action of these drugs is discussed, and other effects noted.

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REFERENCES

1. ARENDT, E. C., PATTEE, C. J. AND MITCHELL, H. S.: *Canad. M. A. J.*, **73**: 269, 1955.
2. KAYE, M.: *J. Clin. Invest.*, **34**: 277, 1955.
3. Summary of Information for Clinical Investigations, E. R. Squibb & Sons, New Brunswick, New Jersey, July 14, 1955.
4. HENNEMAN, P. H. AND CARROLL, E. L.: *J. Clin. Invest.* (Abstract), in press.
5. FRIEDBERG, C. K. *et al.*: *New England J. Med.*, **248**: 883, 1953.
6. ATKINSON, F. R. B. AND WEBER, F.: *Brit. J. Dermat.*, **50**: 267, 1938.

TRICHINOSIS IN CANADIAN ESKIMOS*

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TRICHINOSIS is a public health problem of minor degree in Canada, where the incidence among humans has been estimated at 1.5% in Montreal,[1] 1.75% in Toronto[2] and 4% in Vancouver.[3] In the U.S.A., Gould[4] has estimated the incidence to be about 25%, the majority of cases being subclinical. Hogs have been considered as the source of most human infection. In southern Canada, where a regulation of the Federal Department of Agriculture prohibits the feeding of uncooked garbage to hogs, no valid statistics of its incidence in hogs are available. However, Cameron[5] has shown that it does occasionally occur in them.

Although improperly cooked pork and pork derivatives are the major source of human trichinosis in the more settled areas of our country, pork is rarely eaten in the Arctic regions. Animals of this region which have been shown to harbour *Trichinella spiralis*, include the polar bear,[6] black bear,[7] Greenland bearded seal,[8] arctic fox,[7] arctic dog.[6] and walrus.[9] The incidence of trichinosis among the Canadian Eskimo is unknown, but studies by Brown *et al.*[10] among the Eskimos of Southampton Island, North West Territories, showed 40% to have a positive skin test with trichina antigen.

While the disease has been reported among the Eskimos of northern Canada, the diagnosis has never been proven, to our knowledge, by the actual demonstration of the parasite. The present report describes the cases of two patients in whom the diagnosis was confirmed by autopsy and by muscle biopsy.

The patients were Eskimo siblings who were flown from Labrador to Montreal and admitted to The Children's Memorial Hospital on October 15, 1953. No history was sent with the children. The only information available was a tentative diagnosis of nephritis and bronchial pneumonia in the boy and a "chest condition" in the girl.

CASE 1

On admission the Eskimo boy, about 7 years old, appeared extremely ill. He was listless and dehydrated, with a rapid respiratory rate and persistent loose cough; T 104° F., P 124, R 44. There was œdema of the subcutaneous tissues of the face and extremities; harsh breath sounds and coarse rales were heard throughout the chest. The abdomen was distended and tympanitic, but the liver and spleen were not enlarged. The heart sounds were normal and the blood pressure was 102/48 mm. Hg. There was a minimal pharyngitis associated with discrete pea-sized lymph nodes in the cervical region as well as the axillary and inguinal regions. On examination of the central nervous system it was evident that there was slight but definite neck stiffness with a positive Kernig's sign. The most striking and puzzling feature of the physical examination was the marked hardness and tenderness of the muscles of the extremities.

The initial laboratory findings were as follows: hæmoglobin value 8.2 g./100 ml., white cell count 11,200 with a differential count of 8,600 neutrophils, 1,500 lymphocytes, 700 monocytes and 300 eosinophils. The blood protein level was slightly lowered due to a decrease in the albumin, while the non-protein nitrogen, bilirubin, sodium, potassium and chlorides were within the normal range. The spinal fluid showed a negative Pandy test with a protein content of 29.5 mg./100 ml. The cell content was increased to 26 per c.mm. and all the cells were lymphocytes. Spinal fluid sugar and chloride levels were very slightly lowered, being 41.5 mg./100 ml. and 404.7 mg./100 ml., respectively. Urine examination showed no abnormality. Wassermann, Mantoux and agglutination tests for *Salmonellæ* were negative. Blood and stool cultures were negative.

Chest radiographs showed a pneumonia of the left lower and right lower lobes with right hilar and tracheobronchial lymph node calcification. In addition, there was a diffuse increase in density throughout both lungs which might have represented a mild to moderate degree of pulmonary œdema. There was no evidence of active tuberculosis.

