ureteral colic may be simulated. At operation, a local area of the colon may be acutely inflamed or gangrenous, with or without perforation, and an ulcer crater may be palpable through the bowel wall. In the slowly penetrating form with perityphilitis, a mass may be indistinguishable from carcinoma. The lesion may be confused with diverticulitis, as in the two cases mentioned above, regional enteritis, hyperplastic tuberculosis, dysentery, amœbiasis, or perforation by a foreign body.

Treatment.—When an obviously acute ulcer of the cæcum or colon is encountered at laparotomy, the lesion may be either excised locally and the bowel closed, or the ulcerated area may be oversewn and reinforced with omentum, depending on the extent of the process and the friability of the bowel. In acute perforation, the opening should be oversewn and protected by a piece of detached omentum, and the area drained. If closure is impossible, the perforation may be exteriorized to form a cæcostomy or colostomy. It is questionable whether a bowel resection should subsequently be performed. In any event, a barium enema should be done as a follow-up. A localized abscess must be drained, and further treatment will depend in part on whether or not a fæcal fistula persists. Obstructed cases require appropriate measures for relief of the obstruction primarily. If an indurated area in the bowel is indistinguishable from carcinoma, the bowel must be resected. It is probably better to re-operate after the bowel has been cleansed, and prepared by chemotherapy and antibiotics.

CONCLUSIONS

1. Solitary non-specific ulcer of the large bowel is an uncommon lesion of unknown etiology, involving the cæcum or lower ascending colon in approximately 50% of cases.

2. The usual preoperative diagnosis is appendicitis.

3. The commonest complication is perforation of the cæcum, and in the past the mortality rate in these cases has been high.

4. The ulcer may be indistinguishable clinically from carcinoma.

REFERENCES

1. ROSSER, C.: *Ann. Surg.*, 119: 377, 1944.
2. CAMERON, J. R.: *Brit. J. Surg.*, 26: 526, 1938-39.
3. BARLOW, D.: *Brit. J. Surg.*, 28: 575, 1941.
4. BARRON, M. E.: *Arch. Surg.*, 17: 355, 1928.
5. STEWART, L. S. AND JONES, B. F.: *Arch. Path.*, 31: 37, 1941.
6. BLUM, L.: *Surg. Clin. North America*, 355, April, 1947.
7. MOORE, T.: *Brit. J. Surg.*, 27: 600, 1939-40.
8. PRITZKER, H. G.: *Bull. Acad. Med.*, (Toronto) Dec., 1945.
9. HARRISON, H.: *Arch. Surg.*, 40: 959, 1940.
10. WILKIE, SIR D.: *Surgery*, 1: 655, 1937.

COCCIDIOIDOMYCOSIS*

N. G. B. McLETCHIE, M.D.,
NEIL REID, M.D. and
D. M. SIMPSON, B.Sc., *Halifax*

INFECTION with the fungus *Coccidioides immitis* Rixf. and Gilchr. is endemic in the warm arid regions of the southwestern United States, the Chaco of Uruguay and Argentine and probably northern Mexico, but a rare, sporadic case has been reported elsewhere, *e.g.* Italy and Hawaii.[1] It is the most pathogenic of the fungi, being dangerous to work with in the laboratory, indeed the only case recorded in Britain was a laboratory infection.[2] Jacobsen[3] (1930) mentions Canada at the end of a list of States of the Union and countries where cases have been reported. He does not, however, give the source of the latter information and no Canadian case is listed in the survey of 182 reported cases published the previous year.[4] We have not been able to find records of a case reported from Canada although cases are recorded in Illinois of people who never visited endemic areas. Kurtz and Loud[5] report four cases in New England all of whom had spent a variable period of time in recognized endemic areas. It is our purpose in this communication to record infection with this organism in a man who had never been out of Nova Scotia except to Europe for service in World War I.

In the tissues *C. immitis* is seen in characteristic form as a large spherule (20 to 80 microns) with a doubly refractile wall filled with endospores (Figs. 1 and 2). The fungus spreads by rupture of the spherule wall and release of the endospores which may be carried by the blood or lymph stream to distant regions. We have found that the free endospores in tissue sections can easily be differentiated from small pyknotic lymphocytes by the Hotchkiss-McManus stain which colours the endospore wall red. Intermediate stages of maturation from endospore to spherule are also seen in the tissues.[1] While the characteristic spherule is taken as pathognomonic for the diagnosis in man, for complete identifica-

*From Camp Hill Hospital and Dalhousie University, Halifax, N.S.

tion the recognition of other characteristics in laboratory culture is necessary since a closely related parasite has been isolated from rodents—*Haplosporangium parvum*.[6] This parasite has not been so far identified in human infection.

