

GLANDULAR FEVER: "INFECTIOUS MONONUCLEOSIS"

or "ACUTE BENIGN LYMPHOBLASTOSIS:"

A clinical study with some reference to etiology.

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Glandular fever has usually been regarded as a somewhat rare disease, but there is reason to believe that, during the past few years, epidemics have occurred, and it is not unlikely, considering the mild character of the infection, that many cases may have escaped attention.

Having recognised my first sporadic case in the spring of 1922, I had the opportunity, two years later, of observing a small epidemic which affected about twenty households in my practice. In three patients I was enabled to study the condition closely, from day to day, and to carry out such investigations as might possibly help to identify the disease more clearly. This evidence I was able to corroborate generally, from the epidemic cases.

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In 1889 Pfeiffer described under the title "Drusenfieber," the disease which is now known to us as glandular fever. That he was the first to describe the condition is not quite certain; Filatow of Moscow claimed to have described a similar condition some years earlier, but there can be no doubt, I think, that Pfeiffer's was the first accurate description. He recognised it as an acute infection, which occurred in small epidemics, chiefly amongst children under the age of fourteen years, and characterised by sudden swelling of the cervical and other lymph glands, associated with slight enlargement of the liver and spleen. In this country, Dawson Williams⁽²⁾ first drew attention to the condition and agreed with Pfeiffer in his general findings. Subsequent writers are all in agreement as to the infectious nature of the disease and epidemics have been reported by Hamill, West, Botschowsky, and others. Pfeiffer pointed out in his original article that it usually occurred in small, "house epidemics", that is to say/

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say, where one member of a family contracted the infection, the other children rarely escaped: this feature has been verified by later observers. The disease is endemic in this country and occasional sporadic cases occur and have been, from time to time, reported. There is a distinct seasonal incidence, epidemics occurring in the late autumn,^{and} early spring and there must usually be an interval of several years between the outbreaks. Shortly after the South African War numerous cases were observed in this country and the blankets of returned soldiers came under suspicion as being the source of infection. Strangely enough, during the recent war years, few, if any, cases were reported in the medical journals of this country, but recently Drs. H. Letheby Tidy and E.B.Morley,⁽³⁾ in addition to describing two cases which came under their notice, have given a full and painstaking account of the disease and have shown the diagnostic value of a differential leukocyte count. That the disease was epidemic in this country at that time - 1921 - is proved beyond doubt by the correspondence and comment which their able articles evoked.

In America recent writers have paid more attention to the blood picture than to the clinical findings, with the result that some confusion has arisen with regard to nomenclature. Under the somewhat laboratory title of "Infectious Mononucleosis", T.P.Sprunt, and F.A.Evans⁽⁴⁾ gave an account of six cases, which, from their clinical description, strongly resemble the disease which is known as glandular fever. A very similar group of cases has been described by Bloedorn and Houghton⁽⁵⁾ at the U.S.Naval Hospital, Annapolis, Maryland, under the name of "Acute Benign Lymphoblastosis". Dr.Warfield T.Longcope,⁽⁶⁾ of New York, has recorded ten cases of a similar condition, which he has encountered in the course of thirteen years - 1909 to 1922. In these cases, which occurred in young adults, medical students and young physicians mainly, Longcope recognised the likeness to Pfeiffer's "Drusenfieber", but was unable to satisfy himself that the two conditions were identical. Since this work was/

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 was undertaken, Tidy and Daniel have recorded their observations of an epidemic which occurred in a preparatory school, and have shown that the disease is contagious.

Clinical Features.

Owing to the mildness of the infection in the majority of cases, the incubation period is rather difficult to determine, but in one instance, where the date of exposure was known, the disease manifested itself on the sixth day. From observation of the epidemic cases, seven seemed to be the average and ten days the extreme limit. So far as the age incidence is concerned children between the ages of three and fourteen years, if exposed to the infection, seldom escape, but young adults are also liable and in one instance a woman of fifty contracted the disease from her son, a lad of sixteen years.

The onset is somewhat insidious and it seems to me that there is a prodromal period of from three to four days, during which the patient is "out of sorts", and as a rule extremely constipated: this makes it difficult to observe the disease in its earliest stages.

Lymphatic System.