Progress.—Over the next eight days his condition remained about the same, except for slightly greater weakness and a more marked non-productive cough. The fever persisted and he was in a semi-comatose state. Two days before death he appeared to have severe chest pain and at this time his lungs showed fine crepitant rales over both bases. Both lower lung fields were dull to percussion. On the morning of October 23, the leukocyte count was 25,400 with a differential count of 23,114

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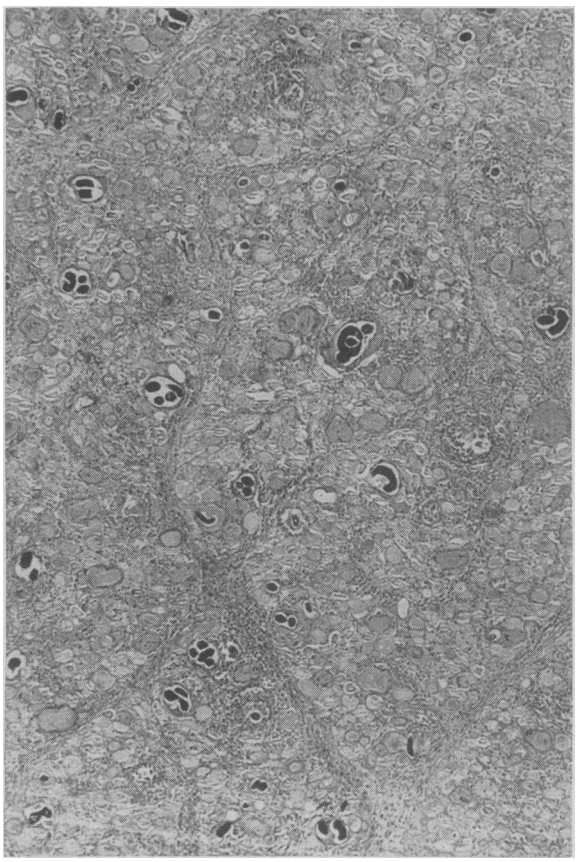

Fig. 1.—Cross-section of vastus lateralis muscle to show the large number of trichinella larvæ present. The larvæ are black and about 40 are present in this field. Periodic acid Schiff. × 50.

neutrophils, 1,016 juveniles and 762 small lymphocytes. The absolute eosinophil count was 56 per c.mm. The blood chemical findings and spinal fluid showed no significant alteration. In view of the hard and tender muscles, the possibility of dermatomyositis was considered and a muscle biopsy was arranged for the afternoon of October 23. However, he suddenly and unexpectedly died that afternoon.

Autopsy.—Autopsy was performed three hours after death. The body was that of a fairly well developed, somewhat undernourished Eskimo boy with the body length of 125 cm. The skin was pale and there was moderate dependent œdema. The pericardium contained 60 c.c. of clear, faintly yellow fluid. The heart weighed 147 g. (normal average weight 100 g.) and the only noticeable abnormality was the presence of pale yellow streaking of the myocardium of both ventricles. The right pleural cavity contained 350 c.c. and the left 135 c.c. of pale yellow clear fluid. Fibrous synechiæ were present over the right middle lobe. The lungs weighed together 550 g. as compared with a normal average of 250 g. They were of rubbery consistency, non-crepitant and bluish-red in colour, particularly the lower lobes. Their cut surfaces showed minimal aeration and presented a wet, bloody appearance, most noticeable in the lower lobes. A calcified nodule was found in the middle lobe of the right lung, with calcified areas in the hilar lymph nodes. The peritoneal cavity contained 150 c.c. of fluid, and the liver was slightly enlarged, weighing 860 g. (normal 680 g.). The spleen was not enlarged. The kidneys weighed 210 g. (normal 140 g.) and were pale but otherwise grossly normal. The brain was of normal weight and showed no gross lesion, although the leptomeninges were moderately œdematous.

The skeletal muscles presented a striking appearance due to their pallor and marked firmness. The degree of change varied from group to group. They showed marked pallor, being almost waxy or parboiled in appearance, were hard, and cut with resistance. These changes were most marked in the vastus medialis, rectus femoris, gastrocnemius, biceps and triceps. The vastus intermedius, diaphragm, strap muscles of the neck and the erector spinæ presented similar but less marked changes. Post-mortem cultures yielded no growth.

