GLANDULAR FEVER

REPORT OF AN EPIDEMIC IN THE CHILDREN'S WARD OF THE
UNION PROTESTANT INFIRMARY

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Glandular fever, an acute infectious disease principally affecting the cervical glands, was first described by Pfeiffer in 1889. Since that time various writers, West, Korsakoff, Gourichon, Terflinger and others, have reported epidemics and written extensively about it, but conclusions as to its etiology, the portal of entry of the organism causing the infection, the extent of the infection, and the complications arising therefrom are very diverse.

The cases reported in this article are nine in number. The first six occurred in children from 2½ to 5 years of age. The last three occurred in the family of Patient 6 after she had left the hospital, and, although not seen in the acute stage, are reported because the clinical history corresponded precisely to that in the cases observed. In this family epidemic only adults were affected. West reported an epidemic of 96 cases occurring in children and Terflinger one of 150 cases occurring in adults, thus showing that this disease, although considered one of childhood, may affect individuals at most any age.

The cases reported occurred in the months of February and March, and made their first appearance two months after the children's ward had been isolated on account of the measles, scarlet fever and diphtheria in the city. The first case began on February 15, the second on the 16th, the next two on the 17th, and the last two on the 18th.

The first case in the family of Patient 6 developed twenty-four hours after the child had reached home. Her mother was the first member of the family affected; none of the family had seen the child for two and a half months previously. From this one would conclude that the incubation period could be as short as twenty-four hours, although most writers think it from seven to nine days.

All the cases showed a leucocytosis from 18,800 to 26,400 during the disease. The variations in the differential count during the disease were as follows:

	Per Cent.
Polymorphonuclear leucocytes	37 to 74
Small mononuclears	20 to 50
Large mononuclears	2 to 11
Eosinophiles	0.5 to 5
Transitionals	1 to 7
Mast-cells	0.5

The small mononuclear elements of the blood seem to be the ones principally increased. The coexistence of tuberculous, gonorrheal and chickenpox infections in some of the cases makes the blood picture somewhat confusing.

Cases 1 and 2 showed a marked leucocytosis according to the absolute count, yet the differential counts were normal. These latter must have been due to an uneven distribution of leucocytes, for it seems very unusual to suppose that all the leucocytic elements of the blood could have been proportionately increased.

Leucocytes after convalescence varied from 5,000 to 8,000.

The variations in differential count after convalescence were as follows:

	Per Cent.
Polymorphonuclear leucocytes	13 to 54
Small mononuclears	30 to 70
Large mononuclears	2 to 14
Eosinophiles	1.4 to 13
Transitionals	1 to 6.5
Mast-cells	0.5 to 2.5

After convalescence there seems to be a still greater relative increase in the small mononuclear elements of the blood.

Throats and tonsils of all the patients were injected, but showed no exudate, and the cultures made showed *Staphylococcus aureus*.

CASE 1.—The patient, R. H., was sent in for treatment of paralysis of left leg due to anterior poliomyelitis. Swelling of glands of both sides of neck was first noted on February 15. At this time his temperature was 101.8, pulse 124. The patient complained of tenderness of cervical glands, stiffness of neck, thirst and loss of appetite. Enlargement of glands was not confined to the cervical group, of which the upper ones, anterior and posterior to the sternomastoid, were chiefly affected, but the axillary and inguinal groups were also enlarged, although to a much less extent. The cervical glands were the only ones tender, and this lasted only three days, after which the swelling began to decrease. No abdominal pain or tenderness present. The patient was constipated. Pharynx and tonsils injected, but no exudate present. Throat culture showed *Staphylococcus aureus*. On February 16 the white blood count was 26,400. The differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	74
Small mononuclears	22
Large mononuclears	2
Eosinophiles	0.5
Transitionals	1

On February 20 the differential count was:

	Per Cent.
Polymorphonuclear leucocytes	65
Small mononuclears	20
Large mononuclears	6
Eosinophiles	5
Transitionals	3

Urinary examination showed absolutely no signs of nephritis. The patient left the hospital March 9 before the swelling of glands had entirely disappeared.