Glandular enlargement is of course the most prominent symptom and usually develops rapidly. In quite a number of cases, stiffness of the neck was the first complaint and drew attention to the condition of the cervical glands.

The glands affected are the deep cervical lying near the sterno-mastoid, at its middle, and extending from the anterior into the posterior triangle of the neck. There may or may not be complaint of sore throat but the glands affected are not those usually involved in septic conditions of the mouth and throat and the absence of tenderness is striking. There is no redness of the overlying skin or oedema of the surrounding tissues.

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James. M. Leighton 2-2-24

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The swelling is usually unilateral to begin with, but in the majority of cases, the glands of the opposite side of the neck are soon affected and the enlargement is accompanied by a rise of temperature. There appears to be no constancy as to the priority of the side involved.

The parotid and submaxillary glands are not affected but in one case enlargement of the thyroid was noticed at a late stage of the disease, and the occurrence of this has been mentioned by some of the American writers.

In all my cases the abdominal glands were markedly enlarged, even when the enlargement of the deep cervical glands was not conspicuous: this, in conjunction with the constancy of abdominal pain, leads me to believe that the mesenteric glands may be involved at a very early, if not the earliest stage of the disease. The pain may be slight and difficult to localise, but in a few cases it was severe. The enlarged glands could be freely palpated - in some cases they assumed the size of a hen's egg - without causing any discomfort. Faecal accumulation may give rise to some difficulty, but unlike the glandular swelling, this can usually be indented by pressure.

The axillary and inguinal glands are fairly constantly affected, but never to the same extent as the mesenteric glands. In some cases the axillary show more swelling than the deep cervical glands, and as in these, the swelling may at first be unilateral. The same may also be said of the inguinal glands.

The mediastinal and peribronchial glands are also involved as the accompanying X-ray print clearly shows, and, as in other regions, the degree of enlargement seems to be very variable. In a few cases there was impairment of the percussion note over the mediastinum and a "pressure cough" was prominent in one.

Enlargement/

Enlargement of the supraclavicular, pre-auricular and epitrochlear glands was noted less frequently.

Suppuration did not occur in any of the affected glands: this is said to be characteristic of glandular fever, but Rudolf⁽⁸⁾ describes a case in his own family, in which the cervical glands suppurated. It is, too, a rather curious coincidence that in the subject of the only recorded post-mortem, the cervical glands had suppurated.

Other Signs and Symptoms.

Most writers, including Pfeiffer, have pointed out the disproportion between the glandular swelling and the condition of the fauces; complaint of sore throat is certainly not a usual symptom and slight reddening of the pharyngeal wall may be all that is apparent.

One of two brothers, under observation at different stages of the disease, developed a typical acute follicular tonsillitis, which was at once reflected in his blood picture by the usual polymorphonuclear leukocytosis.

Rash.

A good deal of stress has been laid on the fact that there is no associated rash, but from time to time, observers have described skin eruptions or rashes in connection with individual cases. Heubner, who took part in the discussion at the reading of Pfeiffer's original paper, described urticarial rashes which he had seen associated with similar symptoms. In one of my patients, a lad of eighteen years, the diagnosis was rendered difficult by the presence of a generalised urticarial rash, but the occurrence of further cases in the family, with no rash, confirmed the diagnosis.

The question of rash naturally leads one to the consideration as to which of the exanthemata glandular fever most closely resembles, and I think there can be little doubt, if we exclude rash, of its similarity to German measles. Both diseases are highly infectious; their/

their course is as a rule mild, and in both there is generalised glandular enlargement.

In several of the patients who came under observation a dry, scaly condition of the legs, trunk and neck was noted.

Epistaxis may occur and has been recorded as being severe. This occurred in two of the epidemic cases at the onset but in neither was it profuse.

Coryza is not usually regarded as a common feature but in one or two cases in debilitated children, it was profuse.

Vomiting may occur at the onset of the disease, especially in children, but it is not constant.

Constipation is usual and may be very intractable: this was noted by Pfeiffer, who also pointed out that it is usually succeeded by diarrhoea with the passage of mucus. The earlier writers thought that the occurrence of this diarrhoea marked the period of defervescence in the disease: constipation is by no means invariable and in quite a number of the patients I observed, the attack was ushered in by severe diarrhoea with troublesome colic.