Microscopic.—Examination of the stained sections of voluntary muscle immediately established the diagnosis, as the fibres showed widespread parasitization by typical *Trichinella spiralis*, many of which were coiled within the muscle fibres. They were strikingly demonstrated by the periodic acid Schiff method, which stained the outer coat a deep rose (Fig. 1). The infestation was heavy and in the most involved muscles there were roughly 45 separate worms in each three sq. mm. of tissue. Extensive muscle fibre damage was indicated by fibre swelling, basophilia, granular degeneration, hyalinization and vacuolization. Many fibres were invaded by histiocytes in varying degrees. Focal collections of histiocytes, lymphocytes and leukocytes were present, both in relationship to degenerating muscle fibres and to naked larvæ (Fig. 2). Eosinophilic leukocytes were present in these areas but were not numerous. The foci were quite localized and there was little diffuse surrounding inflammation. Focal areas of collapse fibrosis were present. Beginning encapsulation of the larvæ was noticed in some fibres as indicated by the thickening and condensation of the sarcolemma, distinctive in its strongly periodic acid Schiff positive reaction. The changes in the voluntary muscles were those typically associated with trichina infestation and the lesions appeared to be of about five weeks' duration. Rough grading showed the gastrocnemii, the thigh muscles, the brachialis and the biceps to be markedly involved, the erector spinæ, triceps, sternohyoid and laryngeal muscles to be moderately involved, and the diaphragm and intercostal muscles only slightly involved.

The myocardium showed a widespread but focal interstitial inflammation with parenchymatous degeneration (Fig. 3). The foci were small with ill-defined borders and contained slight to moderate numbers of histiocytes

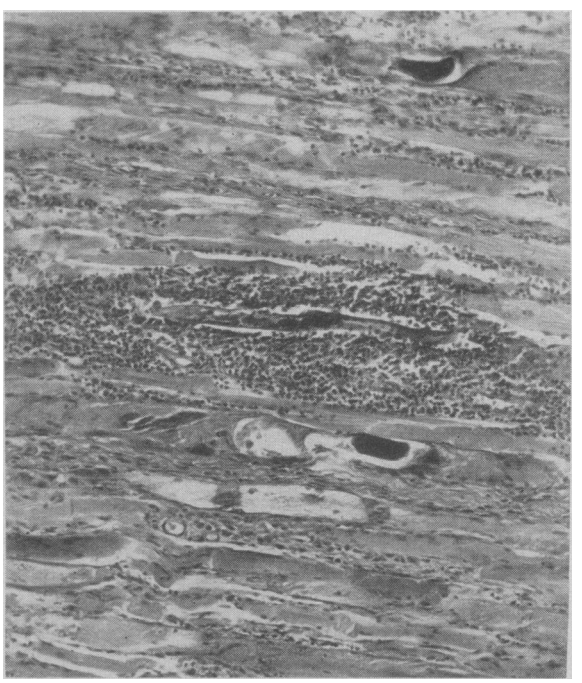

Fig. 2.—Longitudinal section of erector spinalis muscle showing fibre changes and larvæ. Centrally there is a naked larva surrounded by a nodule of inflammation. Periodic acid Schiff. × 100.

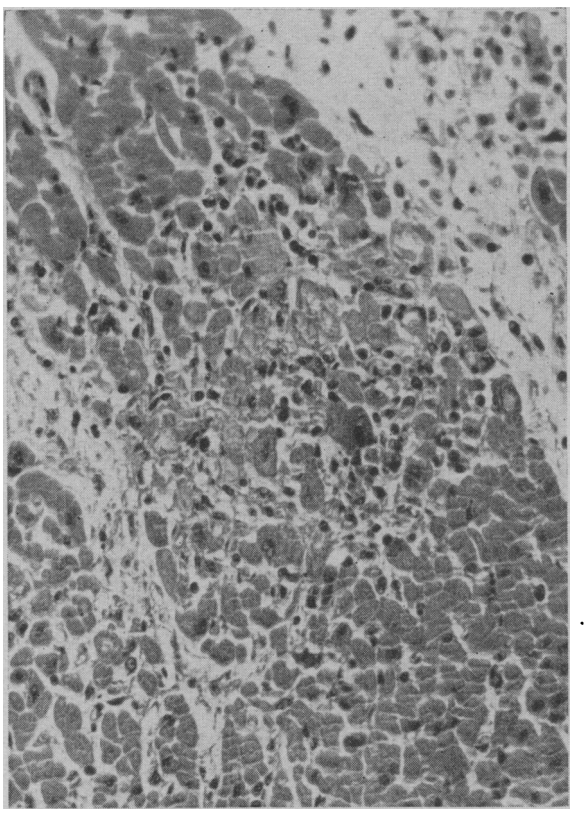

Fig. 3.—Anterior wall of left ventricle showing a focus of muscle degeneration and a thin infiltrate of inflammatory cells. Hæmalum, phloxin, saffron. × 200.

