AN EXPERIMENTAL INQUIRY INTO CIRRHOSIS
OF THE LIVER.*

BY

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PREVIOUS RESEARCHES.

NUMEROUS attempts have been made to gain some insight into the causation of cirrhosis of the liver in man by the artificial production of an interstitial hepatitis in animals.

During the last two years we have been carrying on a series of experiments to obtain a true cirrhosis in animals by various methods, and it is our intention in this paper merely to deal with the results we have obtained by ligation of the bile ducts.

Before describing our experiments it is as well to review shortly the results obtained by other observers on this subject. As early as 1866 Leyden¹ ligatured the common bile duct and obtained degeneration of the hepatic cells; while Meyer² in 1872 found by the same means dilatation of the biliary passages and increase of the intralobular and extra-lobular connective tissue in cats. The same results were obtained by Wickham Legg.³

Charcot and Gombault,⁴ Chambard,⁵ Foà and Salvioli,⁶ experimented on rabbits and guinea-pigs, and the ligation of the bile ducts always caused in these animals, in addition to the results already mentioned in cats, necrotic foci.

Since these experiments were carried out in the pre-antiseptic days it was impossible to say how much might be due to sepsis and how much to the direct ligation of the bile ducts. In fact Litten⁷ considered the increase of connective tissue was not due to the ligation of the bile ducts but entirely accidental, the result of the inflammation of Glisson's capsule.

Lahousse,⁸ Beloussow,⁹ Camalis,¹⁰ E. Pick,¹¹ and Gerhardt¹² all subsequently worked with antiseptics, and claimed that even when antiseptics was carefully carried out they found new connective tissue present in the liver after the ligation of the common bile duct. Steinhaus,¹³ however, working with strict antiseptic precautions, could never find any increase of connective tissue in guinea-pigs thus experimented with.

It might be thought that the differing results obtained by these observers were due to the time which elapsed between the operation and the killing of the animal, as after ligation of the common bile duct most of the animals die within a fortnight. Nasse¹⁴ ligatured some of the hepatic ducts instead of the common bile duct, and thus was able to keep the animals alive for a longer period. He found that the ligatured duct dilated, and the lobe of the liver supplied by the duct showed an increase of connective tissue which finally caused atrophy of the hepatic cells. Josselin de Jong¹⁵ employed the same methods, and kept his animals alive as long as six weeks. When strict antiseptic precautions were employed he found no evidence of diffuse fibrous formation in those lobes of the liver in which the hepatic duct had been ligatured, but merely necrotic areas which afterwards became encapsulated with connective tissue.

From this brief description of the results already obtained we see that there is plenty of room for further investigation on this point, and in order to settle the question more definitely we decided to keep our animals alive for a longer period. As a matter of fact, when we first began our research we were unaware that others had experimented by merely ligaturing one or more hepatic ducts instead of the common bile duct.

OPERATIVE PROCEDURE.

In all cases we employed cats in this research, as so many rabbits suffer from psorospermiasis, and this alone causes an increase of connective tissue in the liver. The animals were operated on under ether with strict antiseptic precautions. Only in one of the cases was there any sign of sepsis; this was the cat which died from peritonitis sixteen days after the

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operation, and happened to have got affected through some of the stitches giving way. The liver was carefully turned upward, and in all the experiments the left hepatic duct was ligatured, the other ducts being left free. As a rule a double ligature was applied, and in some cases the duct divided so as to make sure that the channel did not open up. Afterwards the animals were fed on milk and meat, and appeared perfectly well; in fact, in the majority of cases, except for a slight loss of weight which might be considered due to the confinement, they appeared as if nothing had been done. That the loss of weight was not due to the operation was seen by the fact that the animals which were thin at the beginning gained weight after the operation. In no case was any jaundice present, and the motions passed were the same as those normally seen with cats on this diet.

After a period of from five to six months the animals were killed with chloroform.

MACROSCOPIC APPEARANCES.

