Results

The results I will discuss under headings, including the usual objections to the use of radium therapy—namely, the complaints of discharge and pain following the application.

Bleeding.—A total of 187 cases (94 per cent.) have complete amenorrhoea. Of the twelve cases in which bleeding was not entirely arrested, hysterectomy followed in two cases; two others are still suffering from menorrhagia. The cases in which hysterectomy was performed were those of chronic metritis at ages 33 and 34, the doses being 1,800 and 1,200 mg.-hours, and it seems probable that a larger dose or a further application would have brought about a cure. A case of chronic metritis at the age of 38 (dosage, 1,920 mg.-hours) had no relief at all, and a case of a fairly large fibroid at 48 (1,920 mg.-hours) is in a similar condition. Three women state that they now have normal periods; they are aged 34 (dose 1,800 mg.-hours), 37 (1,200 mg.-hours), and 35 (1,200 mg.-hours). Five state that they have had a period occasionally. Only four patients (2 per cent.), therefore, are dissatisfied on account of abnormal bleeding. As regards the cessation of bleeding after the treatment in the remaining 187, ninety-five had no further loss. In forty-three the bleeding ceased during the first month; it continued longer than a month in fifteen, the longest time being seven months. Thirty had from one to four periods after the operation; two have an occasional period; one had a single slight loss, and one lost for eleven weeks nineteen months after treatment.

Discharge.—This is a most difficult symptom to evaluate, especially as it was present in many cases before the treatment. Eighty-two patients (41 per cent.) replied that they noticed no discharge; thirty-two had a slight discharge, and eighty-one a moderate amount, lasting for varying periods. Two had a profuse discharge—one for a month only; the other, a patient who had no relief from her menorrhagia, still discharges freely. The one significant point I have been able to make on the subject of discharge is that only two patients complain of discharge under the heading "Ill effects of the treatment."

Pain.—It is even more difficult, from the answers to a simple questionnaire, to reach satisfactory conclusions on this symptom. In 138 cases (69 per cent.) there was no pain at all. Pain was slight or moderate in a further forty-eight. Fourteen cases (7 per cent.) had what they consider severe pain for periods of from a few days up to three months. One woman says she had severe pain for a year. Again, it is significant that only one woman mentioned pain in reply to the question on "Ill effects."

Ill Effects.—No ill effect at all was noticed in 123 (62 per cent.) of the cases. Of the remaining seventy-six, seventeen (8.5 per cent.) mentioned definite menopausal symptoms, such as sweats and flushes—a surprisingly small proportion. Three others noticed an increase in weight, seven had headaches, and fifteen complained of weakness and "nerves." Two complain of dyspareunia (I have not been able to examine these patients), one seems to have had a femoral thrombosis, one cystitis, one severe diarrhoea, and one had thyrotoxicosis later, of which the abnormal haemorrhage was probably an early symptom. The remaining few complaints were irrelevant.

Results from the Patients' Point of View.—In response to the question "Was the result of the treatment entirely satisfactory to you?" 184 (92.5 per cent.) replied "Yes," and twenty-eight patients were moved to add notes expressing extreme satisfaction and gratitude with varying

degrees of eloquence. Only fifteen (7.5 per cent.) were less than completely satisfied.

I entered upon this investigation with, I hope, an unbiased mind, and I have been greatly impressed by the almost uniformly satisfactory results. They seem to me striking evidence of the value of radium therapy in selected cases of uterine haemorrhage in women approaching the menopause. I would only add that of 411 cases so treated during the past four years the only death was that of a patient who afterwards proved to be suffering from purpura, a record which I am sure could not have been equalled had radical measures been adopted in all these cases.

DANGER OF PRIMARY ABDOMINAL TUBERCULOSIS IN CHILDREN

BY

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The object of this paper is to present a series of cases of primary abdominal tuberculosis in children which terminated in a fatal meningitis, and to emphasize certain points in order to direct the attention of practitioners to the danger of primary abdominal tuberculosis in the child.

Primary tuberculosis of the lung has been extensively studied in children, and it is well known that in this form of tuberculosis the greatest risk to life results from generalized dissemination of the disease, usually manifested by a terminal meningitis. This risk is particularly great in the first three years of life, so that the prognosis in a case of primary tuberculous infection of the lung depends mainly on the age of the child.