and leukocytic cells. A fairly extensive examination of numerous blocks of myocardium from various parts of the heart failed to reveal any trichinæ.

Numerous sections of the lungs revealed evidence of marked passive congestion, focal œdema, intra-alveolar hæmorrhages and numerous hæmosiderin-laden histiocytes. The lower lobes were almost solid due to the obliteration of the air sacs by red blood cells.

Sections of the brain demonstrated widely separated small foci of encephalomyelitis, mainly in the white matter. These consisted of tiny foci of degeneration infiltrated with macrophages (Fig. 4). In two areas indistinct remnants of degenerating trichinæ were seen. These lesions were present in sections from the cervical cord, pons, cerebellum, medulla, basal ganglia, island of Riel and the rolandic area. The leptomeninges were œdematous and slightly to moderately infiltrated with macrophages and lymphocytes.

The kidneys showed an unexpected lesion in that there was definite evidence of a widespread minimal glomerulitis without changes in any other part of the nephron. The evidence consisted of focal basement membrane thickening, endothelial swelling and an abnormal number of polymorphonuclear leukocytes (Fig. 5). This was obviously a subclinical lesion and presumably related to the primary disease in the absence of evidence of bacterial infection elsewhere. Glomerulonephritis has seldom been reported in trichinosis.[11] The remainder of the organs showed no significant histological lesion.

Anatomical diagnosis.—Widespread acute trichinosis, trichinal myocarditis with cardiac failure and subacute passive congestion of the lungs, meningoencephalomyelitis and glomerulitis.

CASE 2

This girl, aged about 5 years, was a sibling of the patient in Case 1, and was admitted on the same date. On physical examination she was evidently in a much better condition than her brother. She had a barking cough, was dehydrated and showed œdema and muscle tenderness of the extremities. T 102° F. per rectum, P 128, R 44. She had photophobia, a purulent otitis media and a slight enlargement of the cervical and axillary lymph nodes. Breath sounds were harsh except at the right base where they were slightly diminished and no rales were heard. The abdomen was soft and protuberant, with generalized tenderness, and the liver edge was down 1.0 cm. Slight neck stiffness and a positive Kernig's sign were noted.

Blood examination showed hæmoglobin 8.6 g./100 ml., white cell count 25,000, with the following differential count: neutrophils 14,200, juveniles 2,400, lymphocytes 3,600, eosinophils 4,800. An x-ray of the chest showed calcified lymph nodes at the right hilus with an area of calcification in the right lung, as well as a moderate increase in lung density in the right middle and lower lobes. In view of the strong possibility of the child's having active tuberculosis, she was transferred the next day to the infectious diseases hospital.

On October 24, 1953, she was returned to The Children's Memorial Hospital because of increasing œdema and continuance of her symptoms, as well as evidence of hypoalbuminæmia. Gastric washings had been negative on smear and a definite diagnosis of active tuberculosis could not yet be made. Her serum total protein was 6.1 g./100 ml. with 2.65 g./100 ml. albumin and 3.45 g./100 ml. globulin. Lumbar puncture on October 25 showed a normal spinal fluid pressure with a negative Pandy test and a total of 18 cells/c.mm. consisting of 10 neutrophils and 8 lymphocytes. Spinal fluid protein was 47.4 mg./100 ml., sugar 38 mg./100 ml., and chlorides 428 mg./100 ml. Although the heart appeared slightly enlarged on x-ray examination, there was no definite clinical evidence of cardiac failure and the electrocardiogram was normal. The Mantoux test was positive.

