow opening formed by the overhanging margins of the mucous membrane (Figs. 3, 11 and 14). More extensive lesions are seen in which there is invasion and destruction of muscle layers (Fig. 15). The occurrence of intramural hemorrhage is shown in Fig. 16 and the proliferative lesion which in its advanced state results in the production of an ameboma is seen in Fig. 17. The mechanism by which entire layers of the bowel are separated off and sloughed away is well visualized in Fig. 18, where a penetrating lesion is seen undermining the muscle coats. Finally, the end results of necrosis of all bowel layers, where the thickened, inflamed mesentery remains as the sole barrier to perforation, are shown in Fig. 1.

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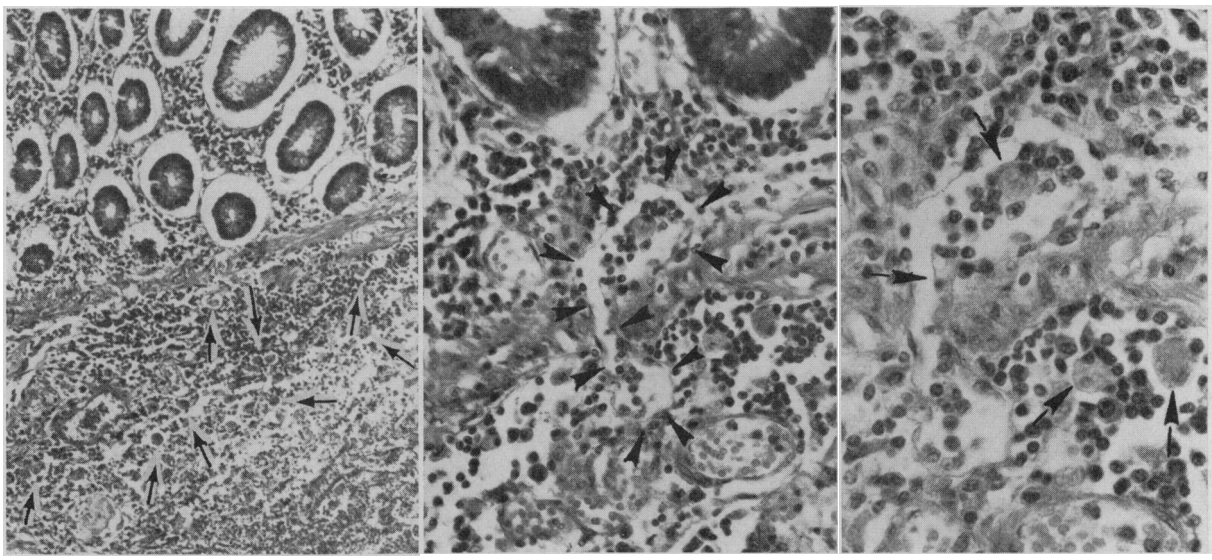

Fig. 19.—Case 1. Section through a submucosal lesion of the colon with numerous amebic trophozoites (arrows) beneath an intact mucosa. (Original magnification, × 145.) **Fig. 20.—Case 1.** A dilated lymphatic channel penetrating the muscularis mucosae, from the lesion illustrated in Fig. 19. (Original magnification, × 400.) **Fig. 21.—An** enlarged view of the lymphatic channel seen in Fig. 20, showing two *E. histolytica* trophozoites (arrows) within the channel and two others in the adjoining submucosal tissue. (Original magnification, × 600.)

Amebic invasion of the mucous membrane was seen only where there was damage to tissue, usually at the margins of deeper ulcers. In the cases under study, amebae were never seen in healthy mucous membrane. Nevertheless the occurrence in mucosa, not contiguous with deeper lesions, of single and groups of amebic trophozoites is seen from time to time. This has prompted some investigators to propose that the mucosa is the site of initial tissue colonization by amebae with subsequent spread to deeper layers.[13-15] Others, including the pioneer investigators Councilman and Lafleur,[16] maintain that the initial lesion is submucosal and that the mucosal lesion is the result of a secondary necrosis. Rogers[17] states further that when amebae appear in the mucosa they usually represent a secondary invasion from the submucosa. Rogers' views appear to be supported by Figs. 19, 20 and 21; Fig. 19, a low-power view, shows a section through an extensive submucosal lesion with numerous amebic trophozoites, while the

