ON THE
HISTOLOGY OF THE SO-CALLED
NUTMEG LIVER.

BY

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IF the liver of a healthy animal be examined immediately after death it will be found to present a uniform red-brown appearance. Soon after, however, the uniform appearance is lost. The surface becomes mottled, and the mottling on further examination will be found to correspond closely with the distribution of the acini of the liver. The circumference of the acinus is pale, while the centre is deeper coloured. The cause of this unequal distribution of colour is to be found in the arrangements of the blood-vessels; the portal vein, which within the liver closely resembles an artery, is distributed to the circumference of the lobule, and, like an artery, empties itself of blood soon after death. The hepatic vein, on the other hand, which arises in the centre of the lobule, remains full of blood, as is the rule with the ordinary systemic veins.

It is an exaggeration of this mottling to which the name of nutmeg liver has been given. Whenever there exists a hindrance to the return of blood from the hepatic vein, this state of the liver may very readily be set up. The radicles of the hepatic vein become gorged with blood, and

a deep brown-red colour is thus given to the centre of the lobule; while the outer part of the lobule, to which the portal vein and hepatic artery are supplied, remains pale. Hence a deep contrast between the centre and circumference of the same lobule.

Kiernan described nutmeg liver under the name of the second stage of congestion, or of active congestion of the liver. "It very commonly attends," he says, "disease of the heart and lungs; the congestion begins in the hepatic veins, and extends towards the portal veins."¹ He has thus accurately enough described the pathology of the disease, so far as it relates to the blood-vessels; before him it was well-nigh impossible to be explained.

Cirrhosis of the liver and nutmeg liver have not always been distinguished. It is clear that five-and-thirty years ago the two morbid states were confounded. Becquerel, in analysing his cases of cirrhosis, sets down heart disease as a cause in exactly one half.² So more recent writers, as Rokitsansky³ and August Foerster,⁴ have mentioned heart and lung disease amongst the causes of true cirrhosis.

Budd appears to have been one of the first to separate cirrhosis and nutmeg liver, and on the ground that simple passive congestion of the organ could never lead to an active inflammation.⁵ Dr. Handfield Jones a few years later expressed his opinion that nutmeg liver does not terminate in the contracted hobnail cirrhosis. As this writer's description of the state of the connective tissue in nutmeg liver seems to me to agree more closely with the facts of the case than those of many other writers, it may be worth while to detail his views more at length. Dr. Handfield Jones regards, as the essential circumstance of the nutmeg liver, the effusion of an unhealthy plasma, not only in the canals and fissures of the liver, that is, in the capsule of Glisson,

¹ Kiernan, 'Phil. Trans. of the Royal Society of London,' 1833, p. 754.

² Becquerel, 'Arch. gén. de Méd.,' 1840, t. viii, p. 40.

³ Rokitsansky, 'Handb. der path. Anat.,' Wien, 1842, Bd. iii, p. 347.

⁴ August Foerster, 'Handb. d. spec. path. Anat.,' Leipzig, 1854, p. 109.

⁵ Budd, 'On Diseases of the Liver,' London, 1845, p. 118.

but in the external part of the lobules. The investing membrane of the lobules is very greatly increased, and becomes much more condensed and more distinctly fibrous. The effused plasma likewise seems to insinuate itself between the cells in the external part of the lobule.¹ With the description of the changes in the lobule itself I am less able to agree. Liebermeister was, I believe, the first to acknowledge that Dr. Jones' view of the changes in the capsule of Glisson was correct, and he has devoted a long chapter in his book on diseases of the liver to this subject.² But, so far as I know, few writers have followed in his steps, Dr. Henry Green being one of the few who describes an interlobular growth as being constantly seen in nutmeg liver.³ Rindfleisch⁴ and Klebs⁵ certainly speak of an interlobular growth, as being sometimes seen, but they evidently look upon it as an accident not to be associated with the essential phenomena of nutmeg liver.

The prevailing doctrines as to the histology of nutmeg liver are, however, altogether different from that of Dr. Handfield Jones. They are those expressed by such authorities as Virchow,⁶ Frerichs,⁷ and Rokitsansky,⁸ and may be stated as follows: that the cells of the liver in the centre of the lobules atrophy from the pressure of the dilated vessels; that their place in the centre of the lobules is then taken by a highly vascular tissue, formed of capillaries and new connective tissue, while the cells of the circumference of the lobules and the interlobular connective tissue remain unaltered. My observations have led me, however, to take a very different view of the

¹ Handfield Jones, 'Medical Gazette,' 1848, vol. vii, p. 1033. It is an abstract of a paper read before the Pathological Society of London.

² Liebermeister, 'Beiträge zur path. Anat. und Klinik der Leberkrankheiten,' Tübingen, 1864, p. 77.