Infection is usually manifest as an acute, benign and self-limiting respiratory infection ("Valley fever", "San Joaquin fever", "desert fever") which may be accompanied by allergic symptoms, particularly erythema and muscular and joint pain ("desert rheumatism"). Occasionally the lung lesion may progress to cavity formation and still be self-limiting. The skin may also, in rare instances, be the primary portal of entry. From either source, progressive and usually fatal disease, coccidiodal granuloma, may develop. Since the primary site of infection may be inconspicuous and even heal, the progressive disease may take many forms, according to the mode of spread. The case we record is of progressive form but is unusual, if not unique, in that it was characterized clinically by muscular pain, spasm, wasting and weakness which all the more emphasizes the opinion of Smith[1] that "mycotic infections occur with sufficient frequency to justify their consideration in the differential diagnosis of every difficult and complicated pulmonary and systemic infection". In addition, in our experience, we would state that they should receive special consideration in reference to the sudden development in adults of pain and swelling in joints, fleeting and flitting, and likely to be labelled as "rheumatism". In three proved fatal cases of pulmonary moniliasis encountered by us, the patients all had initial symptoms lasting six months or more of much pain and incapacity of joints with but little swelling.

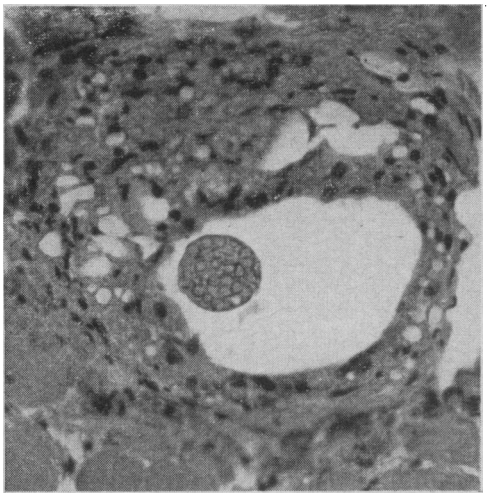

Fig. 1

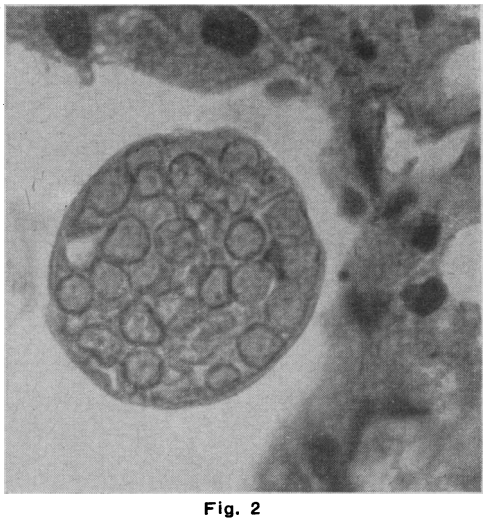

Fig. 2

Fig. 1.—Granuloma in skeletal muscle; the characteristic spherule filled with endospores is seen in the central cyst. X150. Fig. 2.—Higher magnification of spherule of Fig 1, surrounded by foamy macrophages. X550.

CLINICAL HISTORY

The patient, a man aged 61, had been well all his life apart from childhood diseases. He had only been out of Nova Scotia once, during 1915-1918, while serving in the United Kingdom, France and Belgium in the First World War. Since that time he had obtained his livelihood at casual labour which included work handling imported fruit including fruit from California. The patient was too ill to give us further detail.

His present illness began acutely in July, 1949, when he developed a dull pain in the back of his head and at the base of the skull. In the course of a few days the pain spread to involve other parts particularly the left shoulder and arm, and paræsthesia of the left leg, necessitating stopping work. With the pain he noticed weakness of the involved extremities. At the time of hospitalization, one month after the onset, the right arm and leg were also involved.

Gross weakness of the arms and legs was noticed on admission as well as absence of the abdominal and cremasteric reflexes, astereognosis (left), finger-nose incoordination and questionable sensory loss to pain over the left shoulder and distally in the right leg. Limb reflexes were present and equal. Apart from an elevated sedimentation rate of 24 mm. fall in 1 hour (W & L), blood examination showed nothing of note. X-ray examination of the chest on admission was negative. Extensive osteoarthritic changes were noted in the cervical spines, causing narrowing of the intervertebral foramina between C_3 and C_4 and C_5 and C_6. A cervical myelogram revealed no filling defect or other abnormality. Cerebrospinal fluid was within normal limits and the Mastic test was normal, but a slight elevation of the cell count was present. The patient continually showed a slight elevation in temperature with occasional episodes of high fever associated with acute urinary and pulmonary symptoms, which subsided on antibiotic therapy.

