volumes of glacial acetic acid and 10-volume hydrogen peroxide (acid peroxide reagent), which keeps for three months. Wash a white porcelain "spot-test" tile with cavities, rinse with 95% spirit, and allow to dry. Do not dry with a cloth, for fragments of fibre may give false positives. Place a "small knife-point"—about 3 mg. or the volume of a grain of rice—of *o*-tolidine hydrochloride in a cavity; add one drop of urine. Stir with a clean glass rod and add one drop of "acid peroxide." A positive reaction appears as a blue coloration, or spreading blue-green streaks which fade after 5–30 minutes to brown. A negative reaction is pale brown.

Results

The results are shown in the Table. Column A gives the number of cells per ml. which can be detected by the techniques described; column B the corresponding concentration of haemoglobin in mg. per 100 ml. of urine;

Method	A	B	C	D
Microscopical*	5×10^3	0.015	100	Nil
<i>o</i> -Tolidine	5×10^4	0.15	10	Nil
Benzidine	5×10^5	1.5	1	4
Kastle-Meyer	5×10^5	1.5	1	Nil
Amidopyrine	10^6	3.0	0.5	2.5
Guaiac	2.5×10^6	7.0	0.2	5
Spectroscopy*	2.5×10^6	7.0	0.2	Nil

* The sensitivity of both these methods can be increased at least fivefold, as described above under "Technique."

column C the relative sensitivities as percentages of that of the centrifuged deposit; and column D the inhibition caused by ascorbic acid (lowest positive concentration without ascorbic acid divided by lowest positive concentration with ascorbic acid).

Technical Difficulties

In the presence of pus all these tests give false positives, which are prevented by boiling the urine; but this treatment reduces sensitivity at least tenfold. All except the Kastle-Meyer give false positives with iodides, and the *o*-tolidine with bromides.

Guaiac.—The tincture of guaiacum resin must be made up weekly, for its sensitivity diminishes on keeping. Some workers prepare an approximately 2% alcoholic solution of the resin at the time of testing. The tubes used are difficult to clean, and if not quite clean give false positives.

Amidopyrine.—The reagent is stable. Tubes are easy to clean and few false positives develop.

Kastle-Meyer, or Reduced Phenolphthalein.—The reagent is troublesome to prepare, but can be bought from B.D.H. at a cost of less than 1d. a test. It deteriorates little on keeping if a little zinc dust is added, but such solutions may require filtration through a hardened filter paper (Whatman 5, 50, or 54) before use. False positives are few. Ascorbic acid does not reduce the sensitivity.

Benzidine.—The reagent must be made up at the time of use from benzidine, glacial acetic acid, and hydrogen peroxide. False positives occur even when tubes appear to be clean. Ascorbic acid reduces the sensitivity about four times.

Orthotolidine Hydrochloride.—The reagents are stable for at least three months. The test is the most sensitive of all and gives few false positives. Ascorbic acid in the concentration used did not reduce the sensitivity.

Conclusion

No single test can be ideal under all conditions. Microscopy of the centrifugal deposit is at least 500 times more sensitive than the guaiac test, and if the Addis procedure be used the ratio reaches 2,500.

For domiciliary work, and as a ward test, the *o*-tolidine hydrochloride test is convenient, very sensitive, and cheap. The porcelain plate can be replaced by a cavity slide 3 by 1 in. (7.5 by 2.5 cm.) to make it more portable. Although in our hands it is much less sensitive for detecting red cells than was claimed by Zwarenstein, it is still ten times more sensitive than any other chemical test, and rarely gives false positives.

The other tests are much less sensitive. The Kastle-Meyer test is very reliable, but the caustic nature of the reagent makes it unsuitable for domiciliary practice. The guaiac test is expensive, insensitive, and not very reliable; it should be abandoned. Should a test of comparable sensitivity be needed, the amidopyrine test is suitable.