There is no doubt however that the motions are altered and in children the unpleasant odour and character of the motions frequently called for comment.

The spleen is usually enlarged at some period of the disease but I could trace no connection between the degree of enlargement and the severity of the infection. The splenic enlargement was certainly not an early occurrence, was frequently very transient and gave rise to no pain or tenderness.

The liver may also be enlarged but in no case did the enlargement exceed two finger-breadths below the costal margin and its occurrence was not so constant as splenic enlargement.

The temperature is very variable and may be normal at the onset when the glands are already palpable but coincident with the/

the sudden enlargement of any group of glands there is usually a sharp rise to 102°-103°: this level is not maintained for longer than two to three days and the temperature usually falls as rapidly as it rose. In the more severe cases the temperature may go on intermitting in this manner for three or four weeks, but in the majority it is normal by the end of the second week. In none of the cases here reported was there any rigor although in two patients the temperature rose within twenty-four hours to 103°F. Except in the more severe cases there was no great constitutional disturbance and in the apyrexial periods the majority of the patients felt well enough to be up. The accompanying chart illustrates the type of pyrexia in a moderately severe case of the disease with no complications.

The Blood Picture.

This mild disease has recently attracted the attention of observers both in America and in this country on account of its association with curious alterations in the blood picture. Since the publication in July, 1923, of a paper by Tidy and Daniel,⁽⁷⁾ we can take it as proved, that the disease is accompanied by a lymphocytosis which is usually absolute at some stage of the infection, and the blood examinations of the cases here recorded, support this view and confirm the observation that the lymphocytosis takes time to develop. A study of the appended series of blood pictures in two cases, shews that there may be an initial polymorphonuclear leukocytosis, and in one of the epidemic cases in which there was a concurrent acute follicular tonsillitis, the blood picture showed the normal polymorphonuclear reaction. While all the cases examined gave evidence of a definite lymphocytosis, in no case did it reach the height reported by other observers in individual cases. For instance, Longcope records a case which occurred/

occurred in a medical student aged twenty-one, where, at one stage of the disease, the total leukocyte count was 23,000, with no less than 95% of mononuclear cells: Tidy records a case in which the first count showed a leukocyte total of 35,000, with 65% mononuclears. In such cases it would be obviously impossible to distinguish the disease from acute lymphatic leukaemia, by an examination of the blood films alone, and it seems natural to suppose that cases reported as "acute lymphatic leukaemia with recovery" may well have been cases of glandular fever or infective mononucleosis. Professor Arthur J. Hall,⁽⁹⁾ in 1913, recorded such a case as "resembling acute leukaemia" and similar examples have been reported by Ludka, Marchand, Sanders,⁽¹⁰⁾ and by Türk,⁽¹¹⁾ who considered such cases as a key to the etiology of acute leukaemia. Cabot⁽¹²⁾ concluded that "wide-spread streptococcic adenitis of tonsillar origin may be accompanied by a lymphocytosis so pronounced as to suggest lymphoid leukaemia;" but surely in the majority of virulent streptococcal infections the usual reaction is a polymorphonuclear leukocytosis? The frequency, however, with which mild, non-suppurative glandular affections are accompanied by a degree of lymphocytosis with occasional splenic enlargement, is certainly striking enough to call for further investigation.

Type of Cell Encountered.

Other observers have drawn attention to the fact that the predominant type of lymphocyte is distinct from the large and small lymphocyte seen in normal blood smears. It is usually rather larger than the small lymphocyte, its nucleus may be indented or kidney shaped and occasionally may be of the bilobed or so called Rieder type, and the surrounding protoplasm is more distinctly basophilic than in the case of the small lymphocyte. Sprunt and Evans have given a very full and detailed account of the various types encountered and have proved conclusively that these cells are lymphoidal in origin.

Etiology.

That glandular fever is an acute infection which breeds true, is, I think amply proved by a study of the literature bearing on the disease: that its incidence is world-wide seems to be equally true, since epidemics of the disease, or a disease which so closely resembles it as to be indistinguishable by ordinary clinical methods, have been reported in several European countries, in America, in Australia and in South Africa. That there may or may not be obvious changes in the fauces of infected individuals is perhaps responsible for some confusion, since observers have, from time to time, reported epidemics of "cervical adenitis" which may possibly have been outbreaks of glandular fever.

