SOME OBSERVATIONS
ON THE
EFFECTS OF CHOLAGOGUE MEDICINES,
AND SOME REMARKS ON
MORBID CHANGES IN THE LIVER.

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A short summary of the author's views on the structure of the liver may properly precede the following account of the effects produced by certain cholagogue medicines, and some appended remarks on various morbid changes that are incident to the liver.

The mammalian liver consists mainly of a parenchymatous solid mass, marked out by the portal canals and fissures into lobules, which blend at their margins with each other. In the three lower vertebrate classes the lobular arrangement is scarcely to be observed, and is, therefore, evidently non-essential. The parenchyma consists of perfect cells, or nuclei, and diffused granular and oily matter. The ducts do not expand to enclose the parenchyma, nor are they prolonged as intercellular passages through it. They terminate either by closed rounded ends, or, as Kölliker believes, by abutting against the mass of parenchymal cells. The structure of the ultimate ducts is peculiar, consisting chiefly of nuclei, and seems fitted to exert an active elaborating function; they do not resemble mere efferent channels.

The ducts are supplied by the hepatic artery throughout their larger branches; but the ultimate ones are surrounded only by a scanty plexus, as they lie in the interlobular fissures, and are exposed besides to the secretion of the marginal cells. The portal vein is distributed exclusively to the parenchyma, the cells of which lie in the closest relation with its capillaries; the hepatic cells elaborate, out of the blastema supplied by these capillaries, the sugar which is formed in the liver during digestion, and which is again absorbed and carried off by the blood passing out by the hepatic vein. Yellow matter (pigmentary of the bile) is often seen in the cells, especially in the central cells of human livers; it is not nearly so often seen in the marginal, in which oil is much more apt to collect. The yellow matter may be extracted in large quantities by alcohol, and gives the reactions of biliary pigment, but not those of cholic acid and its conjugates. The author believes that these are formed out of oily, saccharine, and albuminous matters by the ultimate ducts, the nuclei of which remaining permanent, exercise constantly a "metabolic" action.

When the development of the liver is traced in the chick, the parenchyma is found to appear first; soon after, an eminence, consisting of dark oily matter, is seen on the wall of the future duodenum, from which two offsets proceed to the parenchyma of the liver: they do not, however, ramify in it, but retrograde and waste, the eminence, however, remaining. The cystic and hepatic ducts begin to be developed at a somewhat later period close to the liver, extend downwards, and open together into the intestine, just exactly at the eminence mentioned. For this eminence the author proposes the name of *colliculus*. The process in fishes and reptiles is essentially similar; in the former it proceeds very slowly; the liver is long a mere parenchymal mass, with a vesicular gall-bladder attached. The hepatocystic duct in tadpoles is lined at one time by a ciliated epithelium.

I now proceed to detail some experiments which I have made relative to the action of cholagogue medicines, in

which a careful examination was made of the intimate condition of the different organs wherever it appeared desirable.

To a healthy cat I gave Hydr. c. Cretâ, gr. v; she was killed by a blow on the head. The liver was found extremely gorged with blood, the gall-bladder containing a very dark yellow bile. The bile contained no visible object but columnar epithelium; its colour was unlike that of the yellow tinted cells often seen—more of a reddish yellow. I examined several thin sections: the capillaries were congested most excessively with blood, and formed an uniform plexus, with circular or elongated meshes. The diameter of the capillaries varied from $\frac{1}{2500}$ th to $\frac{1}{4000}$ th of an inch. The cells everywhere were pale, well-formed bodies, with soft mottled contents, imbedding numerous small oil drops. The envelope and the nucleus were pretty distinct. None exhibited the least yellow tint,—neither the marginal ones, nor those lying near the centres of the lobules. There was no trace of bile in the small intestine. I injected afterwards warm water into the hepatic vein, and washed out the blood; after this I made a watery extract of the part thus freed from its blood, and easily obtained evidence of abundance of sugar being present. This could only have existed in the cells. In this case the dose of the mercurial produced no evident effect, except that of causing considerable congestion.

I then tried the effect of larger and repeated doses. Three doses of calomel, gr. iij, were given to a full-grown cat, at intervals of about twelve hours:—she was killed fourteen hours after the last. The liver was extremely loaded with blood; the gall-bladder, as well as the ducts, contained much deep yellow bile; there was a faint tinge of bile in the middle of the small intestine, which increased towards the lower part, and became very marked there and in the large intestine. On examining thin sections, it was apparent that a prodigious quantity of yellow material had been formed in the cells of the margins of the lobules, and in those extending about half the distance to the centre. It appeared as yellow-coloured oil drops, which were quite distinctly *in* the cells; some few larger masses of reddish-brown or yellow aspect were free.

