Dr. L. J. Davis reported on them as follows: "The film is a 'thin' one in which marrow cells are scanty. Marrow cells of all types are present. Erythropoiesis is normoblastic; although a number of basophil erythroblasts are present, megaloblasts typical of pernicious anaemia in the relapse stage are not seen. No gross abnormality is noted in the white cell series; there is perhaps an increase, however, in the proportion of promyelocytes."

Unfortunately, owing to a technical difficulty, we could not at this time carry out a fractional test meal examination, but on Nov. 25 we were able to do so. It showed a mild hyperchlorhydria, delayed emptying, and bile in the first three and last three specimens. Mucus was present only in the fasting juice.

Liver injections were started on Nov. 20—initial dose 8 c.cm. neohepatex Evans, 2 c.cm. daily for seven days, then 2 c.cm. every other day for two weeks. This was not sufficient, and so 2 c.cm. daily was given from Dec. 10 until Jan. 6, 1943, when it was stopped to see if a relapse would occur. We should like to emphasize that liver was the only haematinic given.

A second sternal puncture done on Nov. 26 showed an essentially similar picture. There were then 6.7% reticulocytes, and the haemoglobin was 73%. Further reticulocyte counts showed: Nov. 28, 3.5%; Nov. 30, 3.6%; and Dec. 2, 2.8%. By Dec. 4 the haemoglobin was 85%, R.B.C. 3,700,000, and C.I. 1.15; and on Jan. 5, 1943, at the end of liver therapy, Hb 92%, R.B.C. 3,900,000, and C.I. 1.25, and the white cells had risen to 7,400. A further count, on Jan. 19, gave Hb 95%, R.B.C. 4,400,000, C.I. 1.1, and W.B.C. 10,700. Reticulocyte counts done during this period were normal.

Meanwhile the patient's clinical condition was steadily improving. The jaundice was slowly disappearing, his appetite was excellent, his liver and spleen were both receding, and he was beginning to gain weight. His condition on Jan. 26 was very good; he had gained 16½ lb. in the last four weeks, and weighed 11 st. 13 lb. He could undertake without fatigue a stiff uphill walk of an hour's duration to his home on the moor-tops. His liver was still palpable and his spleen only just palpable. The faintest trace of jaundice could be seen in his skin and sclerotics. The van den Bergh reaction continued to be positive direct until Feb. 26, but on April 14 and May 14 the results were negative. A blood count on June 9 showed Hb 95%, R.B.C. 4,750,000, and C.I. 1. No trace of jaundice was then to be seen. The liver and spleen were just palpable. The patient's general condition was excellent.

Comment

We feel that the response to liver therapy certainly suggests that the anaemia was due to lack of liver principle; on the other hand, it is conceivable that the improvement in the blood picture might have occurred spontaneously after the patient's recovery from his infective condition. The reticulocyte response would, however, support our own view.

Regarding spontaneous recovery, it is interesting to note that in the only case of macrocytic anaemia associated with acute catarrhal jaundice about which we have been able to read so far (Wintrobe and Shumacker, 1933), spontaneous recovery did occur. In their case, however, the origin of the jaundice was not so clear, there was no splenomegaly, and there was a histamine-fast achlorhydria to begin with. The anaemia cleared in 24 days, whereas in the present case, even assisted by liver extract, recovery to the level of 4,400,000 took 52 days. These authors encountered macrocytosis in 11 out of 43 cases of hepatic disorder, and of these eleven the case quoted above was the only one suffering from acute catarrhal jaundice. They performed necropsies upon 8 cases, and note that the pathologist described the extent of the liver destruction as extreme in the very same four cases in which hydrochloric acid was found in the gastric contents, but that no such comment was made in the other four cases, in which achlorhydria was present.

We are aware that this case is unsupported by mean corpuscular volume figures and that other investigations might with advantage have been carried out, but we feel that the case has sufficient importance to warrant publication if only so that others may be aware of the possibility of a grave anaemia complicating acute infective hepatitis and be prepared for it to be of liver-deficiency type.

We have during the conduct of the case enjoyed the most helpful and encouraging correspondence with Prof. L. S. P. Davidson and Dr. L. J. Davis of Edinburgh. I have to thank them, too, for permission to quote the above report from one of their letters.

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AETIOLOGY OF THE FIBROSITIC NODULE: A CLINICAL CONTRIBUTION

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The term "nodule" is employed in the title of this paper (which expresses my own views alone) as it is one that has been familiarized by custom. It has seemed, however, that the existence of a nodule definite enough to be palpated in the muscles of a sufferer with fibrositis must in most cases be a sign of chronicity of the complaint, and that the "myalgic spot" is probably an earlier stage of what later becomes a nodule if left untreated. The discrepancy in the frequency with which nodules are found in this disease in England and in America can be explained by this hypothesis.

