with various outlooks and experimental accomplishments, and, in particular, that little progress can be made without first-class biochemical work. The other important point is that steady and rapid progress is possible in the clinic only when the clinician has firmly based experimental foundations on which to work. It is easy to exaggerate the importance of antiseptic drugs in surgery, and I have indeed noticed signs of restiveness among surgeons when misguided people have wished to attribute all their success in dealing with septic conditions to penicillin. I have always maintained that the introduction of such drugs demands better, not worse, surgery, and a better understanding of inflammatory processes. And it is, I think, quite clear that penicillin and substances like it will only be used with maximum effect if surgeons have a real appreciation of the properties of the drugs—not only what they can do, but also what they cannot do and the reasons for their limitations.

Perhaps I may close with some words of Lister's written in 1867: "And I may take this opportunity of warning some of your readers that they must not expect carbolic acid to act like a charm; but that, whether they employ this agent or some other of analogous properties, it is only by the light of sound pathology, and strict attention to practical details, that they can hope to attain in their full measure the magnificent results which the antiseptic treatment is capable of affording."

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NEUROLOGICAL COMPLICATIONS OF
INFECTIVE HEPATITIS

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Cerebral changes in fatal cases of infective hepatitis have often been recorded. They have usually taken the form of coma, delirium, convulsions, and incontinence—symptoms which are common to the clinical picture of acute hepatic necrosis of any origin. Other neurological findings are, however, less well recognized, and it is the purpose of this paper to discuss various signs observed independently in cases of infective hepatitis by four persons in different parts of Assam and Bengal during 1944.

The neurological findings have been protean, but it is possible to dissect out four main groups. First, the picture commonly found in the fatal case, which is too familiar to need detailed description. Secondly, a symptom-complex comprising generalized or localized muscular rigidity with increased tendon-jerks, sometimes but not invariably associated with extensor plantar responses; in addition choreiform movements have been observed, and in one case a Parkinsonian tremor. Thirdly, a group of cases with large focal haemorrhages into nervous tissue, which may or may not produce localizing signs. Fourthly, those cases showing signs of peripheral neuritis for whose direct relation to the onset of infective hepatitis there is good evidence.

The Common Type

This group may be illustrated by a "type" case:

S., aged 28, developed anorexia, followed by jaundice and bile-stained urine, on Dec. 19, 1944. He remained deeply jaundiced, and on Jan. 3, 1945, became drowsy and apathetic. The liver dullness was diminished, but there were no objective signs in the nervous system. On Jan. 4 he became alternately stuporous and maniacal. The urine contained no leucine or tyrosine crystals, and the cerebrospinal fluid, under a pressure of 100 mm., contained 60 mg. of protein per 100 c.cm. He died on Jan. 5. Necropsy showed characteristic changes of acute hepatic necrosis in a liver that weighed 750 g. The only demonstrable change in the brain was that of congestion of small vessels in the white matter.

There is nothing unusual about this case, but it illustrates well the short time that often elapses between the first onset of mental change and death. A histogram of this interval in 14 cases is shown in the accompanying figure.

Interval between onset of mental changes and death in 14 fatal cases of infective hepatitis

Some degree of mental depression is very common in infective hepatitis. Any increase in this depression or any behaviour change should be treated as a danger sign and as an indication for such protective therapy as is available.

The Striatal and Pyramidal Group

Nine cases have been observed in this group. The distribution of the relevant physical signs is shown in the accompanying Table. The following are brief histories of Cases 4 and 6.

Case 4.—A British private aged 30 was admitted on May 25, 1944, complaining of anorexia and dark urine for two weeks and jaundice for 10 days. On examination he was afebrile and deeply jaundiced.