Investigations into the fate of children infected with primary abdominal tuberculosis have been chiefly centred on identification of the type of bacillus responsible, human or bovine, or to the percentage incidence as compared with that of primary pulmonary infection, notably by Griffith (1932, 1934, 1937, 1938) and Blacklock (1932, 1935). Many significant facts have emerged from their investigations, two of the most important for the purposes of this paper being, first, that in 80 to 82 per cent. of cases of primary abdominal tuberculosis the infection is due to the bovine type of bacillus, and, secondly, that generalized dissemination takes place from a primary abdominal focus of infection in a high proportion of cases (32.4 per cent. in Blacklock's (1935) series of 372 cases).

For many years it was denied on the Continent that miliary tuberculosis could follow a primary abdominal infection, and only lately has this contention been refuted by the work of Griffith and Blacklock in this country and of Klercker (1931) in Sweden. The clinical importance of their investigations is even greater than is suggested by the figures quoted above, as these results were necessarily obtained by post-mortem examination, and, as will be seen later, the post-mortem figures do not nearly approximate to the total number of cases of miliary tuberculosis in children.

The Incidence of Primary Abdominal Tuberculosis

A survey of the last 3,214 post-mortem examinations at the Hospital for Sick Children revealed tuberculous meningitis as the cause of death in 284 cases—that is to say, this disease accounted for 8.8 per cent. of the necropsies. In forty-one (14.4 per cent.) of these cases the primary focus of infection was in the abdominal lymph glands. Stated differently, tuberculous meningitis resulting from a primary abdominal focus was responsible for death in more than 1.2 per cent. of over 3,000 necropsies. That this figure in no way represents the true mortality may be gauged from the fact that during the period 1933 to 1937 eighty-five children died in the hospital from tuberculous meningitis, but in only thirty-six of these were necropsies permitted—less than half the total number. (It is noteworthy that in the experience of one of us (G. H. N.) there is exceptional difficulty in obtaining permission to hold a post-mortem examination on children dying from tuberculous meningitis, in many cases because the child has been the only one.)

Criteria of "Primary Abdominal Focus" Infection

Our diagnosis of "primary abdominal infection" was based on enlargement with obvious tuberculous infection of the mesenteric lymph glands, with or without caseation, and complete absence of evidence of tuberculous infection of the bronchial or other mediastinal glands. No case was included in this series in which any enlargement whatsoever of the bronchial glands was recorded, or in which there were any tuberculous lesions of the lungs other than the miliary tubercles seen as a result of generalised dissemination of the disease.

Age and Sex Incidence

The next important feature is the age incidence. Former investigators have already stated that the highest incidence of primary abdominal tuberculosis falls in the first three years of life. The exact figures of this hospital were:

0-1 year	..	..	4 cases	3-4 years	..	..	4 cases
1-2 years	..	..	28 "	4-5 "	..	..	3 "
2-3 "	..	..	2 "				

Here the facts only are stated; their significance will be discussed later.

A common and tragic history was that the child had been breast-fed for six to nine months and thereafter had had "ordinary milk diet." In one case, however, recorded in detail as an illustrative case, the parents were emphatic that the child had been given nothing but boiled milk and that there had been no contact with any possible source of human tuberculosis.

Our findings as regards the sex incidence were similar to those of Blacklock and Griffin (1935), who found that tuberculous meningitis following a primary abdominal lesion was commoner in boys than in girls. Twenty-eight of the forty-one cases occurred in boys and only thirteen in girls. Of the total 284 cases of meningitis 152 were in boys and 132 in girls, so that 18.4 per cent. of boys succumbed to meningitis following a primary abdominal lesion and only 9.8 per cent. of girls.

Clinical Features

It may be said that diagnosis of primary abdominal tuberculosis in the living child is almost impossible in the absence of such secondary lesions as tumour-like masses of glands, gross tuberculous peritonitis, or advanced ulceration of the intestine. The first sign of primary abdominal

tuberculosis is only too often the onset of meningitis. It was rare in our series to obtain a history of anything but malaise, irritability, with perhaps constipation or vomiting for a short time, very seldom for more than two weeks. Only in four cases was there a history of illness extending over a period of two months. One of these (Case III below) is quoted as an illustrative case. Two of the other three cases with a long history had frank plastic tuberculous peritonitis, the intestines being matted together by caseating glands and adhesions in the mesentery. In the fourth case a long-standing spinal caries affecting the second lumbar vertebra and complicated by a psoas abscess preceded the meningitis.

Unfortunately an x-ray examination, which is of such invaluable help, if conducted critically, in diagnosis of a primary lung infection, is of little use for the diagnosis of primary abdominal infection. It reveals only calcified glands, a residuum of the infection, when the disease process is no longer active and danger is past. In the present state of our knowledge we can only say that, as clinical diagnosis of the primary abdominal focus is impossible, prevention of the infection becomes of paramount importance.