Some of the earlier writers considered the condition to be an aberrant form of influenza and an epidemic which occurred in Glasgow in 1917, affecting children and young adults, and characterised by swelling of the cervical glands, was popularly known as "Spanish 'flu".

The constancy with which similar symptoms, similar complications and similar blood changes are reproduced in different epidemics, would seem to be sufficiently strong evidence to disprove any connection between this mild disease and the virulent infection, with its protean manifestations and complications, which we know as influenza.

Many writers have suggested the nasopharynx as the seat of infection but since the changes in the fauces are usually remarkably slight, and since the glands affected are not those usually affected in septic conditions of the nose or throat, this seems to be at least doubtful and from my own experience of the condition, I am inclined to think that the bowel is the more likely seat of invasion. As I have already stated, the mesenteric glands appeared to be affected earlier and much more constantly than any other group of glands in the body: this enlargement, too, was greater than in the/

the case of any other group, and these facts in conjunction with the occurrence of constipation and diarrhoea, the frequency of abdominal pain and the manifest alterations in the character of the stools, suggest that the glandular system is attacked in the first instance by way of the bowel lymphatics. This might to some extent explain the peculiar "house-epidemic" character of the infection since a nasopharyngeal focus would be more liable to produce a generalised epidemic.

To the view that the causal organism may be a non-virulent streptococcus, there seems no reasonable objection. The fact that suppuration is rare and that associated with general glandular enlargement there may be slight enlargement of the liver and spleen, would seem to me to favour such a view: in support of this I should like to be allowed to cite one case of streptococcal infection which came under my notice recently. While at work a young man received small abrasions of the forefinger and thumb of the ~~left~~ and right hands respectively: the following day he had marked lymphangitis of both arms, with enlargement of the axillary glands, and two days later he developed an acute pharyngitis with enlargement of all the lymph glands of the body. Meantime the lymphangitis had given place to a purpuric eruption, which followed the line of the lymphatics and stretched from the hands to the axillae. Suppuration did not take place and his throat did not have the appearance of an ordinary follicular tonsillitis, nor was there such elevation of temperature as one usually sees in a primary acute infection.

Bacteriology.

At present there is no general agreement as to the nature of the causal organism: the earlier investigations, which were directed mainly to the culture of organisms found in the fauces, yielded widely/

widely varying results so that streptococci, staphylococci, pneumococci, spirilla and even the influenza bacillus have all come under suspicion. With one exception, cultures from the affected glands have only been attempted in cases where suppuration had occurred, and in all of these streptococci have been found.

Since most of my cases were seen in the course of private practice, it was naturally difficult to carry out the bacteriological investigations as fully as one might have wished. Throat swabs were examined in many cases and in the majority of them, streptococci were found, either alone, or associated with other organisms; this however is such a common occurrence in the examination of throat swabs, even from healthy individuals, that considered apart, no great stress can be laid on such a result.

Catheter specimens of the urine were examined in four cases and in each of these a streptococcus was isolated. Here again it may be urged that, in spite of the most stringent precautions as to catheter and receptacle, contamination is not unlikely, but streptococcal is not so common or so likely as staphylococcal contamination.

In six cases the faeces were examined bacteriologically and in each case streptococci were found to be present in excess of normal.

In three out of six cases examined, streptococci were isolated from material obtained from affected glands. The method employed to obtain the material was as follows:- after surgically cleansing the skin, a few drops of a sterile 1.5% solution of citrate in saline was injected into and withdrawn from the gland, a sterile broth tube inoculated and transferred to the incubator as quickly as possible. On account of their accessibility, the groin glands were most frequently selected for puncture and naturally, on account of its painful nature, the procedure was carried out only in the case of older/

older children and young adults. That in three of the six cases examined, no growth occurred, may, in my opinion, be a result of the difficulty in extracting material from the gland substance by the method employed. Excision and section of the affected gland in each case would have been more conclusive but the accomplishment of this would have entailed more inconvenience and discomfort to the patients than one felt entitled to inflict.