The naked-eye appearance of the liver was little altered; there was no apparent wasting of the left lobe, nor was the right obviously hypertrophied. On a more careful inspection it was seen that there was a slight degree of granulation of the surface of the left lobe, the granules corresponding to the hepatic lobules. This could be easily recognised when compared with the normal appearance of the right lobe. The left hepatic ducts were dilated to the size of a goose quill on the distal side of the ligature, and they contained bile, which in some cases was thickened, but in others little altered. On cutting into the left lobe the dilated biliary passages were seen here and there to contain coloured bile, but macroscopically there was otherwise little difference between the section of the left lobe and a similar section of the right lobe.

MICROSCOPICAL APPEARANCES.

On making microscopical specimens, two sections, one of the left and the other of the right lobe of the liver were mounted on the same slide, so that one was able thus by placing the sections in juxtaposition to observe more accurately the changes following the ligation, and compare any slight degrees of pathological difference in the two lobes.

There was found to be little difference in the microscopical examination in the general appearance of the hepatic cells on the two sides, though on the left the individual hepatic cells were usually irregularly granular, and the cell columns were generally narrower and clearer than on the right. On the left side, however, there was found a development of interlobular tissue separating the hepatic lobules, while on the right side there was no such interstitial tissue, or at the most, in some sections a few nuclei were noted lying between a limited number of lobules. The increase of connective tissue on the left side was most marked in those animals which had been kept alive the longest, and in these cases there was a slight shrinking of hepatic lobules which appeared to contain here and there new cells. Thickened blood vessels were noticeable in the interlobular tissue, the biliary passages were markedly dilated and their epithelial lining considerably folded longitudinally, and the lumen of these vessels sometimes contained greenish coagula. There was no appearance of vitreous degeneration, nor could any necrotic patches be demonstrated.¹⁶

CONCLUSIONS.

We thus see that in these cats we have obtained by ligation of the hepatic ducts increase of interlobular tissue.

So far the animals examined have only lived five or six months, and in none has there been a marked atrophy of the left lobe, as one sees in the true cirrhosis in man. The experiments are being continued for longer periods, when it is hoped to get more marked results.

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ACUTE FEBRILE CATARRH ASSOCIATED WITH INFLAMED GLANDS OF HEAD AND NECK.

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THE main point of interest which concerns the condition treated of in these remarks centres in the fact that they refer to a definite and specific form of disease which apparently has hitherto escaped adequate recognition and is certainly accorded no position in our official nomenclature of disease.

The symptoms suggest that the disease is the result of a general infection of bacillary origin, with local manifestations, confined to the glands of the head and neck. It begins absolutely suddenly, with rigors and pain in the back, pyrexia, rapid pulse, and profuse sweating. The temperature rises to 103° or 104° F., the pulse to 130, the tongue becomes coated, the urine is high coloured and scanty, and there is intense headache. So far this resembles the invasion of atypical influenza, but within twenty-four hours the headache changes in character, and is replaced by a series of exquisitely tender areas over the whole scalp, and each area is soon felt to correspond with an inflamed gland. The patient generally complains of painful bumps, and examination reveals a series of enlarged glands, varying in size from a pea to a chestnut, over the frontal region at the beginning of the hairy scalp; over the occipital region and the posterior cervical glands. At the same time there is usually a fully developed acute tonsillitis of a simple type. The disease easily yields to treatment, and runs its course in a few days. The febrile symptoms subside, the headache diminishes in intensity, and the painful glandular enlargement, which is pathognomonic of the condition, gradually disappears, leaving the patient somewhat prostrate. There is little to distinguish the whole course of an attack from an acute febrile catarrh, except this distinctive and unusually-localised glandular affection. It is difficult to recall any pathological state wherein enlargement of the minute lymphatic glands of the frontal and vertex regions of the scalp exists. We are, of course, familiar with the enlarged suboccipital glands in impetigo and morbus pediculosus, and the enlarged posterior cervical glands of secondary syphilis. The former, however, is a distinctly local affection, and the latter is a manifestation of a general toxæmia of a more acute, but still essentially similar, nature to that of tuberculosis or lymphadenoma. The peculiar glandular inflammation herein described may therefore well claim an independent position in the nosology of disease, having an acute well-defined onset running a definite course with unequivocal physical signs. The morbid process is probably that of a general infection. The *materies morbi* becoming arrested in the glands of the scalp, its nature and point of invasion are matters of speculation. Most glandular enlargements are associated with well-ascertained specific causes. On the other hand we have the glandular inflammation of parotitis, which is the only local manifestation of an acute specific fever, and we have an orchitis of a similar nature. These represent acute inflammation of glands of unknown etiology, with sudden onset and rapid subsidence, but as they do not concern lymphatic glands their analogy with the condition described in this communication is imperfect, but the morbid processes must necessarily be similar.