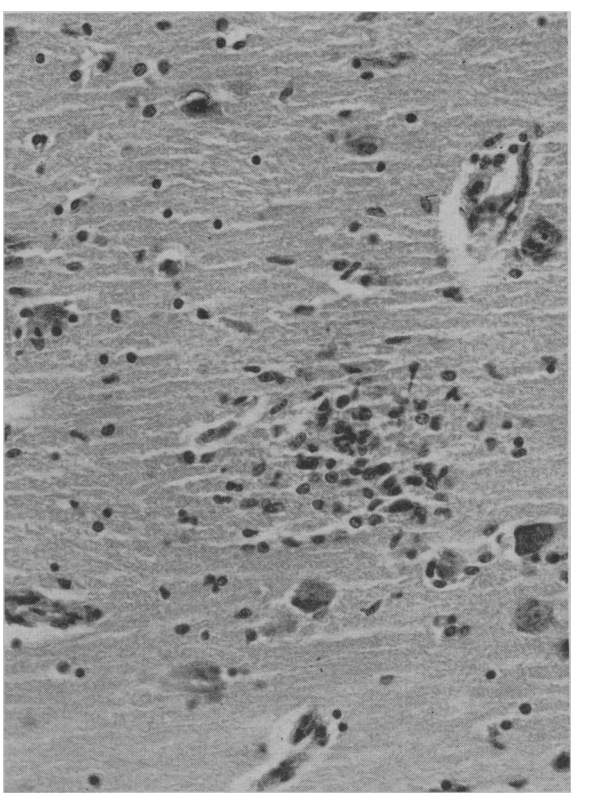

Fig. 4.—Area from brain (basal ganglia) showing focus of degeneration infiltrated with phagocytes. Eosin azur. × 225.

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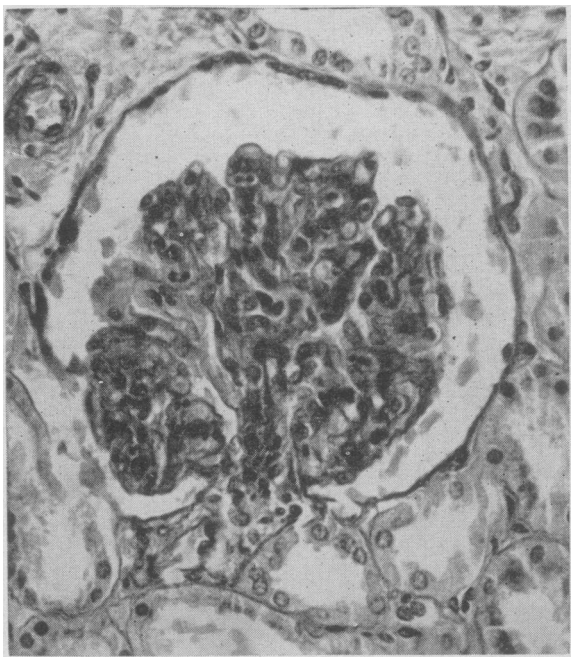

Fig. 5.—Glomerulus showing basement membrane thickening (black) with capillary narrowing and scattered multilobed nuclei of polymorphonuclear leukocytes. Periodic acid Schiff. × 400.

On October 28 it was realized that she must have trichinosis in view of the histological findings on her brother. This was confirmed by biopsy of the gastrocnemius muscle on November 6, 1953. This biopsy showed numerous trichinæ (Fig. 6), but the infestation did not appear to be as heavy as in the brother, a rough count showing about 26 larvæ in 3 sq. mm. of tissue. The inflammatory reaction was somewhat more intense and more diffuse than in the sibling, but otherwise the changes were similar.

The intradermal test with trichina antigen obtained from Dr. T. W. M. Cameron of Macdonald College, McGill University, was repeatedly negative. Gastric washings eventually grew *Myco. tuberculosis.*

Progress.—Her general condition and appetite improved steadily, even though she ran an intermittent temperature of 101° F. for a month. Œdema and muscle tenderness gradually disappeared but the eosinophil count dropped very slowly and five months later was still 2,016. No treatment other than that with antibiotics was given. When she was last seen, seven months later, her tuberculosis was inactive and the trichina skin test was still negative.