Blood culture was attempted in two cases with negative result, and, considering the mild course of the infection, I think such a result was to be anticipated.

Pathology.

In five of the cases reported in the literature under the name of "infectious mononucleosis", glands have been excised and subjected to histological examination, without revealing any typical feature. In some of these the pathologists concerned stated that the appearances could not be distinguished from a very early stage of Hodgkin's disease, in all there was marked lymphoid hyperplasia, with proliferation of the epithelioid cells of the reticulum.

Complications are not common, but nephritis, which is the most important complication, occurred in two of my small series of cases and in these it was, as is usually described, of the haemorrhagic type. The condition became apparent in one patient on the second, in the other, on the sixth day of the disease, which supports the conclusion of previous observers, that nephritis, if it does occur, develops early in the disease. In both cases - and this would seem to be unusual - there was some puffiness of the face and eyelids and in one slight oedema of the ankles; other observers have noted the absence of oedema in these cases.

Otitis media, which occurred in one of my series, must be a rare complication, only four cases having been recorded in a series/

series of something like five hundred cases of glandular fever.

There is no record of cardiac complications except in cases where previous rheumatic infection could not be excluded.

Prognosis.

The prognosis, even in complicated cases, is good: at the end of three weeks in an uncomplicated case, the patient is usually fit to be up and about, but a recurrence of the glandular swelling, with rise of temperature, suggestive of a reinfection, is not uncommon and a slight degree of anaemia may persist for some months, especially in weakly children.

There may be no visible swelling of the glands at the end of three weeks but they usually remain palpable for a considerable period: in three of my cases they were still palpable twelve months after the attack.

Only four fatal cases have been recorded, but it may be well to state here that epidemics of a disease, resembling glandular fever in its infectivity and in its acute affection of the lymph nodes, have been reported and in these endocarditis was a frequent complication and fatal cases were numerous. It is possible therefore that as with scarlet fever, the virulence of the infection may vary greatly in different epidemics.

Diagnosis and Differential Diagnosis.

Of the various diseases with which glandular fever may be confused, acute leukaemia, acute lymphadenoma, syphilis, tubercle, German measles, and septic infections of streptococcal origin, are perhaps the most important.

The blood picture, at a stage when the lymphocytic leukocytosis is fairly well marked, the enlarged lymphatic glands, the enlarged liver and spleen, might suggest the early stage of an acute leukaemia. The early and marked glandular enlargement, the absence of purpuric eruptions and severe anaemia, and the occurrence of abnormal

abnormal mononuclear cells in the blood, together with the mild course of the disease, should serve to differentiate the two conditions.

A sporadic case might well be confused with acute lymphadenoma, but the slight degree of splenic enlargement, the absence of anything suggestive of the Pel-Ebstein type of temperature curve, and the benign nature of the infection, would point to a diagnosis of glandular fever; some help might be obtained from the histological examination of the affected glands.

From syphilis, the acute character of the infection, the blood picture, the result of the Wassermann reaction and, in children, the absence of the other stigmata of congenital syphilis should all help to make the distinction clear.

The extent of the glandular enlargement, the rarity of suppuration, the blood picture and the short course of the disease should serve to distinguish between glandular fever and tuberculous adenitis.

With regard to glandular enlargements secondary to septic infections, there should be no difficulty about the diagnosis, especially in cases where the primary focus is in the naso-pharynx, since the glands involved are not those usually affected in glandular fever, and in cases where there is generalised glandular enlargement following infections elsewhere, as in the case quoted earlier, the discovery of a primary focus would remove all doubt.

From a case of German measles in the prodromal stage when the lymph nodes are already enlarged and the spleen may be palpable, the diagnosis would be difficult if not impossible. Cases of German measles without the usual skin eruption have, according to J.D.Rolleston, (13) been reported by competent observers, and in these instances the only evidence of infection has been the glandular swelling.

Records of blood examinations in cases of German measles are/

are not numerous, but these which I have been able to consult, show that the blood picture in the two diseases is not dissimilar.

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C.B.Ker states that in cases examined by Lyon, "the most constant feature was a relative increase in lymphocytes, which, though occasionally below 40 per cent on the first day of the rash, were invariably above 50% by the third day and averaged 55%, the large mononuclears being much increased in numbers."

