Peyer's patches and from the pin-point abscesses in the thyroid were inoculated into bouillon. I consulted my friend, Dr. J. J. Buchan, M.O.H. St. Helens, who suggested to me that I should try the agglutinating reactions of serum from boys suffering from the disease with the different strains of intestinal bacilli which he had in his laboratory. Dr. Buchan has my sincerest thanks, as, but for the use of his laboratory and materials and the fact that he corroborated and checked my results, I could not have continued the investigations.

Bacteriological Results.

From the spleen, Peyer's patches, mesenteric glands, abscesses in the thyroid, and from the faeces in two cases, a bacillus was obtained which was actively motile. The growth on agar gave the usual *coli*-typhoid appearance. The bacillus was negative to Gram, did not produce indol, did not clot litmus milk. On Conradi-Drigalski plates bluish colonies, much smaller than the red colonies of *Bacillus coli* used as a control, and on picric acid green and McConkey's bile salt media colonies quite distinct from the *Bacillus coli* colonies were grown.

Agglutination Results.

Briefly, the *Bacillus coli*, typhoid bacillus, and Gaertner's bacillus were excluded at once, as even after two hours in a dilution of 1 to 50 there was no agglutination with blood taken from boys who were ill. The laboratory paratyphoid B and the laboratory aertrycke bacillus agglutinated the same serum in dilutions of 1 to 50 almost immediately and 1 to 100 in a few minutes. Some of the specimens taken from boys who had recovered from the disease for some time agglutinated the laboratory paratyphoid B bacillus, but not the laboratory aertrycke bacillus. The bacillus cultivated from the *post-mortem* examination was negative to a case of typhoid, but agglutinated each blood that was positive to the laboratory paratyphoid B.

Whether the bacillus isolated is actually the paratyphoid B or not, there can be no doubt it is closely related to that organism, as it gave similar cultural reactions, and agglutinated the same bloods. Each boy who was ill was positive both to the paratyphoid B and the bacillus isolated. Some of the boys who had not been ill gave negative reactions to both, though some gave positive reactions. Some of these latter admitted having had "the headache," which even in the case of boys who had been evidently affected was almost all that could be obtained in the way of complaint.

The question of the presence of a "carrier" in the school was considered seriously, but the demands of a general practice debarred me from systematically testing the blood of each boy. However, the last *post-mortem* examination I did inclined me more than ever to this idea, though I was not, unfortunately, able to make any further progress in the investigation. The liver in this case was a beautiful specimen of hobnailed cirrhosis. The boy was aged 12, there was no history or suspicion of syphilis. He died after a few hours' illness, but had had an attack of great severity about six months before. It seemed quite a plausible inference that there had been some chronic absorption from the bowel producing cirrhosis of the liver.

I think, then, that this epidemic deserves to be placed alongside of the other recorded epidemics. The descriptions of these resemble the Preston epidemic just as closely as they resemble the Tranent one; and the mere fact that in this latter epidemic the infective agent was the pneumococcus, in view of the atypical form of pneumonia that is present in these epidemics, does not warrant the conclusion that all such outbreaks are due to abortive pneumonia. The diagnosis of the late Professor Gemmell showed his superlative powers as a clinician when he wrote in 1888, "They seemed all to be victims of the same poison, although, in some, owing probably to personal idiosyncrasy, aided by favourable atmospheric conditions, it issued in pneumonia."

The epidemic at Birkdale Farm School, reported on by Dr. Coupland, though diagnosed as pneumonia, was not due to the pneumococcus. It is over two years since I read the report, and I am writing from memory, but I think the organism was said to be a motile bacillus. In this connexion it is interesting to recall the epidemic of

pneumonia in Middlesbrough in 1888, investigated by Dr. Ballard and Professor Klein. There were over 1,600 cases, with more than 300 deaths. According to Professor Klein, the germ at work was a motile bacillus, and from the description of the cultural appearances of this organism on gelatine, given in the *Treatise on Hygiene*, by Stevenson and Murphy, the appearances resembled more those of the *coli*-typhoid group than the pneumococcus. It is also of interest to recall the observation that bacon bought in the infected districts gave rise to pneumonia in mice fed upon it. Considering that paratyphoid B belongs to the meat-poisoning group, this fact may be of importance. However, I made nothing of my investigations in this direction in the Preston cases.