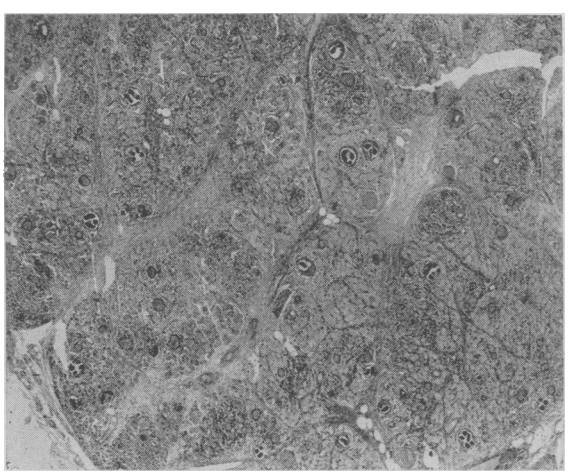

Fig. 6.—Cross-section of gastrocnemius muscle to show larvæ present in Case 2. Larvæ black. Note inflammatory foci. There are about 24 larvæ in this field. Periodic acid Schiff. × 50.

DISCUSSION

Both cases showed some of the classical signs of trichinosis—œdema, muscle tenderness, fever, respiratory distress, meningeal reaction and eosinophilia. It is interesting to note the absence of eosinophilia in the fatal case. Spink[12] has shown that in animals affected with trichinæ, eosinophilia is reduced after secondary bacterial infection. Many others have demonstrated the absence of eosinophilia in fatal cases.[11] A disappointing finding was the persistently negative trichina antigen skin test in the child who survived. However, negative skin tests have been shown by others[13] in about 10% of cases of clinical trichinosis and in some severe or fatal cases.[14]

When contact with this Eskimo family was finally made, through a missionary, a list of foods eaten prior to the illness was obtained. The foods consisted of cod's head, raw mussels, raw bearded seal, raw black bear, boiled cod and, in the month of August, raw arctic char. Trichinosis is known to occur in the bearded seal and black bear and these animals may well have been the source of infection in the present cases. When Eskimos are short of food they will eat almost any animal, including their dogs. This, combined with the fact that the meat is usually eaten raw or half-cooked, suggests that infection with trichina is likely to be common. It is obvious, then, that in dealing with Eskimo patients the possibility of trichinosis must always be kept in mind.

SUMMARY

Two cases of trichinosis in Canadian Eskimo siblings are reported, the parasites being demonstrated at autopsy in one case and by muscle biopsy in the other. Both had fever, œdema, marked muscle tenderness, respiratory symptoms and meningoencephalitis. One patient died from myocardial involvement. Eosinophilia was absent in the fatal case, while the intradermal test, using trichina antigen, was negative in the surviving patient.

It is suggested that the incidence of trichinosis among Eskimos may be high and the possibility of such infection must be considered at all times in dealing with Eskimo patients.

The authors wish to thank Dr. T. W. M. Cameron, Professor of Parasitology, Macdonald College, McGill University, for his information and help in preparing this paper.

REFERENCES

1. CAMERON, T. W. M.: *Canad. J. Research,* **21** Sec. D: 413, 1943.
2. KUITUNEN-EKBAUM, E.: *Canad. J. Pub. Health,* **32**: 569, 1941.
3. BOURNS, T. K. R.: *Canad. J. Pub. Health,* **44**: 134, 1953.
4. GOULD, S. E.: *Bull. New York Acad. Med.,* **21**: 616, 1945.
5. CAMERON, T. W. M.: *Canad. J. Research,* **17** Sec. D: 151, 1939.
6. KUITUNEN-EKBAUM, E.: *Canad. J. Pub. Health,* (abstract), **41**: 34, 1950.
7. BRANDLY, P. J. AND RAUSCH, R.: *Arctic,* **3**: 105, 1950.
8. THORBORG, N. B., TULINIUS, S. AND ROTH, H.: *Acta path. et microbiol. scandinav.,* **25**: 778, 1948.
9. KUITUNEN, E.: *Canad. J. Pub. Health,* Laboratory Section Supplement, **45**: 30, 1954.
10. BROWN, M. *et al.*: *Canad. J. Pub. Health,* **40**: 508, 1949.
11. GOULD, S. E.: Trichinosis, Charles C Thomas, Springfield, Ill., 1945.
12. SPINK, W. W.: *Arch. Int. Med.,* **54**: 805, 1934.
13. MCCOY, O. R., MILLER, J. J., JR. AND FRIEDLANDER, R. D.: *J. Immunol.,* **24**: 1, 1933.
14. HEATHMAN, L. S.: *Am. J. Hyg.,* **23**: 397, 1936.

A CASE OF MERSALYL (SALYRGAN) OVERDOSAGE

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THIS CASE is presented because the patient received 15 c.c. of Salyrgan (mersalyl) intravenously in a period of 46 hours, and recovered.