CASE 2.—F. R., male, aged 2½ years, epileptic, had swelling of cervical glands of both sides first noted on February 16. On February 15 the temperature rose to 100.6 and on the 16th to 101.6 and then gradually declined.

On February 17 the patient's neck was painful and stiff. The soreness lasted one day. After this the glands began to decrease in size, but those on the left are still somewhat enlarged. Axillary and inguinal glands not involved. Pharynx and tonsils injected, the latter enlarged, but showed no exudate. Throat culture showed *Staphylococcus aureus*. No abdominal pain or tenderness. The patient is habitually constipated. There was loss of appetite.

On February 16 the white blood count was 22,100. The differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	63.5
Small mononuclears	30
Large mononuclears	2
Eosinophiles	1
Transitionals	2.5
Mast-cells	0.5

On February 20 the differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	66
Small mononuclears	25
Large mononuclears	5
Eosinophiles	1
Transitionals	2

The patient is still in the hospital and doing apparently as well as before the attack of glandular fever.

CASE 3.—E. McD., male, aged 3½, had Pott's disease (high dorsal); swelling of cervical glands of both sides first noticed on Feb. 17. Axillary and inguinal glands not involved. No rise of temperature. Swelling and tenderness of glands, and stiffness of neck lasted until February 20, after which time the tenderness and stiffness disappeared, and the swelling gradually decreased. The patient held his hands to his ears as if suffering with earache. No abdominal pain nor tenderness. The patient was not constipated; had no sore throat. He had loss of appetite; has had swelling of glands of neck three times previously.

On February 20 the red blood count was 4,200,000; white blood count, 21,800; differential count, as follows:

	Per Cent.
Polymorphonuclear leucocytes	44
Small mononuclears	43
Large mononuclears	6
Eosinophiles	3
Transitionals	3
Mast-cells	0.5

On March 27 the leucocyte count was about 6,500; the differential count, as follows:

	Per Cent.
Polymorphonuclear leucocytes	44
Small mononuclears	49
Large mononuclears	5.3
Eosinophiles	1.4

The patient is still in hospital and general condition seems about the same as before he had glandular fever.

CASE 4.—P. K., male, aged 5, had tuberculosis of hip (left) and lumbar kyphosis; swelling of cervical glands of both sides first seen on February 17. Axillary and inguinal groups not involved. No tenderness of cervical glands. Some stiffness of neck. Swelling increased until February 20 and then began to subside. On February 17 the temperature rose to 100 and on the 21st to 100.1. It then gradually fell to normal. The pulse showed no peculiarities. No abdominal pain nor tenderness. Pharynx and tonsils somewhat injected but patient complained of no sore throat. No exudate present. Throat culture showed *Staphylococcus aureus*. The patient was not constipated.

On February 20 the differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	48
Small mononuclears	38
Large mononuclears	9.5
Eosinophiles	3
Transitionals	3.3

On March 27 the leucocytes were about 5,000; the differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	27
Small mononuclears	49
Large mononuclears	6.8
Eosinophiles	13
Mast-cells	2.5
Transitionals	1

The patient is doing well. Cervical glands still somewhat enlarged.

CASE 5.—M. H., female, aged 5, had tuberculosis of hip (left) and chickenpox; bilateral swelling of cervical glands first noted on February 18; no other glandular involvement. On this day the temperature rose to 100.8, pulse to 120. The temperature gradually fell to normal by February 23, by which time the tenderness of glands and stiffness of neck had disappeared, and swelling of glands was beginning to decrease. The patient complained of earache. Pharynx and tonsils injected, but no exudate present. Throat culture showed *Staphylococcus aureus*. The patient lost her appetite and was constipated. No abdominal pain or tenderness.