The liver was palpable and tender. Otherwise there were no abnormal signs. There was bile in the urine, and a diagnosis of infective hepatitis was made. There was normal progress up to May 31, when the jaundice was barely discernible, except that he had been found sleep-walking on the nights of May 29 and 30. He was not, so far as he knew, in the habit of sleep-walking. On May 31 he was drowsy all day, but took food and answered when spoken to. In the evening he became distant and unapproachable, and the same night was incontinent of urine. Examination revealed slight spasticity of both arms. On June 1 he was in coma. There was deep jaundice and the liver was still palpable. Both arms were spastic, adducted, and pronated. Both legs were spastic, adducted,

Distribution of Striatal and Pyramidal Signs in 9 Cases of Infective Hepatitis

Case No.	Muscular Rigidity	Increased Jerks and Clonus	Involuntary Movements	Extensor Plantar Responses	Outcome
1	+	—	—	—	Death
2	—	+	—	—	"
3	—	+	— *	—	"
4	+	+	— *	—	"
5	+	+	— †	—	"
6	+	+	—	+	"
7	—	+	—	—	Recovery
8	+	+	—	+	"
9	+	+	—	—	Death

* Frank choreiform movements. † Parkinsonian tremor of hands.

and extended. Plantar responses were flexor. All tendon-jerks were very brisk and there was sustained left ankle clonus. The pupils were not dilated and gave normal reactions; corneal reflexes were absent; fundi were normal. During the day these physical signs remained unchanged, but there appeared in addition choreiform movements of both arms, more marked on the right side, and purpuric spots on both upper arms. He died early on June 2 with more purpura on the right hand and a sharp terminal rise of temperature. Lumbar puncture revealed no abnormality. A white blood count showed a slight polymorph leucocytosis. There were no malaria parasites in repeated blood slides. There was no albuminuria.

At necropsy there were numerous subpleural, subpericardial, and mesenteric petechial haemorrhages. The liver was not diminished in size; it had a red-and-yellow blotchy appearance and the architecture was clearly destroyed in patches. The brain showed no macroscopic abnormality, there were no malaria parasites in brain smears; and there was no bile staining of brain tissue.

Histology.—Liver:—Marked degeneration of the parenchyma with a moderate amount of fibrosis and cellular reaction. Proliferation of bile ducts and formation of new parenchyma very pronounced. Evidence of degeneration even in newly formed epithelial cells. Brain:—Generalized oedema of white matter. No perivascular cuffing or general increase in cells. No cellular degeneration. Virchow-Robin spaces widely separated from the vessels. A small extravasation of red cells into the brain tissue from one vessel in the midbrain.

Case 6.—A British N.C.O. aged 24 was admitted on Sept. 16, 1944, complaining of anorexia for five days and dark urine for three days. On examination he was moderately jaundiced and there was bile in the urine. There were no other abnormal signs. Infective hepatitis was diagnosed. On Sept. 19 he became drowsy yet restless. Jaundice was more intense and the liver dullness was diminished. There were no abnormal signs in the nervous system. Later in the day he became delirious. On Sept. 20 he was still more deeply jaundiced and in coma. The pupils were dilated but not fixed, and the fundi were normal. There were bilateral extensor plantar responses, but no alteration in muscular tone and no involuntary movements. Later in the day his temperature rose slightly. Both legs became spastic and were held adducted and extended. There was bilateral sustained ankle clonus. The temperature rose steadily to 105° during Sept. 21, coma deepened, and the physical signs remained unchanged. He died early on Sept. 22. There was never any purpura. The urine contained no albumin, and repeated blood smears were negative for malaria.

Necropsy revealed endocardial petechial haemorrhages. The liver was small and flabby with a shrunken capsule, and the cut surface was blotchy yellow and red. The brain showed no macroscopic abnormality, no bile staining, and negative smears for malaria parasites.

Histology.—Liver:—Extensive parenchymatous degeneration with marked leucocytic infiltration. Brain:—Generalized oedema, especially of the white matter. Perivascular lymph spaces greatly enlarged. No haemorrhages. No degenerative changes. Occasional vessels in the caudate and lentiform nuclei showed a few round cells, perivascular, but the appearances were not suggestive of an encephalitis.

In all fatal cases the liver showed the characteristic pathological changes of acute or subacute hepatic necrosis. Histological sections of the brain are available in five cases, including the two detailed above. They consisted of scanty round cells, perivascular around the basal ganglia, in the meninges, and in one case in the subcortical white matter. A greater or lesser degree of cerebral oedema was always present, and extravasation of small numbers of red blood cells throughout the brain was sometimes observed. These changes are in alignment with those found by Baldwin Lucké (1944) in his excellent analysis of fatal hepatitis in the U.S.A., except that in one of our cases lymphocytic infiltration was found in the subcortical white matter as well as in the meninges and basal ganglia.