In the laboratory it is preferable to examine a centrifuged deposit. If information on the degree and persistence of haematuria alone is needed, then it is justifiable to examine a 1 in. (2.5 cm.) layer of urine with the hand spectroscope; if positive, haemoglobin equivalent to about 2,500,000 red cells per ml. is present; and if negative, then the deposit from 12.5 ml. of urine should be suspended in 0.5 ml. and examined in a Fuchs-Rosenthal chamber.

REFERENCES

- Barach, J. H., and Pennock, L. L. (1943). *J. Amer. med. Ass.*, **114**, 640.
 Harrison, G. A. (1947). *Chemical Methods in Clinical Medicine*, 3rd ed. Churchill, London.
 Kohn, R., and Watrous, R. M. (1938). *J. biol. Chem.*, **124**, 163.
 Zwarenstein, H. (1949). *J. clin. Path.*, **2**, 145.

GLANDULAR FEVER WITH NEUROLOGICAL COMPLICATIONS

BY

J. S. CROWTHER, M.D., M.R.C.P.

Senior Medical Registrar, Chase Farm Hospital,
Enfield, Middlesex

Epstein and Dameshek (1931) are usually credited with the first description of involvement of the central nervous system in glandular fever (infectious mononucleosis), though Longcope (1922) and Glanzmann (1930) had suspected the association.

I have been able to find only 24 cases of glandular fever, confirmed by a positive Paul-Bunnell test and involving the nervous system, in the literature since 1931 (Sucher and Schwarz, 1936; Gsell, 1937; Pietzonka, 1939; Thomsen and Vimtrup, 1939; Marshall, 1939; Thelander and Shaw, 1941; Landes *et al.*, 1941; Richardson, 1942; Zohman and Silverman, 1942; Hiller and Fox, 1943; Coogan *et al.*, 1945; Ricker *et al.*, 1947; Field, 1948; Bercel, 1948). However, several cases of neurological involvement in clinical glandular fever with a suggestive blood picture but without a positive Paul-Bunnell test have been reported, the most recent being that by Kløvstad (1950); and several cases of proved glandular fever without clinical involvement of

the nervous system have been found to have abnormal cerebrospinal fluids, notably those of Schmidt and Nyfeldt (1938) and Huber (1938). Of the above 24 cases only four had pure encephalitis, the others showing encephalomeningitis, meningitis, cranial nerve lesions, or peripheral nerve lesions. Several of the cases had a radiculo-neuritis of the Guillain-Barré type with raised protein but normal cells in the C.S.F.

The following case of encephalitis in glandular fever is presented because of its rarity.

Case Report

A draughtsman aged 20 had a mild sore throat with pyrexia to 99.6° F. (37.6° C.) for two days and then returned to work although feeling weak. Two days later he had nausea, and next day vomited undigested food. Anorexia, nausea, and occasional slight vomiting of food and bile continued daily until admission to hospital 12 days after the onset. The day before admission he complained of dizziness on sitting up, but not of double vision, and at no time was there pain or headache; he was afebrile after the first two days. There was nothing relevant in either his past or his family history.

On admission to hospital he was afebrile, alert, and co-operative, though preferring to lie on his back with only one pillow, as movement caused dizziness, nausea, and sometimes vomiting. The pulse rate was 76. The only abnormal physical signs were slight injection of the fauces, pea-like glands bilaterally in his neck and axillae, and a doubtfully palpable spleen. Although glandular fever was strongly suspected on clinical grounds, and a blood count and Paul-Bunnell test were requested, a lumbar puncture was also performed. The C.S.F. showed: pressure, 80 mm.; clear; no block; protein, 15 mg. per 100 ml.; Pandy, negative; cells, *nil*; W.R., negative.

Other tests were:—Blood count: white cells, 5,300 (polymorphs 45%, eosinophils 6%, lymphocytes 46%). Sedimentation rate, 7 mm. in one hour. Paul-Bunnell test, positive to 1 in 12,800 after guinea-pig kidney absorption and 1 in 3,200 after ox cell absorption. Blood W.R. negative. Liver-function tests: Van den Bergh direct, delayed positive; indirect, 0.7 mg.; thymol turbidity, 6; alkaline phosphatase, 8; cephalin-flocculation test, ++++. Plasma proteins: albumin, 4.8%; globulin, 2.5%.