(15)
Hess has shown that there is usually a polymorphonuclear leukocytosis during the incubation period.

Case No.1. A sporadic case of glandular fever.

On 8th April, 1922, T.B., a boy of seven years, previously healthy, except for measles at four and mumps at five years complained of frontal headache, was sick and vomited, and remained in bed. Next day he felt well and remained so until the 18th April when he complained of stiffness of the neck and pain on attempting to extend his head, slight headache and loss of appetite. There was no complaint of sore throat or earache, but his aunt, in whose charge he was at this time, had noticed with some anxiety, that the glands on the right side of the neck were slightly swollen - a younger brother, the subject of tuberculous glands of the neck, having died ten months previously of tuberculous meningitis.

When first seen, on 19th April, the patient was found to be a well nourished, healthy-looking boy of good physique. Temp., 100°F. Pulse 90. Respiration 18.

The lymphatic glands behind the angle of the jaw, on both sides, were markedly enlarged, the enlargement being more marked on the right side, where there was a central mass about the size of a walnut, surrounded by a number of smaller, discrete, "shotty" glands. There was/

was no redness of the skin or oedema of the surrounding tissues and palpation gave rise to little or no pain. The tongue was slightly furred and there was an unpleasant odour from the breath. There was no oral sepsis and apart from a slight injection of the pharynx examination of the ear, nose and throat was negative.

The heart and lungs were normal.

No tenderness was elicited on examining the abdomen, but enlarged glands were palpable in the left iliac fossa; no enlargement of the liver or spleen was detected.

During the next two days there was a general spread of the glandular enlargement; the deep cervical glands, in relation to the sterno-mastoid, both anterior and posterior, were involved, as were also the supra-clavicular, the axillary, and the glands in the groins.

On the 24th April he was pale and slightly puffy about the eyes; his urine was scanty and gave a very marked blood reaction, but there was no oedema of the feet or ankles.

The swelling of the glands increased and the enlargement continued to be more marked on the right side of the neck.

On the 28th April he was still passing a very small quantity - four to five ounces - of bloody urine in the twenty-four hours and there was still some puffiness of the face. Next day there was little change in the general glandular condition, but the spleen was now definitely palpable. As the urinary output remained very low and presuming that the risk of infection was slight, I advised his removal to a general hospital for further observation and on the 29th April he was admitted, as an acute haemorrhagic nephritis, to the Victoria Infirmary, under the care of Dr. Douglas Russell. On May 1st the general glandular enlargement was still present and on percussion over the upper end of the sternum and inner ends of the first and second interspaces on the right side, an impaired note was elicited, due probably, to enlargement of the mediastinal glands.

The/

The spleen was still palpable and the urine contained 9% Esbach, abundant deposit of red blood corpuscles, renal epithelial cells and epithelial casts.

Two days later the enlargement of the cervical glands was not so marked, but in the case of the axillary glands it was greater.

On May 5th the swelling of the glands was considerably less in all areas, the face was less puffy and the boy's general condition had greatly improved, but he was decidedly paler and had obviously lost weight.

The area of cardiac dulness was normal, but a soft systolic murmur was audible in the pulmonic area.

The following day he complained of headache and slight sore throat; the temperature which had been normal for two days rose to 103°F., the cervical glands were again enlarged and his general condition suggested a reinfection which was reflected in the blood picture by a sudden increase of the lymphocytosis.

On the 9th May he felt very much better, but the temperature was still rising to 101°F. or higher each day. The cervical glands were less swollen but the glands in the axillae and groin were more so; the glands in the left and to a less extent in the right iliac region were easily palpable and the tip of the spleen could still be felt. The skin, throughout the illness, had been very dry and scaly, especially on the neck, arms and legs; constipation had been very troublesome and the breath retained its unpleasant odour.

From now on, the glandular swelling gradually subsided until, on the 26th May, five weeks from the onset of the illness, the principal lymph nodes were just palpable.

No enlargement of the spleen could now be detected and the boy felt well. He was passing twenty-five ounces of urine daily, with no blood and but a slight haze of albumen, and was discharged from/

from hospital on the 27th May.

A month later, after a holiday at the coast, the boy looked and felt fit, but there was still a trace of albumen in the urine and a few groups of glands were still palpable.