The myalgic spot is an area of hyperaesthesia in the substance of a muscle or its tendinous sheath which gives rise to pain either in the same locality or referred to a distance, when stimulated. We owe mostly to Kellgren the description of this referred pain and its distribution. These spots are generally multiple, and occur in the powerful muscles of the back and of the gluteal region, often towards the edge of the muscle where it blends with the more fibrinous portion. They may also occur, but less often, in the peripheral muscles, and in the anterior muscles of the trunk.

The aetiology and pathology of the myalgic spot or nodule are unknown, although trauma is believed by most observers to play a part in its development. It is thought that the observations recorded below throw some light on the aetiology in a proportion of cases.

Observations of Acute Myalgia

An epidemic of influenza was recently studied in which severe pain in the lower back was an early and prominent symptom in nearly every case. Some patients also complained later of pains in the thighs, calves, and arms. The cases comprising this epidemic were all of the "febrile" type described by Horder and Gow (Price's *Medicine*, 1941) as being of abrupt onset, with pyrexia and associated malaise and headache in addition to the pains described above. The pyrexia was high for three to five days, and was accompanied by a moderate degree of catarrh, chiefly affecting the eyes. Defervescence was by rapid lysis, and a leucopenia was present in most cases. None of the 40 patients examined had any previous history of rheumatism.

It was noted in the course of this epidemic that, although the acute lumbar pain was diffuse, severe, and resulted in spasm in some cases, by careful examination it could be found that it radiated from localized hypersensitive areas in the adjacent muscles, and that the position of these areas approximated to those usual in cases of ordinary lumbago. The same observation was made in cases in which the pain was in the limbs. In one instance severe "crampy" pain in the upper portion of the rectus abdominis muscle was also present—the clinical picture being comparable to that of epidemic myalgia (Bornholm disease). This pain was entirely relieved by an injection of procaine at the focal point.

The subjective pain disappeared after two or three days, but these myalgic spots were found by palpation to be still present, although the patient was not aware of them. When found and pressed on, he felt a sudden sharp pain which made him wince momentarily and which was—in about half the cases examined—referred in addition to the whole area previously affected. The number of such spots which could be discovered in any patient tended progressively to decrease as time went on.

The same group of patients were again examined two months after their influenza, when it was found that only in rather less than half of them could these spots still be found. In these cases, as before, the patient was himself unaware of their presence until examination. Three cases deserve special mention.

Reports of Three Cases

Case 1.—A civilian aged 40 had a sudden onset of headache, with pain behind the eyes, sweating, and malaise. Pain in the back had occurred several hours previously, and this got progressively worse. For this reason the patient preferred walking about to lying in bed, although his temperature was 102.6°. On examination he looked ill and was sweating profusely. The eyes were congested and the tongue furred. Pain in the back was evidently severe, and the muscles appeared to be in spasm. Urine and stools were normal, and no malarial parasites were present in the blood. The white cell count was 5,000. Next day he was much better. There was still pain behind the eyes and in the back. The temperature was normal. Myalgic spots were found in the lumbar region. The patient made an uninterrupted recovery until three weeks later, when he developed mumps. The pain then returned to the lumbar region as at first, although not so severely, for two days, during which the temperature was raised above 100° F.

Case 2.—A civilian aged 27 complained of sudden onset of severe pains in head, back, and legs, with a feeling of pyrexia, the previous afternoon. Temperature was 101.6° and pulse 90 when seen, and he was sweating profusely. No shivering; bowels rather loose on previous day but now constipated. Patient looked ill; tongue lightly furred. On examination nothing abnormal was found in the abdomen, and there were no malarial parasites in the blood. W.B.C. 3,400. The pains had prevented much sleep previously, but sedatives gave some relief. One week later pain and other symptoms had entirely gone, and the patient had resumed work. Pain could, however, be provoked momentarily by pressure on the myalgic spots which still persisted in the lumbar region and along the border of the ilium on both sides. Two weeks later the condition was unchanged, excepting that fewer of these spots could be found. Those present were carefully marked. Five c.cm. of blood, taken in the first 12 hours from a patient who had just developed sandfly fever, was then injected intramuscularly—by permission—and on the next day a pyrexial attack with a maximum temperature of 101° developed, and lasted 36 hours. The patient complained of lumbago from the onset of this pyrexia, and on examination it was found that this pain was originating from the spots which had been marked. It was easily abolished by injecting 1% novocain into them. One month later this patient was still found to have three myalgic spots in the lumbar region of which he was completely unaware.

Case 3.—A gunner aged 22 experienced a sudden onset of severe occipital headache with pains in back and legs. Temperature 101°. On examination he looked, and felt, very ill. There was marked congestion of the conjunctivae, and the bowels had been rather loose for two days. Tongue moist, with light-brown fur; abdomen normal; stools and urine normal; W.B.C. 4,200. Pains disappeared on third day; temperature normal and all symptoms gone on fifth day. Two weeks later the patient stated, when seen, that he was perfectly fit, but well-defined myalgic spots were found in the lumbar region. On pressure these referred a pain down the legs entirely comparable to that which had occurred during onset of fever. This patient was seen again a month later for another reason, and volunteered the information that similar pains had returned, although in a less degree, for a short period a few days previously while a cold in the head was developing.