Progress

The spleen became easily palpable two days after admission. Anorexia, nausea, and sporadic vomiting continued for a further 10 days in spite of varied symptomatic treatment, while dizziness was provoked on the slightest attempt to sit up. Sixteen days after admission, and 30 days after the onset of the sore throat, he was noticed to be drowsy and confused, his speech was slurred, and on questioning he complained of severe frontal headache and double vision since the previous day. He also had some difficulty in initiating micturition. He was apathetic and still afebrile. The glands and spleen were still palpable. There was a suggestion of bilateral ptosis; the pupils reacted to light and accommodation but hippus was present, and the fundi were within normal limits. Ocular movements showed limitation laterally, left more than right, with nystagmoid jerks, and gross limitation of upward movement with definite nystagmus. There was diplopia on looking laterally. Other cranial nerves were normal. Neck rigidity was not present. The arms were normal. Abdominal reflexes were absent. Knee- and ankle-jerks were very brisk but equal; ankle clonus was present, but Kernig's sign was negative. There was no response to plantar stimulation.

A diagnosis of glandular fever with encephalitis seemed justified. The following investigations were done:—C.S.F.: clear; pressure, 80 mm.; protein, 15 mg. per 100 ml.; Pandy, negative; cells, less than 1; chlorides, 730 mg. per

100 ml.; glucose, 61 mg. per 100 ml. Paul-Bunnell test with C.S.F. negative. Lange curve, no change. The W.B.C. numbered 5,800, with 55% lymphocytes, many atypical.

The following day his condition appeared worse, he was stuporous, and in his confusion during the night he attempted to get out of bed and fell, but without sustaining any injury. Chloramphenicol was begun because of favourable reports by Hirsch (1949) and by Lewis (1949) on its use in uncomplicated cases. He was given 3 g. daily in four divided doses for two days, followed by 2 g. daily for a further eight days, a total of 22 g. After two days the patient was definitely less drowsy, and able to take a light diet. The physical findings were unchanged, except that the plantar responses were possibly extensor.

A week later he had some dizziness and frontal discomfort on moving his head or eyes quickly, his diplopia was slight and only on looking to the extreme right. The ocular movements were full, and without nystagmus. His speech was normal, abdominal reflexes were present, lower limb reflexes were still brisk, but ankle clonus had vanished. Plantar reflexes were not obtained. The cervical glands were subsiding; the spleen was impalpable. Ten days after this his only complaint was of easy fatigue and lack of concentration—for example, when playing cards or reading. Physical examination was negative, the plantar reflexes both being flexor and the C.S.F. normal. He was discharged for convalescence after 11 weeks in hospital. During this time repeated blood counts never showed haemoglobin below 100% or W.B.C. more than 6,500 per c.mm., with a persistent lymphocytosis of 46 to 65% and even 53% on the day of discharge. Liver-function tests a week before discharge still showed thymol turbidity 4, but plasma globulin had diminished to 1.9 g.% and the cephalin-flocculation test was now only doubtfully positive.

He was seen as an out-patient two months after discharge. Apart from tiring easily, he had no symptoms or signs. W.B.C. numbered 6,400 per c.mm., 52% lymphocytes (none reported as abnormal). The Paul-Bunnell test was still positive; unabsorbed serum was 1 in 40, after guinea-pig kidney absorption 1 in 320; after ox-cell absorption there was no agglutination.

Discussion

This case appears unusual in several respects. At no time after admission to hospital was the patient febrile. It is well known that glandular fever can show afebrile periods, but in the cases reported with nervous complications a raised temperature was present at some time.