Blood Examinations.

Date.	Hb.	C.I.	R.B.C.	W.B.C.	Polymorphs %	Large Lympho- cytes.%	Small Lympho- cytes %	Eosino- philes. %	Large Hyal- ine %	Mast Cells %	Mono- nucleat %
2.V.22.	74%	.74	5,050,000	10,600	61.75	12.75	23	1.25	1.25	-	35.75
5.V.22.	76%	.7	5,730,000	8,800	79	6.25	9.75	2.75	1.5	0.75	16
8.V.22	73%	.7	5,280,000	9,600	74.25	15	14	3	3.75	-	29
11.V.22	72%	.7	5,160,000	14,200	58	29	7	1	4.5	0.5	36
15.V.22	72%	.72	5,060,000	14,200	55	28	12.5	1.5	0.75	2.25	40.5
18.V.22	70%	.73	4,700,000	13,200	61	22.25	14.5	1.25	0.5	0.5	36.75
23.V.22	70%	.66	5,300,000	9,600	53.25	29.5	13	3.25	0.5	0.5	42.5

Bacteriology.

26.IV.22. On culture the urine yielded streptococci.

8.V.22. Throat swabs gave cultures of streptococci after 48 hours' growth.

3.V.22. Faeces gave cultures of streptococci analogous to those found in the urine.

Blood culture was not attempted in this case.

Case No.2.

This case occurred as a result of T.B's admission to hospital.

R.K.C., male, aged four years, occupied an adjoining cot and had been in the ward for over a month during which period his temperature was normal.

On May 4th, six days after T.B's admission, his temperature rose to 100°F., and two days later it was noticed that his cervical glands/

glands were swollen.

The rise in temperature was associated with drowsiness, loss of appetite, and extremely obstinate constipation, a large faecal mass being palpable in the iliac colon. On examination the throat was found to be congested, with inflammation and swelling of both tonsils and a day or two later he developed a muco-purulent nasal discharge.

On 17th May, the enlarged cervical glands formed a visible swelling in the neck, the enlargement being more marked on the left side. The enlarged glands were firm, elastic and discrete, and there was no redness or tenderness and no oedema of the surrounding tissues. Enlarged lymph nodes were also felt in both iliac fossae, more marked in the right where they attained to the size of walnuts and rolled easily under the fingers.

During the next four days, the glandular enlargement continued and the patient was so constipated that hard faecal matter was now palpable in the transverse and pelvic colons.

On the 21st May, the deep cervical glands anterior and posterior to the sterno-mastoid remained enlarged and the submaxillary group on either side were now affected. The axillary, groin and abdominal glands remained as before, and the epitrochlear glands were now palpable - all firm and discrete.

The salivary glands were not affected; there was no enlargement of the liver and the spleen was not palpable.

The boy lost flesh rapidly and his mucous membranes were much paler than they had been prior to the illness. The urinary output was not affected and the urine contained neither albumen nor blood.

A week later the glandular swelling began to subside and on May 29th., the lymph nodes were still easily palpable, but not obviously swollen. By May 30th, that is, rather more than three weeks from the onset, the boy was putting on weight and obviously very/

very much better. He was still pale, however, and the glandular enlargement remained and persisted until his dismissal from hospital on June 21st.

When seen twelve months later, the superficial lymph glands were all easily palpable.

Blood Examinations.

Date.	Hb.	C.I.	R.B.C.	W.B.C.	Poly-morphs. %	Small lympho-cytes. %	Large lympho-cytes. %	Eosino- philes. %	Large Hyaline. %	Mast Cells %	Mononu- clears. %
19.V.22	70%	.85	4,130,000	8,800	68.5	10.5	16.5	1.5	2.75	.25	27
22.V.22	70%	.77	4,560,000	9,200	63.25	9.25	24.5	0.5	2.5	-	34
25.V.22	70%	.68	5,620,000	6,400	34	35	27	3	1	-	62
29.V.22	72%	.85	4,290,000	9,200	48	16.5	31.5	1	3	-	48
2.VI.22	72%	.75	4,820,000	12,600	47.5	24	23.5	0.5	0.5	4	47.5
7.VI.22	-	-	4,880,000	15,200	67	18	14	0.5	0.5	-	32
13.VIII.22	70%	-	5,345,000	7,400	41.5	29.5	20	4	4.5	0.5	49.5

Bacteriology.