Case I.

J. C., aged 1 year 8 months, was quite well until two weeks before admission to hospital on June 4, 1937, when he became drowsy and disinclined to play. His appetite became poor. About a week later he had a convulsion and became unconscious. Since then he had been comatose and difficult to rouse. For several days he had vomited after meals. He was a normal full-term infant and was breast-fed (period not stated). There was no history of contact with tuberculosis. There was one other child, a boy aged 6 years, who was well. The parents were healthy.

On examination the child was comatose. The head was retracted. There was marked proptosis of both eyes. The optic fundi were normal. The Mantoux reaction (1 in 1,000) was strongly positive. The cerebrospinal fluid was examined on June 10, and contained 15 lymphocytes per c.mm., 95 mg. of protein per 100 c.cm., and 690 mg. of chlorides per 100 c.cm. No tubercle bacilli were seen. The chlorides fell terminally to 590 mg. per 100 c.cm. The child died a month after admission.

Necropsy Findings.—A typical tuberculous meningitis was present. There was a considerable degree of hydrocephalus. No tuberculomata were found in the brain. Many miliary tubercles were scattered throughout both lungs. There was no tuberculous infiltration of any of the bronchial or mediastinal glands. Miliary tubercles were present in the liver, spleen, and kidneys. A mass of enlarged tuberculous glands was situated in the mesentery. Caseation had not yet begun. No tuberculous ulceration was found in any part of the intestinal tract.

Case II

D. I., aged 1 year 6 months, was admitted to the Hospital for Sick Children on December 9, 1937. For two weeks he had had pyrexia and had lost his appetite. He had vomited occasionally. There was no history of contact with tuberculous patients. The other members of the family were healthy.

When admitted he was drowsy, with a temperature of 102° and a pulse rate of 128. There was neck rigidity, and a positive Kernig's sign was obtained on both sides. No papilloedema and no choroidal tubercles were observed. Examination of the cerebrospinal fluid showed 275 cells per c.mm., 2 per cent. being polymorphs and 98 per cent. lymphocytes; and 100 mg. of protein per 100 c.cm. Reduction of Fehling's solution was poor. Chlorides amounted to 670 mg. per 100 c.cm., and tubercle bacilli were present. The child died six days after admission.

Necropsy Findings.—Well-marked tuberculous meningitis was present. There was a considerable degree of hydrocephalus. A few miliary tubercles were found in both lungs. There was no tuberculous infiltration of any of the bronchial or mediastinal glands. Many miliary tubercles were present in the liver and spleen, but none were observed in the kidneys. There were one large and several smaller tuberculous glands in the mesentery. These had undergone caseation and were becoming liquefied. No definite tuberculous ulceration was found in the small or large intestine.

Case III

J. S., aged 1 year 3 months, was admitted to the Hospital for Sick Children on July 16, 1938. He had been well until two months previously, when he developed intermittent vomiting, lost his appetite, and became constipated. Ten days before admission he had three convulsions. Later he became drowsy and eventually relapsed into coma. There was no history of tuberculous contact. The parents were healthy. The child since early infancy had been fed on "accredited" milk, which the parents declared was always boiled.

The patient, on admission, was comatose and had Cheyne-Stokes respiration. The abdomen was retracted. A mass was felt near the umbilicus and another in the right iliac fossa. Early papilloedema was present, but no choroidal tubercles were seen. The cerebrospinal fluid was not under pressure; it was opalescent and slightly yellow; the chlorides amounted to 650 mg. per 100 c.cm.; and culture was sterile. The child died the day after admission.

Necropsy Findings.—There was only a thin fibrinous exudate containing a few miliary tubercles at the base of the brain and limited to the infundibular space. A few very small miliary tubercles were scattered throughout both lungs. There was no tuberculous infiltration of any of the bronchial or mediastinal glands. The spleen was slightly enlarged, and contained many rather large miliary tubercles. A few miliary tubercles were present in the kidney and liver. There was extensive ulceration of the mucous membrane of the last few inches of the ileum and of the caecum. The ulcers were irregular, and were situated transversely to the long axis of the gut. There were many miliary tubercles on the peritoneal surface. No ulceration was present in the rest of the small intestine or in any part of the large intestine. One large caseous tuberculous gland was situated alongside the second part of the duodenum and a large mass of tuberculous glands was present in the mesentery of the ileo-caecal angle. These glands were in various stages of caseation.