Another surprising feature, considering how severely ill the patient was and with such marked neurological signs, was the continued normality of the C.S.F., which was tested once before the onset of definite clinical neurological involvement three times during and once after all neurological signs and symptoms had subsided. Bercel (1948) states that some cases may be missed if the symptoms are slight, as the C.S.F. changes occur late, and this may account for several cases being reported with normal fluid. Among the other reported cases all combinations of raised cells and/or protein were found.

I have been able to trace only four fatal cases (Thomson and Vimtrup, 1939; Ricker *et al.*, 1947), all the others having made complete recoveries without any specific treatment; and indeed Tidy (1948) has pointed out that improvement in neurological cases begins within a few days of the patient's lowest ebb. Nevertheless, this patient appeared so desperately ill at one stage that it was decided to use chloramphenicol. Of the two reported cases treated with chloramphenicol, one, that of a child who responded clinically within 24 hours of beginning the drug, was given the drug for three days

only, but she relapsed a week later. She again responded promptly when again given the drug, and this was continued for one week without further relapse. The other case, of seven months' duration, responded promptly, and had not relapsed three months after discontinuance of the drug. Although most cases of glandular fever are relatively benign and require only symptomatic treatment, some severe ones often leave behind a state of depression and debility which may predispose to more serious illness (indeed, I have seen two cases which within a few weeks returned with a tuberculous pleural effusion), and in these cases if chloramphenicol is likely to shorten the illness it may be worth a trial.

Summary

A case of glandular fever with encephalitis is reported. The Paul-Bunnell test was positive, and the blood showed typical cell changes.

In spite of the clinical encephalitis, the cerebrospinal fluid was normal on the five occasions it was tested.

Chloramphenicol was used in treatment: its use in glandular fever is discussed.

I wish to thank Dr. C. Allan Birch, into whose ward this patient was admitted, for his interest and help in the preparation of this article.

REFERENCES

- Bercel, N. A. (1948). *J. nerv. ment. Dis.*, **107**, 537.
 Coogan, T. J., Martinson, D. L., and Mathews, W. H. (1945). *Illinois med. J.*, **87**, 296.
 Epstein, S. H., and Dameshek, W. (1931). *New Engl. med. J.*, **205**, 1238.
 Field, W. W. (1948). *Amer. J. Med.*, **4**, 154.
 Glanzmann, E. (1930). *Das lymphomaeide Drüsenfieber*. Karger, Berlin.
 Gsell, O. (1937). *Dtsch. med. Wschr.*, **63**, 1759.
 Hiller, R. I., and Fox, M. J. (1943). *Marquette med. Rev.*, **7**, 152.
 Hirsch, F. G. (1949). *Nav. med. Bull., Wash.*, **49**, 1081.
 Huber, W. (1938). *Schweiz. med. Wschr.*, **68**, 892.
 Kløvstad, O. (1950). *Acta med. scand.*, **139**, 67.
 Landes, R., Reich, J. P., and Perlow, S. (1941). *J. Amer. med. Ass.*, **116**, 2482.
 Lewis, P. L. (1949). *J. Pediat.*, **35**, 630.
 Longcope, W. T. (1922). *Amer. J. med. Sci.*, **164**, 781.
 Marshall, E. A. (1939). *Amer. J. clin. Path.*, **9**, 298.
 Pietzonka, H. (1939). *Dtsch. Arch. klin. Med.*, **185**, 153.
 Richardson, J. S. (1942). *Lancet*, **1**, 618.
 Ricker, W., Blumberg, A., Peters, C. H., and Wideman, A. (1947). *Blood*, **2**, 217.
 Schmidt, V., and Nyfeldt, A. (1938). *Acta oto-laryng.*, **26**, 680.
 Sucher, A., and Schwarz, E. (1936). *Wien. klin. Wschr.*, **49**, 1417.
 Thelander, H. E., and Shaw, E. B. (1941). *Amer. J. Dis. Child.*, **61**, 1131.
 Thomsen, S., and Vimtrup, B. (1939). *Nord. Med.*, **4**, 3295.
 Tidy, Sir H. (1948). *Blood*, **3**, 823.
 Zohman, B. L., and Silverman, E. G. (1942). *Ann. intern. Med.*, **16**, 1233.