The patient was a 75-year-old white male, diagnosed as having carcinoma of the stomach. He was admitted to hospital on July 27, 1954, for gastric resection. His complaints then consisted of a weight loss of 12 lb. in two months, anorexia and upper abdominal discomfort of increasing severity over the same period of time, with recent constipation. He had had a prostatectomy in 1952 and no genitourinary complaints of note since. A half-sister had died of carcinoma of the liver. No other significant data were noted in the history.

General physical examination revealed only pallor and emaciation; the blood pressure was 136/78 mm. Hg. Abdominal examination was also non-contributory, the abdomen being flat, soft and non-tender with no palpable masses.

His preoperative course was uneventful. A sterile Levin tube was inserted the morning of the operation (July 30) and Demerol 75 mg. with atropine 1/150 grain was given hypodermically. He received 1,000 c.c. of blood during the operation. His blood pressure remained stable at 132/68 to 136/80 postoperatively. Morphine 1/6 grain was given as required for pain. The Levin tube was removed at 2 p.m. on July 30.

At 4.15 p.m. on July 30, the patient received 5 c.c. of Salyrgan in 10% Travert in water due to misinterpretation of the surgeon's handwriting. In the following 46 hours a total of 15 c.c. of Salyrgan was given in this manner before the mistake was discovered. During this time, the patient became progressively more restless, complained of bladder discomfort, used the urinal frequently and had to be catheterized on occasion. Eventually, an indwelling Foley catheter was established, and although it was draining freely, the patient continued to complain of bladder cramps and the desire to void. He was very nervous, jumping about at times. His pulse was noted as weak and irregular. His urinary output began to fall in spite of his large fluid intake. On irrigation of his bladder, the return was seen to be bloody. On August 2, his condition was considerably worse. He was perspiring profusely and his skin was cold and clammy. His B.P. was 78/50 and his pulse was again recorded as weak and irregular. He was placed in the Trendelenburg position. Consultation at this time revealed complaints of muscle cramps, a state of dehydration was noted, and the erroneous administration of 15 c.c. of Salyrgan was recognized. At this juncture dimercaprol (BAL) therapy was begun. The urinary output was approaching oliguric levels. After 7.5 c.c. of BAL had been given, the patient's urine output began to rise. The blood urea nitrogen level, which had been 15.9 mg. % preoperatively, rose to 66 mg. % as the urinary flow fell. As the urinary output returned to normal, the blood urea nitrogen went down, 30 mg. % being the last recorded value. Urinalysis on August 4 showed albumin 0.03% whereas previously it had been negative. A total of 8.5 c.c. of BAL was given. His subsequent course was uneventful and he was discharged on August 19, 1954.

He was readmitted on October 20, 1954, complaining of weight loss, nausea and vomiting. A recurrence of his carcinoma was diagnosed. The patient went downhill rapidly and died on November 11, 1954.

At post mortem, the adenocarcinoma of the stomach was widely disseminated involving the peritoneum, liver, gallbladder, left ureter, left and right pleuræ, diaphragm, œsophagus, anterior abdominal wall and the mesenteric, aortic and left supraclavicular lymph nodes. Gross examination also showed brown atrophy of the myocardium and a left hydronephrosis. Microscopic examination of the left kidney showed a moderate degree of dilatation of the convoluted tubules and a moderate infiltration within the interstitial tissue of the kidney proper. The glomeruli and small arterioles were normal. There was a moderate degree of arteriosclerosis within the larger arteries.

DISCUSSION

The undesirable and toxic effects of the mercurial diuretics were not quickly made known to the profession. In 1920 Heilig and Saxl published an account of their first case of heart failure treated with Novasurol. The second patient died from the effects of the drug. This case did not appear in the literature until 1950. The following complications are now well known:

1. Local necrosis.

2. Dehydration and salt depletion:[3, 16, 21] (a) weakness; (b) cramps; (c) restlessness; (d) delirium; (e) tetany;[12] (f) gout; (g) hemiplegia;[17] (h) coronary artery thrombosis.[2]

3. Hypersensitivity reactions: (a) urticaria and exfoliative dermatitis;[6] (b) sudden death.[1, 22]

4. Toxic effects: (a) acute pre-renal uræmia;[5, 10] (b) nephrosis;[8] (c) poisoning.[3, 20]

5. Acute urinary retention.[19]

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