The pyramidal and striatal signs may be accounted for by one of three theories: a mutation of the infective hepatitis virus, giving it a neurotropic character; a specific attack upon the basal ganglia and pyramidal systems by products of autolysed liver cells; or by toxins from the gut which are allowed to pass through an incompetent liver.

The virus theory is improbable on account of the following facts. The onset of striatal signs coincides with a sudden increase in liver damage and not with the onset of the infection. The cellular reaction round the small vessels of the brain is very slight and can hardly be considered to indicate a meningo-encephalitis. It is conceded, however, that the tempo of the disease, once cerebral changes have appeared, is so swift that more dramatic histological changes may have no time to appear; again, it is possible that special methods of staining which were not available might have demonstrated more extensive damage.

The chemical theory is more likely. It is interesting to note the relation between striatal and pyramidal disease and diffuse liver damage in such diverse conditions as kernicterus (Hawksley and Lightwood, 1934), umbilical infection (Biernacki and van Crefeld, 1937), Kinnier Wilson's disease (Greenfield, Poynton, and Walshe, 1924), Laennec's cirrhosis (Waggoner and Malamud, 1941), and such metabolic disturbances as haemochromatosis and the lipidoses (Brouwer, 1936). Many of these conditions are characterized by diffuse liver disease of a chronic nature in which there is no active autolysis of liver cells. It is for this reason that we prefer the last explanation—namely, that of poisoning of nervous tissue by the passage of intestinal toxins through an inefficient liver.

The pathogenesis of these signs is probably the same as that of the "type" picture, but the association between hepatic and striatal damage in so many diseases is too frequent to be pure coincidence and demands further investigation.

The Haemorrhagic Group

It is the rule rather than the exception to find diffuse petechial haemorrhagic phenomena in fatal cases of infective hepatitis as in any disease causing liver failure. We have observed three cases which are worth noting, since they showed massive haemorrhages—into the caudate nucleus in one case, and forming a subdural haematoma in the other two.

Case A.—A British officer became ill on July 1, 1944, with nausea and vomiting followed by jaundice. On July 14 he became unconscious and incontinent; the plantar responses were both extensor, but later in the day the right response became flexor. On July 18 there was a petechial rash and he bled extensively from ulcers on his scalp, shoulder, and wrist. Necropsy on July 22 showed the common hepatic changes of necrosis; the brain contained an area of softening lateral to the right lateral ventricle and a large haemorrhage into the right caudate nucleus. Histology demonstrated small extravasations of blood into the meninges and into the Virchow-Robin spaces in the pons; there was also slight perivascular round-cell infiltration.

Case B.—A sapper developed infective hepatitis on July 26, 1944. There were small subconjunctival haemorrhages and haematemeses. Blood slides showed a few benign tertian rings. On Aug. 3 he suddenly lapsed into coma and died the same day. Necropsy showed a right parietal subdural haematoma. The surface vessels of the brain were congested and there were petechial haemorrhages throughout the white matter. Brain and spleen smears showed no malaria parasites, and the liver changes were those of acute hepatic necrosis.

It is suggested that in the first case the lesion (possibly a venous thrombosis) giving rise to the area of softening occurred at the same time as the extensor plantar response was observed. The caudate haemorrhage which gave no signs was probably

terminal. The subdural haematoma both in the case quoted and in the other was silent.

This is a small and somewhat artificial group which should be regarded aetiological as a gross manifestation of the general haemorrhagic tendency in liver failure.