³ T. Henry Green, 'An Introduction to Pathology and Morbid Anatomy,' London, 1871, p. 244.

⁴ Rindfleisch, 'Lehrbuch d. path. Gewebelehre,' Leipzig, 1867, p. 383.

⁵ Klebs, 'Handb. d. path. Anat.,' Berlin, 1869, p. 424.

⁶ Virchow, 'Würzburger Verhandlungen,' 1854, Bd. iv, p. 349.

⁷ Frerichs, 'Klinik der Leberkrankheiten,' Braunschweig, 1858, Bd. i, p. 374.

⁸ Rokitsansky, 'Lehrbuch der path. Anat.,' Wien, 1861, Bd. iii, p. 247.

disease, and have caused me to support in general the statements of Dr. Handfield Jones and Professor Liebermeister.

The observations which follow were made upon twenty livers which showed a well-marked nutmeg appearance, met with in the post-mortem room of St. Bartholomew's Hospital during the last two years. Parts of the livers were either hardened altogether in weak chromic acid, or first kept for a few days in weak chromic acid and then put into spirit of wine. The thin sections were in all cases coloured with carmine and mounted in glycerine. The following descriptions must be understood of sections examined with Hartnack's microscope, ocular 3, objective 9, *à immersion* :

In the earlier stage of the disease the chief morbid appearance is to be found in the centre of the acinus, and is caused by a dilatation of the radicles of the hepatic vein. In the section these vessels may be seen distinctly enlarged and still completely filled with red corpuscles. Their appearance varies according to the direction of the section of the blood-vessels. When the cut has fallen lengthwise upon the vessels, they are seen as long channels passing between the liver-cells ; when the vessels are cut directly across, they are then surrounded by a ring of liver-cells varying in number. The liver-cells themselves seem to be at first not much changed in character. Their outline is, however, hard to make out, so that they cannot be readily counted ; they show a large nucleus and granular contents.

In the later stages the dilatation of the capillaries becomes very great. The vessels in the centre of the acini are dilated to twice or three times their natural size, and in this way grave changes are wrought upon the tissues immediately around them. The rows of liver-cells between the vessels, at first only somewhat lengthened and flattened, become so much pressed upon that their shape becomes almost linear ; a nucleus can scarcely be made out, and their contents are seen to be dark and granular.

The latest stage of all is that in which the centre of the lobule becomes little more than a network of vascular tissue,

between the meshes of which a few highly granular and pigmented liver-cells lie. On looking at specimens in this stage with a low power (Hartnack, oc. 3, obj. 4), the outer part of the acinus is seen to be formed of a ring of almost colourless liver-cells, while the centre is filled with a red tissue, studded with pigmented liver-cells; and this tissue, as seen with a low power, looks very like connective tissue. But on examining the specimen with higher powers, this tissue is found to be made up of channels, the walls of which are exceedingly delicate and transparent, and within which red blood-corpuscles can yet be made out. No nuclei can be seen in the midst of this tissue as in the interlobular tissue, but studding the field are numerous rounded or slightly polygonal cells, with highly pigmented contents, and containing no discoverable nucleus. These cells I hold to be the remains of liver-cells.

This last stage of the disease is rarely met with, but it is clear that it is this stage which Rokitansky has endeavoured to portray in the woodcut which shows an intra-lobular vessel surrounded by a highly nucleated connective tissue, in which a few pigmented liver-cells are seen. I am quite unable, however, to agree with the statement that the tissue in the centre of the lobule is an overgrowth of the connective tissue. It is rather to be regarded as the transparent wall of the vessels. The only other change which I have been able to make out is a thickening of the wall of the hepatic vein in the centre of the lobule.

These changes in the vessels and cells rarely go beyond the middle zone of the acinus; I have not found them exceed this in any of the specimens which I have examined. Fatty infiltration of the cells of the outer border of the lobule is not so common or so usual as from the writings of others I had been led to believe. In a very few only did the amount of fat in these cells exceed what is natural. In the few cases in which there was more fat than is common the excess was very great, and the border of the acinus showed cells filled with large fat drops for some depth towards the centre.

The connective tissue of the capsule of Glisson is the seat of important changes. The centre of the acinus is not the only part of the liver which suffers; a large part of the connective tissue of the liver becomes actively engaged in the disease. In the earlier stage the capsule of Glisson may be found increased in size and with numerous lymphoid corpuscles present in it. This may be seen very early. In a child of eight years, in whom, so far as could be made out, the heart disease has lasted only three weeks, a considerable increase of the connective tissue of the liver was observed, and the connective tissue itself was studded with lymphoid bodies. In the earlier stage of the disease this appearance, however, is not always met with. The connective tissue may be increased in amount, but no lymphoid corpuscles seen among the fibres. When these are present they are most abundant in the sheath of the vessels; and it is around the interlobular vessels that the increase of the connective tissue is most marked. There can then be no doubt as to activity of the process going on in the connective tissue of the liver, but if these lymphoid bodies be absent it is a matter of some nicety, requiring considerable experience in the histology of the natural liver, to decide if an increase of the connective tissue have really taken place.