In view of the positive finding of the pneumococcus in the Tranent epidemic and the positive finding of a bacillus of the *coli*-typhoid group in the Preston epidemic, I think the search for a solution of the problem may well continue. It is only too likely that a chance for further investigation will present itself before long, considering the histories of the industrial schools of the country. I am, however, not sure that this type of disease is limited to the inmates of these institutions, as I cannot help being struck with the frequency with which at coroners' inquiries, deaths from acute conditions of a few hours' duration are returned as deaths from acute pneumonia. It seems to me possible that there are toxæmias of alimentary origin masquerading up and down the country as malignant influenza, gastric influenza, and fulminant pneumonia, in addition to the undoubted diseases of these names. It is in the hope that some one with sufficient time, and the fortune to meet cases of this class, may still further investigate the subject, and to keep the question of the naming of the disease open till we have further knowledge, that I have written this communication.

NOTES OF A CASE OF "NODULAR LEUKAEMIA."

BY

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G. M., a boy aged 10, was seen by Dr. Reid, on November 2nd, 1912, for pain in his right hip and leg. As no improvement followed rest in bed, Dr. Reid admitted him to the Throne Children's Hospital on November 13th. The pain closely resembled that of right hip-joint disease, and splints were applied; but the pain soon developed in the other side. On December 8th enlarged glands were found below the left lower jaw; some teeth were loose and were removed. Within a few days a swelling appeared above the right zygoma, and subsequently above the left, and later in the groins. He was rapidly losing flesh, but there were as yet no head symptoms.

On December 15th there was loss of vision in the right eye and later in the left, and slight proptosis. Some spinal fluid was withdrawn by Mr. Stevenson and examined by Dr. Thomson. On December 27th he was seen also by Dr. Calwell and Dr. Thomson, and at this date his condition was much worse; he was only partially conscious; he did what he was told if he was given time; his answers were fairly intelligent, but delayed, and were chiefly in monosyllables; there were large symmetrical swellings above each zygoma, and the proptosis was more marked; there were sordes on the lips; the abdomen was full and tender; it was examined with difficulty, but no enlargement of liver, spleen, or kidney was detected; all the lymphatic glands—cervical, axillary, inguinal—were enlarged and shotty; on the skin generally, and on that of the abdomen in particular, there were palpable minute millet-seed-like nodules; there was some head retraction, well-marked Kernig's sign, and priapism; he was now blind, and later became deaf; there was also paralysis of

both lower extremities with anaesthesia, and unconscious action of both bowels and bladder; flexion of legs caused pain; one optic disc presented some neuritis, the other was clear. There was also epistaxis a day or so before death. The temperature varied from 98° F. to 100° F., but on December 26th it began to be sharply intermittent, and reached 104° F. on January 1st; it was subnormal before death, which took place on January 3rd. Unfortunately a photograph was not obtained nor a *post-mortem* examination allowed.

REPORT BY DR. THOMSON.

The spinal fluid sent to me was so haemorrhagic that a cytological examination was of no value; a slight growth on agar was due to a staphylococcus, and as it was not again discovered it was probably a contamination.

At a subsequent examination of the patient on December 27th the following results were obtained:

Blood.—The coagulability was delayed; the serum showed distinct lipaemia; fat was extracted from it.

Red cells	...	...	2,800,000 per c.mm.
Haemoglobin	...	...	55 per cent.
Colour index	...	...	1 (practically).
White cells	...	...	5,640 per c.mm.
Differential count:			
Polymorphonuclears...	...	...	12 per cent.
Large lymphocytes	...	...	49 "
Small lymphocytes	...	...	17 "
Transitional	...	...	12 "
Myelocytes	...	...	10 "

There was no poikilocytosis; no nucleated reds were found and no chromatophilia.

A blood culture gave a negative result.

Urine.—No albumen, no sugar, no Bence-Jones's substance. Nucleo-proteins were present in rather increased amount.

Lumbar Puncture (made by Dr. Thomson).—The fluid escaped at high pressure and again seemed almost like pure blood; fat was again present in large amount in the serum; a culture gave a negative result.

It was intended to confirm or modify these results of the physical examination and of the blood count by repeated similar investigations, but the rapid course of the disease prevented the accomplishment:

REMARKS BY DR. CALWELL.

Although these notes are not complete, we thought the case of sufficient importance to warrant us in putting on record such facts as we have. There seems to be little doubt that it falls under the broad category of "nodular leukaemia," as described by Dr. Gordon Ward in the Section of Medicine of the Royal Society of Medicine in 1912, and in type it most closely resembles "chloroma." The zygomatic swellings were marked; the early pain in the hip and leg, which finally developed into paraplegia, was presumably due to analogous deposit in the spinal column, and such a deposit would no doubt account for the deeply blood-stained fluid removed on both the occasions of lumbar puncture. The blindness, the deafness, the priapism, are all classical symptoms; the rapid course of the affection was in keeping with the diagnosis.