Peripheral Neuritis

In the Arakan in 1944 there was a small and short-lived outbreak of peripheral neuritis which coincided precisely in time with the development of jaundice in each case. This outbreak will be reported elsewhere by Byrne, who considers, with some reason, that the symptoms and signs of peripheral neuritis were due to the emergence of a neurotropic element in the virus of infective hepatitis. We have observed one such case:

A British private aged 38 complained of a painful heel on July 26, 1944. He had cellulitis of the heel, which cleared up by Sept. 20. There was no open ulcer. He then noticed difficulty in walking (the difficulty involved both legs), and a week later he developed infective hepatitis. Jaundice was persistent, the weakness of the legs became gradually worse, and the arms became weak also. On Nov. 12 (the last day on which he was seen, as he developed amoebic dysentery and had to be evacuated) examination showed normally reacting pupils, no cranial nerve lesion, general weakness of the upper limbs with absent tendon reflexes, and general weakness of the legs with absent knee- and ankle-jerks. There was wasting of the dorsiflexors, with blunted touch sensation on the legs and slight Rombergism.

It seems doubtful whether the peripheral neuritis in this case was causally related to the infective hepatitis. Hurst (1943) observed similar cases in Gallipoli in the 1914-18 war, and it is by no means certain that they did not represent the simultaneous occurrence of two fairly common diseases.

Summary

The neurological complications of infective hepatitis are reviewed. Four main groups are illustrated by cases observed in Assam and Bengal in 1944.

It is concluded that neurological changes may appear in association with infective hepatitis due to a number of causes, most of which are still a matter for speculation.

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A TRICK TEST TO DETECT NIGHT-BLINDNESS "MALINGERERS"

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The tests that have so far been evolved to examine scotopic vision—pentagon, hexagon, and the various adaptometers—are all subjective in nature and therefore demand the full co-operation of the subject. From the military point of view this is of little value in eliminating the few genuine cases of night-blindness from the many who simulate the condition. To help in sifting these cases the following test was devised and preliminary experiments have been carried out.

It was thought that if it could be shown that the subject was co-operating fully, then more reliance could be placed upon the subjective results of one of the above-mentioned night-vision tests. A mass of experimental data (Hecht and Williams, 1922; Hecht and Mandlebaum, 1939; McDonald, 1940; Mandlebaum, 1941) indicates that red light stimulates the cones of the retina only and that the rods are unaffected. On this basis, subjects with normal central vision—that is,

adequately functioning cones at the macula—should be able to identify a pure red light at minimal intensity even if the rest of the retina is diseased or defective.

Experiments performed by us have shown that the minimum threshold for pure red falls within a very narrow range of intensity of illumination (Fig. 1). An individual with defective night vision but with normal cones—that is, normal macular function—should theoretically be able to see red light within this narrow normal range of minimal intensity. This hypothesis has been confirmed by the few cases of early retinitis

FIG. 1.—Range of minimum threshold for red light of 100 subjects chosen at random and including those with hypermetropic and myopic errors of refraction.

pigmentosa, diffuse choroido-retinitis (maculae unaffected), and advanced glaucoma with very contracted fields but good central vision which we have so far been able to test. One possible exception, suggested by the literature (Wald, Jeghers, and Arminio, 1938; Wald and Steven, 1939; Hecht and Mandlebaum, 1939; Mandlebaum, 1941)—for we have not been able to find such a case—is severe nutritional deficiency (vitamin A), because it is reported that in experimentally induced vitamin A deficiency the cone threshold for white light, and therefore we presume the red threshold as well, is raised. In practice, however, this exception can be dismissed, as this condition cannot arise on Army diets and would, in addition, show other well-marked features. Finally, it is necessary that known cases of night-blindness (familial) with no signs of disease or abnormality of the fundi should be tested to ascertain if such cases fall within the above established normal range of minimal thresholds. This would substantiate the universal application of the test.

Method

The test evolved is briefly as follows. The individual who complains of night-blindness at the out-patient clinic is given a careful routine examination including colour vision, then placed in a dark room, given dark goggles, and left to dark-adapt for 20 minutes. Other patients are seen meanwhile, so that no time is wasted. After 20 minutes' adaptation the "night-blind" patient is asked to state when he can just see the faint red light which is shown him and increased gradually in intensity; as soon as he can see the light it is dimmed and the test repeated a few times until a constant result is obtained. It is simple to deduce whether the patient is co-operating or not. The general procedure of the test suggests to the subject that his night visual ability is being tested, and the malingerer reasons that he must not admit seeing the light until it is very bright; but this, of course, does not tally with the results of the general routine investigation, which shows that he has normal macular function. Further, the several readings