The course of the disease was steadily progressive with much pain, muscular weakness and atrophy with severe muscular spasms in the early stages. During this phase he also had bouts of diarrhœa and vomiting. Early in the period of hospitalization neck traction was applied without benefit, similarly there was no benefit from a course of radiation to the cervical spines. During the terminal 6 months the patient had had little pain but he

remained a helpless invalid unable to move his left arm or legs and only feebly able to move the right arm. In May 1951 a biopsy was taken of the left deltoid muscle. This revealed a granulomatous condition associated with the characteristic parasitic stage of *C. immitis* which will later be discussed under the autopsy findings.

A coccidioidin skin test was done in June 1951 using 0.1 ml. of 1:100 dilution of the antigen intradermally. This remained negative after 24, 36 and 48 hours. Such results are encountered in widespread systemic infection. He became very emaciated and expired in August 1951, with the clinical and laboratory picture of an overwhelming pyogenic infection and uræmia.

SUMMARY OF AUTOPSY

Gross emaciation; gross wasting and patchy fibrosis of muscles of limbs, chest, abdomen and shoulder girdles; scattered throughout all lobes of both lungs numerous abscesses often with central liquefaction, from miliary to 1.5 mm. in diameter; gross pyelonephritis with large abscesses in both kidneys, cystitis; slight splenomegaly; small scattered early softenings in brain; all other organs showed wasting only.

HISTOLOGY

The renal substance was practically destroyed by acute abscesses in which a variety of bacteria were identified. It was evident that, secondary to a cystitis associated with the indwelling catheter, gross pyelonephritis had developed and that there was a terminal pyæmia, since the lung and cerebral lesions were all acute necrotizing abscesses in which there was no evidence of a granulomatous process, and in which prolonged search with special stains has not revealed fungi. Outside of muscle, only a few chronic granulomatous lesions were recognized. Those were all in the kidneys and in one a disintegrating spherule was identified.

Sections of numerous muscles from the limbs, chest and abdominal wall showed atrophy, fibrosis and patchy recent necrosis. There was a fairly generalized interstitial round cell infiltration and numerous small granulomata consisting mainly of foamy phagocytes and giant cells. Sometimes the phagocytes were orientated round spaces which contained typical spherules (sporangia) pathognomonic of *C. immitis* (Figs. 1 and 2) (with the reservation already stated). These spherules were very brittle and were generally dislodged in the cutting of the paraffin blocks so that they were found outside the cysts. In addition in some areas there were numerous free endospores and occasional larger yeast-like bodies intermediate between endospores and spherules.

At the autopsy it could hardly have been appreciated that the lung lesions were all terminal and that the fungus was almost exclusively confined to muscle. Unfortunately only the lungs were retained for culture. Both were retained intact. One was preserved in formalin. The other was frozen for culture. Both were serially sliced without revealing a primary focus. All standard media for the culture of fungi were utilized on the frozen lung, as well as cupric sulphate media stated to be specific for *C. immitis*. All media failed to produce growth of fungi and intratesticular guinea pig inoculation was negative.

DISCUSSION

While the organism was not identified by culture the appearance in the tissues is so characteristic that one must assume that the pathogen was *Coccidioides immitis* or a closely related fungus; the organism was probably imported rather than of local origin and the history of working with imported fruit is suggestive.

It was obvious from sections that the sporangia rupture and liberate endospores. Since lesions were present in the muscles of all limbs spread must have been by the blood stream. The failure to find specific granulomata outside muscle except for small resolving foci in the kidney must indicate that endospores lodging in other organs had been successfully phagocytosed and the infecting organism must have been of a strain which found the environment of muscle a specially favourable soil. Since the only significant portal of entry is the respiratory tract one must assume that the primary lung lesion was minimal and its identification made even more difficult by the numerous terminal lesions. While the localization to muscle is unique in the literature, progressive fungal diseases are protean conditions and the uniqueness is more likely a "breach in the observance" on the part of others.