Korea is a highly malarious country with much of the population infected with the disease. In addition, the work of combating the anopheles mosquito has been complicated both by the innumerable breeding grounds provided in rice paddies and by the frequently harassing tactical situation. However, with the use of chloroquine, which became available throughout the entire combat area late in the summer of 1950, the incidence of malaria in Korea has been kept low compared with the second world war rates. Chloroquine is an excellent suppressant; but, like mepacrine and quinine, it is neither a preventive nor a complete cure for malaria. It was developed by the Germans in 1939 as a relative of pamaquin. Recently the U.S. Army Medical Service has concentrated much of its research on a new drug, primaquine, which appears particularly effective against the tissue phase of the disease because it attacks the stubborn parasites in the liver cells. This is chemically another close relative of pamaquin, merely differing in having a primary amine instead of a tertiary amine at the end of its side chain. A preliminary report appeared in the *Journal of the National Malaria Society*, 1950, **9**, 285.

TENOSYNOVITIS OF THE WRIST

BY

MAURICE ELLIS, F.R.C.S.

(From the General Infirmary, Leeds)

Gray's *Anatomy* (1949) describes this disease in the following words: "The tendons of the abductor pollicis longus and the extensors of the thumb are liable to become strained and their sheaths inflamed (tenosynovitis) after excessive exercise, producing a sausage-shaped swelling along the course of the tendons." In three standard textbooks of surgery, tenosynovitis is described similarly as a disease of these three muscles of the thumb. One of them amplifies this description by stating that it is a disease of the "tendon sheath of the extensor ossis metacarpi pollicis (abductor pollicis longus) and of the extensores longus and brevis pollicis . . . and as the sheath surrounds not only the tendons but, as can be anatomically demonstrated, also extends some way up around the muscle bellies, movements of the affected parts are painful" (Romanis and Mitchiner, 1948).

Examination of 44 cases since the beginning of 1949 has made me very dissatisfied with this anatomical description. The disease as met with in the casualty department of the General Infirmary, Leeds, presented the following anatomical features. A sausage-shaped swelling was present on the radial side of the lower part of the dorsal surface of the forearm. This swelling was always about 1½ in. (3.8 cm.) long, and appeared to be slightly oblique to the long axis of the forearm. The lower limit of this swelling never extended distally beyond a point about 2 in. (5 cm.) from the lower articular margin of the radius. Thus, even allowing for a tendon sheath extending around the muscle bellies as described by Romanis and Mitchiner, the swelling seemed to be too high in the forearm to have any connexion with the extensors and long abductor of the thumb.

To investigate this point, therefore, a number of dissections were made on the lower forearm in the post-mortem room. My dissections all showed conclusively that the muscle bellies and tendons of the three dorsal muscles of the thumb crossed obliquely over the radius in its lower 2 in., and thus were unlikely to have any connexion with the swelling of tenosynovitis as seen clinically. Injections of water into the sheaths surrounding the tendons of these muscles did confirm the description given by Romanis and Mitchiner of the tendon sheath continuing up over the bellies of the muscles of the thumb, but the swelling produced by this distension of the sheath did not in the least resemble the shape of the swelling seen clinically, and was situated too near the wrist to correspond with the site of the swelling seen clinically. Dissections further up the forearm show that, immediately proximal to the muscles of the thumb, the tendons of the extensores carpi radialis longus and brevis are lying subcutaneously and that these tendons pass deep to the muscles of the thumb as they proceed distally to their insertion. These tendons emerge from their appropriate muscle bellies at a point about 1½ in. proximal to the upper border of the muscles of the thumb. Injections of water into the areolar tissue surrounding these tendons always produced a sausage-shaped swelling exactly similar to that seen clinically in tenosynovitis. The apparent obliquity of the swelling is shown to be produced by the oblique passage of the muscles of the thumb over the tendons. If the muscles of the thumb