On February 20 the white blood count was 18,800; the differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	37
Small mononuclears	50
Large mononuclears	10
Eosinophiles	2.2
Transitionals	2

On March 27 absolute leucocyte count was about 5,000; the differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	27
Small mononuclears	59
Large mononuclears	6
Eosinophiles	2.5
Mast-cells	0.5
Transitionals	4

The patient is doing well. She has entirely recovered from both her chickenpox and glandular fever without any ill effects.

CASE 6.—N. S., female, aged 3, had gonorrheal arthritis of hip (left). On December 29 patient developed tonsillitis; on January 27 left tympanic membrane ruptured due to purulent otitis media; on January 30 patient first showed signs of chickenpox, and on February 18 swelling of cervical glands (left side) was first noted. On February 19 the patient's temperature rose to 101.6, pulse to 144. Cervical glands were tender and neck stiff. Axillary and inguinal glands also somewhat enlarged. By February 23 tenderness of glands had disappeared and swelling was beginning to decrease. At onset pharynx and tonsils were injected. Latter were also enlarged. Throat culture showed *Staphylococcus aureus*. There was no abdominal pain or tenderness. Bowels were regular. On February 20 the differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	42
Small mononuclears	40
Large mononuclears	11
Transitionals	7
Mast-cells	0.5

Patient left the hospital on February 28 with cervical glands still somewhat enlarged.

On March 23 I was told by Dr. W. S. Baer, orthopedist to the Johns Hopkins Hospital, that he had heard that several members of the family of Patient 6, who is a patient of his, had glandular fever. Through the kindness of their family physician, Dr. William T. Watson, I was permitted to see them. On arriving at their home I found that three members of the family had had what clinically seemed to be glandular fever. The last patient had recovered two days previously, but all showed some enlargement of the cervical glands still. Throat cultures and blood smears were taken from all three and from Patient 6. Culture from the latter showed *Staphylococcus aureus* as before, and differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	13
Small mononuclear leucocytes	70
Large mononuclear leucocytes	14
Eosinophiles	0.5
Transitionals	3

The leucocyte count was about 7,500; and the cervical glands were still slightly enlarged.

CASE 7.—The patient, the mother of Patient 6, aged 25, was apparently a healthy woman; she had not seen her daughter for two and a half months and had been perfectly well until the latter's return home on February 28.

On the evening of March 1 the patient says she felt tired and ached all over, and on the morning of March 2 both sides of her neck were swollen and painful. Her neck was stiff, throat very sore; she had a headache, and ached all over. She

was very thirsty, had no appetite, and was constipated. The neck was swollen and painful for one week, after which time it began to subside. At the onset the patient was nauseated and vomited. No abdominal pain nor tenderness.

On March 23 leucocytes were about 5,000; the differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	49
Small mononuclears	34
Large mononuclears	4
Eosinophiles	4
Transitionals	6.5
Mast-cells	0.5

Throat cultures showed *Staphylococcus aureus*. Glands of neck still somewhat enlarged.

CASE 8.—The patient, grandmother of Patient 6, aged 50, apparently healthy, on March 13 had headache, ached all over, and had chills. At the same time both sides of neck began to swell and become painful. The neck was stiff and throat very sore. The patient was very thirsty, had no appetite, and was constipated. Swelling and tenderness of glands of neck lasted about one week, after which time it subsided. No abdominal pain or tenderness.

On March 23 the leucocyte count was about 7,500; the differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	49
Small mononuclears	41
Large mononuclears	2
Eosinophiles	3.5
Transitionals	4.5

A throat culture showed *Staphylococcus aureus*. Glands of neck still somewhat enlarged.

CASE 9.—Patient, maternal uncle of Patient 6, aged 20. General health good. Bilateral swelling of neck first noticed on March 15. At this time patient had a headache and a feeling of general malaise. The neck was stiff and throat very sore. The patient was thirsty, lost his appetite and was constipated. Swelling and tenderness of neck lasted about one week. No abdominal pain or tenderness.

On March 23 the leucocytes were about 5,000; the differential count was as follows:

	Per Cent.
Polymorphonuclear leucocytes	54
Small mononuclears	30
Large mononuclears	12
Eosinophiles	2
Transitionals	3

Throat culture showed *Staphylococcus aureus*. Axillary and inguinal, as well as cervical glands, still somewhat enlarged.