From these observations it seems that infection with the organisms of influenza will produce acute muscular pain which can be shown to be referred from myalgic spots that develop in the region of the affected muscles. The spots appear to resemble those found in cases of ordinary lumbago. A large proportion of the spots which were seen to develop in the present series of cases disappeared a few days after the termination of the influenza, but some of them survived.

It does not seem that these myalgic spots are a specific reaction to the virus of influenza as such, however, in view of the fact that the pain returned temporarily in the same areas during an attack of mumps which one of the patients (Case 1) developed spontaneously during convalescence. This view was confirmed experimentally by inducing an attack of sandfly fever artificially in a patient convalescent from influenza (Case 2), with the same result. It also seems possible (Case 3) that periodical attacks of the common cold or other mild virus infection may prove to be a factor in keeping myalgic spots which have arisen in this way active, although confirmatory evidence is lacking. If this were found to be so it suggests an analogy with the "maintenance dose" in other fields.

Observations on Myalgia following Exanthemata

It is well known that acute muscular pains may arise in the course of, or after, many of the acute infectious diseases other than influenza—chiefly, it would seem, those of virus

origin. A considerable number of patients complaining of pain that had arisen in this way have been examined during the past year. These pains have also in the majority of cases been found to have their origin in well-defined hypersensitive myalgic spots from which the patient's myalgia or "neuritis" (muscular tenderness) was referred. The diseases which most commonly give rise to this syndrome appear to be sandfly, glandular, undulant, and scarlet fevers, measles, and rubella. Myalgic spots arising during the course of one of these diseases have been found to be still present two months later, this being the longest period during which a "follow-up" proved possible in this series.

The description already given of the myalgic spots arising during the epidemic of influenza applies equally to those arising in this series, and justifies the belief that they may appear during the course of almost any acute infectious fever, and that a certain proportion will persist unknown to the patient until such time as they may subsequently become reactivated.

It seems probable that factors such as chill, damp, trauma, and mild focal infection, which have sometimes been held to be causative, are in fact of secondary importance, and will provoke an attack of fibrositis or myalgia only in the presence of latent myalgic spots formed previously in this way. The method by which they actually provoke an attack may possibly be by inducing a local oedema in the sensitive area, whereby the victim becomes aware of the myalgic spot and of the pain referred from it. If this is so it accounts for the nodular feeling which is not infrequently remarked at these points, and the fact that this can sometimes be rubbed away by a skilful masseur.

Summary

The role of "myalgic spots" or "rheumatic nodules" in fibrositis is discussed.

In a recent epidemic of influenza in which lumbar and other pain was a prominent feature it was observed that this pain was also referred from small hypersensitive areas in the muscles. These were indistinguishable from "rheumatic" myalgic spots. On re-examination of the patients after one and two months these spots were still found to be present, although in diminishing numbers. The patient was, however, invariably unaware of this fact until pressure from the examining finger disclosed them. None of these patients had any previous rheumatic history.

Myalgic spots which had arisen during influenza were reactivated in one patient by an attack of mumps which arose spontaneously during convalescence. In another case this occurred as the result of the artificial induction of an attack of sandfly fever by the inoculation of infected blood. It appears, then, that myalgic spots can arise *de novo* in the course of acute influenza, and that these will persist in a proportion of cases. They can, however, be reactivated by infections of other types. In one case there was evidence suggesting that the common cold provided the means for maintaining the activity of the myalgic spots.

Rheumatic pains are a characteristic sequel of many of the exanthemata, mostly those of virus origin. Observation has shown that these pains, which tend to arise in a less acute manner, are also generally of the focal type.

The final suggestion is therefore that the myalgic spots which it is now widely agreed form the basis of many of the rheumatic syndromes of later life are sometimes a legacy from acute infections in earlier years. It is important to remember that the victims are often unaware of their presence until they become activated by factors such as chill, trauma, or focal sepsis. These factors should consequently be regarded as secondary and no longer causative in such cases.

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Thirteen out of 20 patients with eclampsia were found by M. Rosenbaum and G. L. Maltby (*Arch. Neurol. Psychiat.*, Chicago, 1943, 49, 204) to have electro-encephalograms indicative of cerebral dysrhythmia. They compare this with the finding of similar changes in only 2 out of 20 patients with pre-eclampsia. Twelve of the eclamptic patients had a family and personal history of convulsive disorders. The authors therefore suggest that in eclamptic patients there may be a primary cerebral dysrhythmia, and that the associated toxæmia may be the "trigger mechanism" which sets off convulsions.