In the later stages the increase of the connective tissue becomes far more marked, and the lymphoid bodies are never absent throughout the whole of the liver. At least, I have always been able to see them in some part of the liver in all the cases of advanced nutmeg liver which I have examined. The connective tissue is strewn with them just as in primary cirrhosis. They are often very abundant indeed; but they do not show any linear arrangement as in cirrhosis, but are scattered irregularly through the tissue. This lack of arrangement may be due to the fact that but a small piece of the connective tissue is visible at one time under the microscope, so that it is well-nigh impossible to follow for any long distance the same tract of overgrown connective tissue.

The connective tissue is not always developed to the same

degree in every part of the same liver. Often quite close to spots where the interlobular tissue is actively engaged, crowded with lymphatic corpuscles, and much increased, a spot may be found quite free from these lymphatic bodies, and seemingly not greatly increased in bulk. This is an exceedingly common appearance in nutmeg liver, and one for which the observer must be prepared in forming a judgment upon it.

I have not found the connective tissue in any of the specimens which I have examined so greatly increased as to penetrate within the lobules themselves, although I can well conceive such an appearance in far advanced specimens of the disease to which the name of atrophous nutmeg liver has been given. I must still, however, be allowed to doubt, with Dr. Handfield Jones, if the growth of the interlobular tissue ever becomes so great as to give a hobnailed appearance to the liver.

It has been laid down as a pathological law by Sir William Jenner that, whenever an organ is mechanically congested for any length of time, the part becomes indurated, and also that an overgrowth of connective tissue takes place, although this is rather a matter of inference from Sir William's words than a direct statement¹ of his. He found in cases of congestion of the heart that the interstitial tissue lying between the muscular fibres was increased. It is also well known that one of the results of long-continued mechanical congestion of the kidney is an overgrowth of the intertubular connective tissue. It is not, therefore, surprising to find like changes in the interlobular tissue of the liver in mechanical congestion of that organ. The overgrowth cannot be due, as Rindfleisch implies,² to a mere coincidence, as I have found it in almost all the specimens which I have examined, even in the earliest stage of the

¹ William Jenner, 'Med.-Chir. Trans.,' 1860, vol. xliii, p. 200. The exact words are: "It is a pathological law that mechanically induced congestion, if long continued, slowly formed, and intermitting altogether or in degree, has for effect induration, and also *when the fibrin exuded is not of the powerfully contractile variety*, permanent increase in bulk."

² Rindfleisch, 'Lehrbuch der path. Gewebelehre,' Leipzig, 1867, p. 383.

disease; nor can it be merely an early stage of cirrhosis caused by habits of intemperance, for I have found the same interlobular overgrowth in four nutmeg livers of children varying from eight to twelve years in age, and who were unlikely to have been of intemperate habits. The presence of the lymphoid corpuscles I look upon only as evidence of the activity of the interlobular growth, and in no way related to a chronic inflammation.

The shrinking in the after stages of nutmeg liver is, in my opinion, due to the same cause as in cirrhosis, that is, to an overgrowth in the capsule of Glisson. A decrease in size cannot be caused by an atrophy of the parenchyma of the liver, so long as this atrophy is commensurate with the pressure upon the parenchyma by the dilating blood-vessels, for the decrease in size of the cells will be exactly counter-balanced by the increase in size of the blood-vessels. According to many authors, a new growth springs up in the midst of these dilated vessels, and it is by the growth of this new tissue that the decrease in size of the liver is brought about. I think this is but an imperfect explanation of the decrease in size, and it would seem more probable that if there be an interlobular growth, that the shrinking of the liver is due to the same cause as in cirrhosis.

In conclusion, I should like to add a few words as to the name of red atrophy which has been given to the atrophous nutmeg liver by Rindfleisch. Nothing can be more confusing than to have the same name given to two different states. The name of red atrophy was years ago given by Virchow¹ to a rare state of liver met with after wasting diseases, such as typhoid. This name has been accepted in this sense by pathologists such as Rokitsansky² and Foerster,³ and it is scarcely worth while to introduce a disturbing element into the nomenclature when the name of atrophous nutmeg liver is sufficiently good, and no advantage can be attained by change.

¹ Virchow, 'Arch. f. path. Anat.,' Bd. v, p. 289.

² Rokitsansky, 'Lehrbuch d. path. Anat.,' 1861, iii, 244.

³ Foerster, 'Handb. d. path. Anat.,' 1863, ii, 169.