Some Points in Morbid Anatomy

Two of the above cases illustrate the salient feature of the morbid anatomy of tuberculous meningitis resulting from a primary abdominal focus—that is, the small size of the lesion in the abdomen which can give rise to a fatal meningitis. In many cases only *one* enlarged infected gland could be found in the mesentery, and no trace of ulceration could be discovered in the bowel. Reference has already been made to the few cases in which gross peritonitis or ulceration of the bowel was present. Widespread dissemination of miliary tubercles was almost invariable; only in three cases was there a meningitis without miliary tubercles in the viscera. Often only a few tubercles were scattered over the pleural surfaces of the lungs and on the surface of the liver, spleen, and kidneys; but in view of Blacklock and Griffin's series (1935), in which they found 27.8 per cent. of cases with meningitis following a primary abdominal lesion without generalized miliary tuberculosis, it is rather remarkable that only three similar cases (7.3 per cent.) should have occurred in our series.

A macroscopic tuberculoma was found in the brain in only one case, in which a hard mass the size of a cherry stone occupied part of the right crus and the floor of the third ventricle. The rarity of tuberculomata in meningitis

following a primary abdominal lesion contrasts with the frequency with which they occur in meningitis resulting from a primary lung infection; for in the whole series of 284 cases of meningitis, tuberculomata were present in thirty-five (12.3 per cent.).

Geographical Distribution

Both Griffith (1938) and Blacklock (1932) have pointed out that primary abdominal tuberculosis, owing to the high percentage of the bovine type of bacillus found in this form, is more prevalent in rural districts than in cities. It is noteworthy that in our admittedly small series of forty-one cases twelve children came from one particular county and from a radius in it of not more than thirty miles. Central London furnished only fifteen cases and "Greater London" another four.

Discussion

Our observations on a series of children who were investigated both clinically and pathologically afford striking evidence of the danger to which children are exposed by infection with primary abdominal tuberculosis. This danger may take the form of generalized miliary tuberculosis with or without a terminal meningitis, or, rarely, of an isolated fatal meningitis. The admirable work and statistical surveys of pathologists and bacteriologists such as Blacklock and Griffith in this country and Klercker in Sweden are apparently not fully appreciated by practitioners. This is the more deplorable because the mortality revealed by their studies and also by our investigations represents only part of the morbidity due to primary abdominal tuberculosis, which results also in many cases of "surgical tuberculosis."

One of the most important points with which we have dealt is the reflection of age incidence on the prognosis. We found that twenty-eight cases of the forty-one came to necropsy during the second year of life, and that no case occurred after the age of 5 years. In order to explain this age incidence many factors must be considered. It is possible that younger children are more susceptible subjects for implantation of the tubercle bacillus in the intestine, as it is well known that their intestines form a *locus minoris resistentiae* for many intestinal disorders which occur at this age. But a more likely possibility seems to be that in the very young there is *difficulty in localizing* the disease process. This opinion is supported by the parallel series of cases of generalized miliary tuberculosis with meningitis resulting from primary lung infection published by one of us (S. E.) in 1924 and 1930. In these cases failure of localization was revealed by anatomical evidence. In the younger children bronchial glands at a distance from those primarily draining the primary tuberculous focus in the lung were larger and much more often affected than in older children. The slight tendency for younger children to localize the tuberculous process was thus proved by ocular demonstration. It has not yet been possible to bring forward similar evidence in primary abdominal infection owing to the small number of cases personally observed.

Another point to be mentioned is the effect of the difference in feeding which takes place during the second half of the first year. This change from breast milk to cow's milk could be held responsible for the high incidence of fatal cases in the second year of life. We consider that the infection originates in this way in the vast majority of cases, but that the high mortality at an early age is due to the deficient power of localization mentioned above. It is common knowledge that primary abdominal tuber-

culosis is most often due to the bovine type of bacillus which is conveyed in milk. The researches of Blacklock and Griffith leave no doubt on this point, as they found the bovine type of bacillus in 80 to 82 per cent. of cases with primary foci in the abdomen. We are therefore entitled to assume that in our cases also the bovine type of bacillus predominated. This assumption is sustained by the fact that a majority of the children came from rural areas where children are more often fed on raw milk.

It may be remarked that in Case III the parents declared that the child had been given only boiled milk. The possibilities in this case are, first, that the infection was of the human type, which is rare; and, secondly, that the milk had been insufficiently or not always boiled. To omit to boil milk properly on a single occasion is quite sufficient to allow the tubercle bacillus to enter the body and give rise to infection.

Conclusions

Primary abdominal tuberculosis is a commoner disease in children than is generally supposed, and the true incidence is much higher than post-mortem figures indicate.