- 19.V.22. Blood cultures sterile.
 21.V.22. Throat-swabs - streptococci grown.
 21.V.22. Urine - streptococci grown on culture.
 21.V.22. Faeces yielded a streptococcus which had the same sugar reactions as that obtained from the urine.

Case No.3.

J.McL., male, aged 13 years, came under observation on February 2nd, 1924.

Previous health:- He had measles in childhood, enteric fever three years ago and acute rheumatism a year later when he was treated in the Victoria Infirmary.

On/

On the 28th January, 1924, while at school, he had an attack of vertigo accompanied by profuse sweating. The following day he had severe frontal headache and was confined to bed. On January 30th he complained of pain in the lower abdomen, and in the lumbar region. His throat felt "husky" and he noticed that he was passing less urine than usual and that it was blood red in colour. He had pain at the commencement of micturition and complained of a burning sensation in the urethra after voiding urine.

On February 2nd he had severe nausea but there was no vomiting. He was admitted to hospital that day and was found to be a well developed boy for his age, with high colour, some "puffiness" of the face, but no oedema of the feet or ankles. The deep cervical glands on both sides of the neck were enlarged and very slightly tender.

The axillary and groin glands were also enlarged, the biggest being about the size of a hazel nut. The glands were firm, discrete and slightly tender but there was no redness of the overlying skin. The teeth were good, the tongue pale and furred and the breath had an unpleasant odour. The tonsils were enlarged and the tonsillar crypts were very prominent but there was nothing suggestive of an acute tonsillitis. There was no enlargement of the liver or spleen throughout the illness and the temperature which was of the intermittent type did not rise above 100°F.

On February 20th he complained of pain in the abdomen and during the night he passed two loose, foul smelling stools which contained mucus and a little obvious blood. Prior to this the stools had been abnormally light in colour. On the 22nd February, the thyroid gland was noticeably swollen but the swelling was transient and at the end of three days no enlargement could be detected.

On March 25th he developed an ordinary acute follicular tonsillitis/

tonsillitis and the effect on his blood picture was striking.

On admission the urine contained a large quantity of blood, one part of albumen on the Esbach scale, epithelial and blood casts, and he was passing a very small quantity - four ounces - in the twenty four hours. By the end of a week he was passing fifty ounces daily with a mere trace of albumen, but the haematuria persisted for six weeks.

Examination of the lungs revealed nothing abnormal, but there was a systolic murmur at the mitral area which was present during the entire period of observation. That this was a result of his previous rheumatic infection (1921) was proved by a reference to his old hospital case sheet, and it was still present at the time of his discharge from hospital on the 9th April, 1924. When seen two years later he looked and felt well but there was still a trace of albumen in the urine and the superficial lymph glands were all easily palpable.

Blood Examinations.

Date.	Hb.	C.I.	R.B.C.	W.B.C.	Poly- morphs %	Large Lympho- cytes. %	Small lympho- cytes. %	Hyaline. %	Mast Cells. %	Eosinophiles. %
9.II.24.	.70%	.7	4,860,000	7,300	43	33	19	4	-	1
14.II.24.	.61%	.72	4,240,000	8,600	63.75	10.5	21.5	2.75	.75	.75

A few cells showed polychromatophilia and punctate basophilia.

9.II.24. Wassermann reaction negative.

Bacteriology.

14.II.24. Urine cultures sterile.
Gland cultures sterile.
Throat swabs: Staphylococci; streptococci and micrococcus catarrhalis.

Since the compilation of the foregoing, an epidemic presenting similar clinical features has occurred in Glasgow, (Spring, 1927) and it is interesting to note that one attack does not confer immunity, as three of the patients had suffered from the affection during the previous epidemic.

Further efforts are at present being made to identify the causal organism.

In conclusion I wish to express my indebtedness to Dr. Douglas W. Russell for access to the patients under his care; to Dr. John Anderson, Pathologist, Victoria Infirmary, and his assistant, Dr. Florence Kirk, for their kindly help with the bacteriological investigations.

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