The result of the blood examination shows a remarkable smallness of white blood count; whether this paucity would have been found to be a constant factor on further examination cannot be argued; such a number has been found, and enormous rises and falls in the white blood count have been put on record by most authorities; in one case it is given as 800 per c.mm. The differential count is also interesting; the great increase of large lymphocytes and the presence of a considerable number of myelocytes is characteristic. Gulland and others say that the blood picture in leukaemia is by no means constant; so that the blood examination in this case confirms what has been already so often noticed, that neither in number or character of the red, nor in differential count of the white, have we a definite and final arbiter in the subclassification. In this case, however, the blood count sharply differentiates it from the series of cases given by Robert Hutchison, in the first number of the *Quarterly Journal of Medicine*, of suprarenal sarcoma in children with metastases in the skull, in which temporal swellings were present; but a blood count showed a simple marked secondary anaemia. Frew, however, in a later number endeavours to prove that such cases come under the term "carcinoma," and gives details of cases in which the

differential count shows a very marked disturbance; such cases would widen the boundaries still further.

The usual conception of "leukaemia" rests on the differential count of the white corpuscles; in the acute form there is an excess of lymphocytes and profound constitutional disturbance, and often an early fatal issue; in the chronic or marrow form, symptoms are frequently delayed till late in the course of the disease, and we find an excess of myelocytes. In his paper Dr. Gordon Ward describes "nodular leukaemia" as embracing all cases of leukaemia in which nodules of leukaemic growth have been found in various parts of the body, and have been obvious to sight or inference during life. It is purely a clinical term. He mentions a great variety of titles, such as mycosis fungoides, chloroma, Mikulicz's disease, and others, and points out that lately facts have come to light which, apparently, link the affections described under these names closely together: cases of mycosis fungoides occur with a blood picture of leukaemia; cases of leukaemia occur in which nodules indistinguishable from those of mycosis fungoides have developed; similar nodules are found in chloroma; the green colour of chloroma may be present only in a minority of skull tumours, and may be found in the glands and marrow of leukaemia in which there were no tumours.

Whether we can rope in all the affections enumerated by Dr. Gordon Ward, and also by Dr. Treadgold,¹ is a matter for future investigation. We can distinguish the leukaemias from even extreme cases of leucocytosis, and also from cases of pure sarcomatosis; the blood picture, however, varies, not only in different patients, but also in the same patient from time to time; probably these differences are due to the type of cell becoming more and more primitive. "The variety and severity of the affection," says Treadgold, "varies with the part of the haemopoietic apparatus affected, with the intensity of the stimulus, and with the ability of the organism to withstand it." And one has thorough sympathy with him in his complaint regarding the cumbersome terminology that is suggested in each new article.

It might be considered more correct to use the term "infiltrating leukaemia" and not "nodular"; the collections of cells are not always circumscribed; oedematous infiltration may be found about the face, neck, scalp, and this may at times have a greenish colour; definite nodules of fair consistency are most common in the bones, especially those of the skull, but have also been found in the pelvis and vertebral column; they may occur also in the skin and subcutaneous tissue—indeed, wherever lymphoid tissue is found. The nodules vary in size, from that of a pin's head to that of a fist. They do not occur in the epidermis, but may ulcerate through it. The colour varies from that of the surrounding skin to yellow, red, purple, greenish. Minute nodules are found on the gums and in the submucous tissue of the alimentary tract. Parkes Weber points out that the pre-mycotic infiltration of mycosis fungoides may be sufficient to make the skin fall in rolls, and that this affection corresponds to Kaposi's lymphodermia perniciosa.

The more constant employment of the oxydase reaction, as described by Dunn in the April number of the *Quarterly Journal of Medicine*, 1913, may in future prove of service. His conclusions state that the occurrence of a positive indophenol-oxydase reaction in large non-granular cells in acute leukaemia is a certain proof of their myeloid nature, and enables a diagnosis of acute myeloid leukaemia to be readily made from blood examination; but that the reaction is negative in the more embryonic forms of marrow cells; cases of acute myeloid leukaemia may occur, in which the type of blood formation is so embryonic that the oxydase reaction is valueless for differential diagnosis; but even in such cases the histological characters of the large leucocytes may render a diagnosis possible. It seems, however, thus to fail us just where it would have been of great service—namely, the origin of the embryonic type of white cell.

REFERENCE.

¹ *Quarterly Journal of Medicine*, 1908-9.

SURGEON-GENERAL GEORGE BIDIE, C.I.E., Honorary Surgeon to the King and formerly to the Viceroy of India, left personal estate of the total value of £2,943.