In primary abdominal infection, as in cases with a primary lung infection, the prognosis depends on the age of the child: the younger the child at the time of infection the worse the prognosis.

We are unable to accept the current view that primary abdominal tuberculosis can be more lightly regarded in children than can a primary lung infection: the bad prognosis in young children refutes this view. Diagnosis in cases of primary abdominal tuberculosis in the living child is extremely difficult; consequently early treatment is rarely possible. Prevention of infection is therefore all-important. Many cases of tuberculous meningitis, miliary tuberculosis, and crippling deformities could be prevented. We should endeavour, as an ideal, to secure for children milk from tuberculin-tested herds only, but at present it is impossible to provide this for the whole population. Therefore the greatest measure of protection is afforded by milk which has been boiled or efficiently pasteurized.

We wish to thank Dr. D. N. Nabarro, Director of the Pathological Department, Hospital for Sick Children, for the interest he has taken in our work, and the honorary medical and surgical staff of the hospital for permission to use their case reports and post-mortem records.

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The regulations governing the award of Commonwealth Fund Fellowships have been amended since the publication in the *Journal* of October 15 (p. 804) of the announcement regarding the fellowships. The chief alterations are as follows: Candidates must be unmarried and must not have attained the age of 30 on September 1 of the year of award; fellowships are vacated by marriage; they are open to men only; and are tenable for two years. Readers of the *British Medical Journal* who are interested are advised to apply to the secretary of the Commonwealth Fund Fellowships, 35, Portman Square, W.1, for copies of the revised regulations.

APLASTIC ANAEMIA WITH COMPLETE RECOVERY

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When treating a patient with aplastic anaemia it is difficult to decide as to how long it is worth while keeping him alive by repeated blood transfusions in the hope that his bone marrow will ultimately revive and so maintain his cure. There are types of so-called idiopathic aplastic anaemia in which the bone marrow fails to recover and the disease is progressive and fatal. Blood transfusion probably does no more than postpone their death by a few months. There are other types of aplastic anaemia, usually the result of poisoning by drugs, in which the bone marrow quickly recovers its function and effects an automatic cure with or without the aid of a few blood transfusions. It is between these extremes that we are faced with the difficulty of deciding the number of transfusions to be given.

The case whose story is reported here is that of a man with aplastic anaemia following salvarsan therapy who in 1935 was kept alive for nine months with blood transfusions and is now (three years afterwards) in good health. At first no history of treatment by salvarsan was obtained, and in the absence of any apparent exposure to a noxious drug he was regarded as suffering from idiopathic aplastic anaemia. With the haemoglobin falling to 18 per cent. and the patient almost blind from retinal haemorrhages, there appeared to be no hope of recovery. He continued in this state for five weeks while transfusions were given to him two or three times weekly. In all, twenty-five transfusions were given in nine months.

Case History

The patient, a confectionery baker aged 50, began to complain of lack of energy and shortness of breath on exertion, and in April, 1935, his friends noticed that he was getting pale. A blood count done at that time showed 50 per cent. haemoglobin with colour index 1.1, and in spite of intensive oral and intramuscular liver therapy his condition rapidly became worse. He was first seen in May, and was admitted to hospital on the 30th of that month. He was then in a very critical condition, with dyspnoea on the slightest exertion. His mental processes were distinctly sluggish, his manner morose, and the history was given in a distant and hesitant manner which did not lead one to place much reliance on his statements. There were widespread haemorrhages into the skin and mucous membranes, and these were so thickly scattered in the retina that he was scarcely able to see. There were a few superficial ulcers with their sloughs on the buccal surface of the lower lip. Apart from some distension of the bladder, which could be palpated without discomfort, and absent ankle-jerks, examination was negative. The Wassermann reaction was very weak positive, and the van den Bergh normal, and radiographs of the femora revealed no encroachment on the medulla.

A blood examination resulted as follows: red cells, 1,380,000; haemoglobin, 23 per cent.; colour index, 1.02; reticulocytes, 0.6 per cent. The red cells were normal in shape, size, and colour. There was a slight amount of anisocytosis, but no poikilocytosis or polychromatophilia. No early forms were seen. Platelets numbered 38,600 (over 500 erythrocytes), and the white cells 2,187. The differential count showed: polymorphs, 16 per cent. (350 per c.mm.); lymphocytes, 72 per cent. (1,575); monocytes, 9 per cent. (197); eosinophils, 1 per cent. (22); basophils, 1 per cent. (22); myelocytes, 1 per cent. (22). The lymphocytes were mainly large in character. No primitive forms were seen. The