SUMMARY

A case is described of infection with *Coccidioides immitis* or a closely related fungus. The victim was a male aged 61 who had never been out of Nova Scotia except over twenty years before the infection for military service in Europe. The fungus was almost exclusively confined to muscle where the granulomatous reaction to it led to gross wasting, fibrosis and contracture of the limbs producing a most painful

Canad. M. A. J.
Dec. 1952, vol. 67

and crippling malady. Death was brought about by a terminal pyelonephritis and pyæmia.

We are indebted to Dr. Walter Leslie for his clinical notes, to Dr. C. M. Harlow for the gross findings at autopsy, and to Dr. T. E. Kirk, S.T.M.O., for permission to publish.

REFERENCES

1. SMITH, C. E.: *M. Clin. North America*, **27**: 790, 1943.
2. NABARRO, J. D. N.: *Lancet*, **1**: 982, 1948.
3. JACOBSEN, H. P.: *Arch. Dermat. & Syph.*, **21**: 790, 1930.
4. CUMMINS, W. T., SMITH, J. K. AND HALLIDAY, C. H.: *J. A. M. A.*, **93**: 1046, 1929.
5. KURTZ, R. H. AND LOUD, N. W.: *New England J. Med.*, **237**: 610, 1947.
6. EMMONS, C. W. AND ASHBURN, L. L.: *Pub. Health Rep.*, **57**: 1715, 1942.

IMMUNIZATIONS IN INFANCY

GEORGE E. WHITE, M.D., *Windsor, Ont.*

IMMUNIZATIONS IN INFANCY has been selected as a subject for this meeting, for the reasons that, as yet, there is no universal agreement as to the age to begin immunization, and there are variations in the choice of immunizing agents.

One finds doctors beginning at the age of one month and one reads in the literature that immunization should be started at three months, five months, and six months; all agree that immunization should be completed for diphtheria, whooping cough, tetanus and smallpox by the first year. In the prospect that we can arrive at a standardized routine, I present this subject hoping that a standard may be established for the whole of Canada because of the movement of peoples from one province to the other. Thus we will know all have been immunized by the first year for these diseases. In the *American Journal of Public Health* (**40**: 674, 1950) on simultaneous immunization of newborn infants against diphtheria, tetanus and pertussis, production of antibodies and the duration of antitoxin levels, the writer concludes that "in the first year, the capacity to produce antibodies in response to antigenic stimulation definitely increases with advancing age." The results of immunization may not be as good as obtained in the older child but a significant degree of protection may be obtained by starting prophylactic immunization injections in the newborn and it is suggested that triple combined immunization be postponed until three months of age and thus the critical period of immune mechanisms will have been passed.

The American Academy of Pædiatrics has a committee that is constantly reviewing the research and assaying the subject of immunization and therapeutic procedures for all infectious diseases. They publish a booklet every two years keeping the members informed of these accepted procedures and therapy. The 1951 booklet is just printed and many of my statements will be from this book as well as from the Connaught Laboratories Research Department.

DIPHTHERIA, TETANUS AND WHOOPING COUGH

It is practically universal to give immunization for diphtheria, tetanus and pertussis in a combined mixture. However, the choice of material varies. Diphtheria and tetanus toxoids are available in two types: (1) Those containing alum precipitate or aluminum hydroxide. (2) Those not containing these substances; these are called fluid toxoids.

The combined antigens containing alum precipitate or aluminum hydroxide adsorbed diphtheria and tetanus toxoids and *H. pertussis* vaccine are preferred by the American Academy of Pædiatrics Committee and are in use in the majority of the states of the United States. The fluid toxoids of diphtheria and tetanus and *H. pertussis* vaccine are the choice in Canada and some of the States. The reasons are:

The alum precipitate or aluminum hydroxide adsorbed diphtheria and tetanus toxoids with *H. pertussis* vaccines are preferred because: (a) There is a more prolonged antitoxic immunity produced. (b) Greater effectiveness as immunizers against pertussis in early infancy. (c) Less likelihood of producing systemic reactions by reason of lower protein content and slower absorption.

The committee feels these factors far outweigh the two advantages of the non-adsorbed fluid mixtures which undoubtedly all have greater speed in achieving immunizations, and freedom from formation of the occasional sterile abscess.

In giving the combined alum precipitate or aluminum hydroxide adsorbed toxoids attention must be given to the following details:

1. Agent must be injected intramuscularly, (and a small amount of air to follow to wash out the agent), at intervals of not less than one month and preferably not more than three months elapsed between injections.
2. Minimum injections should be three. If dosage has been lowered by reason of reactions, then more injections must be given.
3. Total dosage of *H. pertussis* not less than 40 billion. This dosage is adequate to protect 4 out of 5 infants for