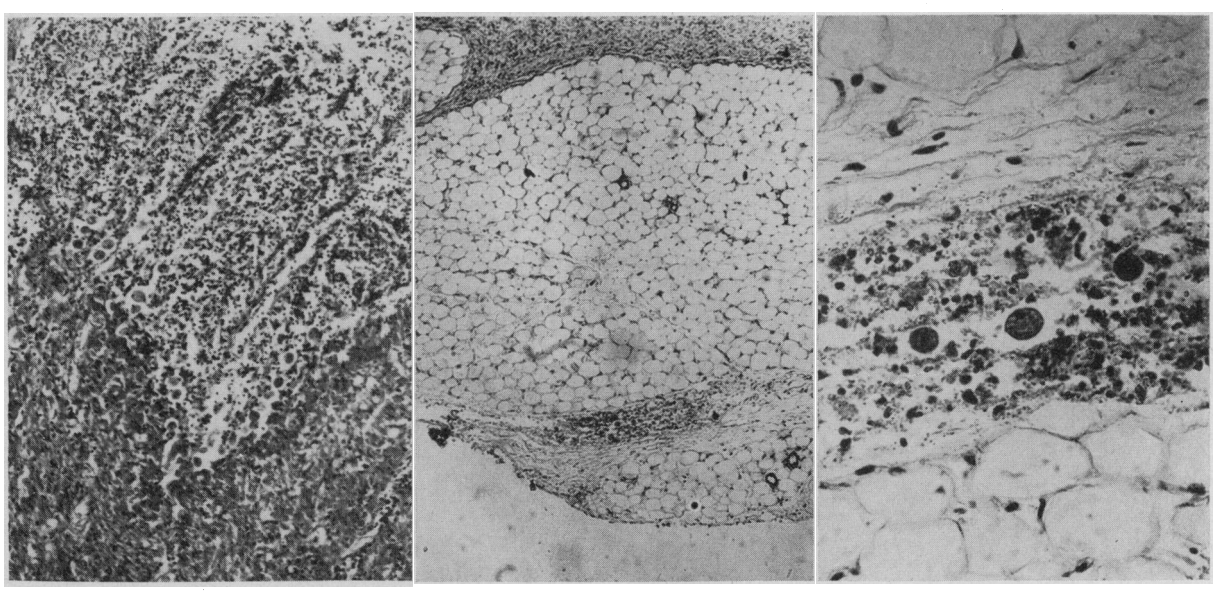

Fig. 22.—Case 1. Ulcer of colon with base in muscle coat showing the distribution of amebic trophozoites along the ulcer margins adjoining viable tissue. (Original magnification, × 145.) **Fig. 23.—Case 1.** Inflammatory focus with *E. histolytica* trophozoites in mesenteric fat isolated from main amebic ulcer in colon wall. (Original magnification, × 45.) **Fig. 24.—Mag**nified view of Fig. 23, showing amebic trophozoites. (Original magnification, × 400.)

overlying mucosa is undamaged and free of amebae, while in the high-power views (Figs. 20 and 21) of an adjoining portion of this lesion a small lymph vessel is seen penetrating the muscularis mucosae and serving as a channel for two amebae present therein. As numerous amebae are seen deep to the muscularis and none superficial to it, there is a strong probability that the amebae in the channel originated in the submucosa and are en route to the mucosa.

A study of lesions from one patient (Case 1) shows that the amebae are confined almost exclusively to the lesions and are often concentrated at or near their periphery (Fig. 22). In only one instance were amebae seen in an isolated focus at any distance from a principal lesion, and this was in a small inflammatory focus (Figs. 23 and 24) near the outside margin of thickened mesentery serving as the sole remaining layer of an area of deep and extensive bowel ulceration. In another patient (Case 3), on the other hand, the amebae were found widely scattered in the tissues and usually restricted to lymph spaces, lymph capillaries, and in one instance within a vein (Figs. 6, 7, 8, 9 and 10). The difference in the distribution of amebae in Cases 1 and 3 is probably explained by the difference in the interval between death of tissue and its fixation. Tissues from Case 1 were obtained at colectomy and presumably fixed soon after removal from the body. In Case 3 the necropsy was not performed until 36 hours after death and the tissue showed advanced autolytic changes. Amebic trophozoites remain alive and motile after the death of the host; Councilmann and Lafleur[16] noted that as long as 36 hours after death a few viable amebae could still be found at autopsy. The scattered *in situ* locations of amebae seen in Case 3 were probably due to postmortem migrations and should not be interpreted as an accurate indication of their location in the tissues of the living host. The distribution of amebae seen in the tissues of Case 1 undoubtedly offers a more accurate picture of the *in vivo* positions of these parasites.

Summary Five fatal cases of amebiasis in Reserve Indians from bands in the Loon Lake area of Northern Saskatchewan are described. The patients ranged in age from 1 to 83 years; four had amebic ulcerative colitis and the fifth had an amebic liver abscess. Specific chemotherapy was delayed until it was apparently no longer possible to alter the fatal outcome of the disease. This was either because the patients failed to present themselves for medical care until the disease was far advanced or because the medical attendants did not consider the possibility of amebic infection sufficiently early. The clinical status of one patient was complicated by tuberculosis and pregnancy. The nature of the lesions seen in these patients is described in some detail. The *in vivo* location of vegetative amebae is discussed.

Résumé Les auteurs présentent cinq cas fatals d'amibiase survenus dans des Réserves indiennes de la région de Loon Lake en Saskatchewan du nord. L'âge des malades variait de 1 an à 83 ans. Quatre souffraient de colite ulcéreuse d'origine amibienne et un cinquième avait un abcès du foie de même origine. La chimiothérapie spécifique a été retardée jusqu'au moment où il ne semblait plus possible de modifier l'issue fatale de la maladie. Ceci s'est produit soit parce que les malades négligeaient de se présenter à la visite médicale, du moins pendant qu'il en était temps encore, soit parce que le personnel médical n'ait pas envisagé assez tôt la possibilité de l'infection amibienne. L'état général d'une malade était compliqué par la tuberculose et son état de grossesse. L'article décrit, avec certains détails, la nature des lésions observées chez ces malades. Il discute également la question du siège *in vivo* des formes végétatives des amibes.

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