In the first six cases the enlargement of the cervical glands occurred at the same time on both sides, with the exception of Case 6, and in the last three cases there was a history of simultaneous enlargement of the glands of both sides of the neck. In only one instance, that of Case 6, was there a unilateral involvement. The swelling of the glands seemed to increase on both sides at the same rate, and with the tenderness seemed

to reach a maximum on the third day, after which time the tenderness disappeared and the swelling began to decrease gradually. The upper glands of the chains anterior and posterior to the sternomastoid muscle were the ones chiefly swollen and tender. All the glands involved were hard and discrete. Stiffness of the neck seemed to disappear with the tenderness of the glands and was due most probably to the latter symptom. The axillary and inguinal group were slightly enlarged and hard in two of the cases. None of the cases showed any signs or gave any history of the occurrence of suppuration of the involved glands.

The only definite period of incubation that could be determined with any certainty was that of Case 7, for both the patients in the ward and those on the outside may have become infected at the same time from the same source, or later from other patients. Yet, on account of the varying degrees of individual resistance, the period of incubation would vary greatly. Patient 7 had not seen her child (Patient 6) for two and a half months previously, nor could she remember having been near any one suffering with this disease until she took her child home. This incubation period of twenty-four hours is, as far as I have been able to ascertain, the shortest one recorded.

In all the cases observed there was injection of the pharynx and tonsils, but no exudate was present, and all the outside cases gave a history of an intense pharyngitis. This would seem to indicate the probable location of the portal of entry of the organism causing the infection and the finding of *Staphylococcus aureus* in all the throat cultures might mean that this was the etiologic factor. The chief objection to this latter assumption is that in pyogenic infections the blood usually shows an increase in the polymorphonuclear leucocytes, whereas in this infection, as has been shown above, there is an increase in the small mononuclear elements, both during and after the disease. Cases have been reported in which suppuration occurred and its non-appearance in our cases could not be used as an argument against the pyogenic theory of infection.

A feeling of general malaise with, in some cases, a slight rise of temperature on the day preceding the enlargement of the cervical glands were the first symptoms noted. Later stiffness of the neck, swelling and tenderness of the cervical glands, thirst, loss of appetite, and constipation were the most constant symptoms. Patient 8 had chills at the onset. Nausea and vomiting occurred at onset in Case 7, and this, excepting the constipation which occurred in nearly all the cases, was the only symptom indicating that possibly the disease might be due to an autointoxication from the intestinal tract, as has been thought to be

the case by some writers. None of the patients had any abdominal pain or tenderness.

The pulse showed nothing beyond an increase in rate in some of the cases, the volume tension, force and rhythm being unchanged. The temperature varied from 101.8 F. to normal at the onset, and in cases of a rise fell by lysis. In the case of the tuberculous patients whose temperature curve was not normal the superadded infection made very little, if any, change.

The urine was examined where it was possible and showed absolutely no signs of nephritis, either during or after the disease; in fact, no change in its condition from what it had been previous to the infection was noted.

NOTE.—The following articles may be found of interest on this subject:

Gourichon: Thèse de Paris, 1895.

Arch. Pediat., 1896, xiii, 889.

Jahrb. f. Kinderh., 1889, xxiv, 257.

Arch. f. Kinderh., 1905, xli and xlii.

Ztschr. f. klin. Med., 1907, lxii, 170-178.

Monchau-Beuchant: Pédiatrie prat., 1908, vi, 223-227.

Kühner: Kinder. Arzt, 1908, xix, 121-125.

Werner: Tidsskr. f. d. norske Lægefor., 1908, xxviii, 345-349.

Crane: Ohio Med. Jour., 1908, iv, 143-149.

Terflinger, F. W.: Epidemic of glandular fever. Jour. Am. Med. Assn., 1908, i, 765.

Jones: Amer. Jour. Med. Sc., 1908, new series, cxxxv, 346-351.