During the last three years at least six cases of this acute inflammation of the scalp glands have come under my notice, and one of them merits detailed description owing to the extraordinary tendency it displayed to relapse.

The patient is a lady aged 35 years, who until 1895 had good health. On January 18th she had what appeared to be an ordinary attack of influenza

with pains in limbs, headache and sickness, and temperature 104°. The symptoms abated in a few days and rapid convalescence ensued. On January 26th, soon after leaving her bed, a relapse supervened with similar symptoms. Subsequent relapses occurred again on February 9th, 16th, March 1st and 10th, and another during April, in each attack the headache was agonising and the sickness very distressing. And each attack was accompanied by a series of inflamed and enlarged glands, mainly over the occipital region, varying in size from a pea to a filbert nut, and exceedingly tender. In all the patient had fourteen similar attacks, the last being on October 28th, 1896. She was then three months pregnant, and she remained free until April, 1898, when she suffered another attack precisely similar in all details, the enlarged lymphatic glands in the scalp being the most prominent feature.

The extraordinary tendency of this case to relapse suggested a malarial origin, but no antecedent history of this diathesis could be ascertained in this or in the other cases, and the exhibition of quinine did not prevent the recurrence of the attacks. On the whole it presents the closest analogy to epidemic catarrhal fever or influenza, which for some undetermined reason attacks especially the glands of the head and neck, as other varieties attack the lungs, nervous system, or intestines. The classical accounts of this disease do not, however, mention this peculiar manifestation. The only references to a similar condition in recent literature contain an epidemic of acute catarrhal fever associated with enlargement of the carotid lymphatic glands, which prevailed in Eastern Ohio from 1893 to 1896, described by Dr. Park West; and a glandular fever of childhood affecting mainly the cervical glands, reported by Dr. Dawson Williams.

MEMORANDA: MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, Etc.

EPISTAXIS—A SIMPLE METHOD OF TREATMENT IN SOME CASES.

EPISTAXIS may of course be caused by many surgical affections of the nasal cavities. These require their appropriate treatment; for such cases I do not propose to make any suggestion. In many, however, apparently the cause is not strictly merely local, but is due either to the condition of the blood or to some degeneration of the coats of the blood vessels. In some of these cases I have found a simple application successful, when, as sometimes happens, position—local application of astringents, hot water douches, and pressure have failed. Sometimes too as in the country, astringents and other appliances are not at hand, and under such circumstances I would suggest the trial of the application to the back of the neck of very hot poultices, which I have found useful on more than one occasion. I am quite aware that the use of hot water bags to the spine has been proposed, and I presume they act in the same way as hot poultices, but hot water bags are not often at hand, whilst hot poultices can readily be obtained in the poorest houses and most remote districts. I have used linseed meal to make the poultices, but any other heat-retaining material would do equally well. The rationale of the success of the method is the effect produced on the vessels through the vasomotor system.

I may quote shortly one case in illustration. Many years ago I was asked at 7 A.M. to see an old lady whose nose had been bleeding for three hours. I found her very weak, and the bleeding not severe, but continuous. Local pressure and astringents had been tried without success. I applied a very hot linseed poultice to the back of her neck, and the bleeding at once stopped. This lady subsequently went to the country, and she informed me that when she again got a return of the bleeding, and it continued any time, she doctored herself successfully by the application of the hot poultice. The bleeding in her case was evidently due to degeneration of the coats of the blood vessels; she had a rigid radial artery.

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TRAUMATIC APHASIA.
IN connection with the case related under this heading in the BRITISH MEDICAL JOURNAL of November 19th, I wish to put briefly on record a case which resembles that in the substitution of a less familiar language after a brain injury.