On dissecting out the ducts nothing different from their ordinary condition was observed. The nuclei were not tinged yellow. The lungs contained numerous whitish masses of varying size, consisting of well-formed granular cells, nuclei, &c.; they were not of the nature of tubercle, but rather of exudation. In this instance I am satisfied that the quantity of yellow matter seen in the exterior cells was the result of the calomel that had been given; some bile was also poured out into the intestine.

Another cat, for the sake of confirmation, was dosed in a similar manner. No bile was found in the small or large intestine; the gall-bladder and the ducts were full of dark-coloured secretion, as in the former cases. The cells of the parenchyma were found exceedingly loaded with oil; in some parts large masses of big oil drops were seen, or huge single oil drops. The cells about the centres of the lobules contained distinct yellow matter, either in the form of granules or molecules, or as a diffused fluid. There were seen here and there largish, reddish, or reddish-yellow, or brown masses, of a somewhat angular form, which were probably pigment matter. The smaller ducts were found perfectly natural; the larger ones and trunks often stained of a decided yellow colour. The lungs were healthy. I am inclined to think the enormous accumulation of oil in the liver was partly the effect of the mercurial as well as the accumulation of yellow matter in the cells, which, it is interesting to notice, was deposited not only in the cells but also *free* in their intervals.

To a kitten two or three weeks old I gave Hyd. c. Cretâ, about gr. vij, and killed her four hours after. There was a good deal of mucus in the intestinal canal, and the gall-bladder contained much dark yellow bile. The lobules of the liver on their margins, where they bound the fissures and spaces, were decidedly tinted with yellow matter, which contrasted remarkably with the pale, granular, and oily condition of the larger remaining parts. The cells were usually pale, granulous particles, well and definitely formed; they contained some oil drops, and were imbedded in oily matter,—but this was less abundant than usual: the yellow matter was seated

in the cells. On dissecting out the ducts, yellow tinted cells and bright deep-yellow particles were seen adhering to the Glissonian sheaths; none were seen in the ducts. The ultimate branches of these, as is usual in young creatures, were not completely formed,—not of a definite shape; their nuclei were more widely *espacés* than in the adult, and less isolated from the sheath itself.

I will also quote an earlier observation which I made upon a large, rough greyhound dog. He had Calomel, gr.v, given him, and was killed sixteen hours afterwards. The gall-bladder was full of healthy bile. The liver was much congested with blood: the cells were of a pale granular aspect, well defined, containing generally a few yellow molecules. Those situated on the margins were especially the seat of the yellow matter; it was seen in this situation constituting yellow sheaths or patches. The arrangement of the cells was plexiform rather than linear; there was but little oily matter in them. The structure of the ultimate ducts was quite natural; but among the nuclei numerous yellow molecules were seen clustering, as it were, over them: these were very similar to those in the hepatic cells. This observation, as well as the preceding, leave no doubt on my mind that the action of mercurials on the liver is to produce a greater quantity of yellow matter in the cells. While I regarded yellow matter as identical with bile, relying solely on the indication of colour, I felt no doubt that this was biliary matter, and supposed that these experiments afforded even more positive proof than we had before, that the action of mercurials increases the production of bile; that is to say that it not merely increases the *flow* of bile, by emulging the ducts and gall-bladder of their contents, but actually causes a greater quantity to be formed. And, indeed, it may still be so; the quantity of glycocholate of soda, the organic salt of the bile, may really be increased; but of this the above experiments do not give any proof. It will, however, be interesting to compare the above results with those obtained when other cholagogue medicines were given, some of which influenced the *flow* of bile much more decidedly than mercury.

Colchicum.—To a healthy young dog a rather large dose of the wine was given. It produced vomiting and several clay-coloured evacuations. The liver presented hepatic venous congestion of first degree very well marked; the gall-bladder was greatly distended with greenish-yellow bile. The stomach was empty; its mucous membrane was of a pale white, with a blush of red here and there; its secretion faintly acid. The duodenum was empty; its surface covered with a quantity of watery and mucous fluid deeply bile-tinged; its capillary plexus was injected here and there. The small intestine was covered on its inner surface in the upper half of its extent by a layer of deeply yellow-tinged mucous fluid; the lower half, or rather more, was paler, not covered by fluid, and without any yellow tinge; the limit to which the bile-flow had reached was very marked. The last two inches of the small intestine, as well as the cæcum and large intestine, were covered by a red grumous fluid, which consisted of a tenacious, transparent, partly granular plasma, containing multitudes of mucous or puriform globules and blood discs. The mucous membrane covered by this red fluid was in parts injected and softened. In a section it was seen that there was thickening and granulous deposit around the Lieberkühn tubes, and some enlargement perhaps of the solitary glands. In the liver the capillaries surrounding the intra-lobular vein and the interlobular veins also were congested with blood. The cells were pale granular bodies, without any yellow tinge; they lay in a granulous basis matter, which also contained free nuclei and small groups of free oil drops. In some few cells here and there were seen bright yellow particles extremely distinct; but none such existed in the vast majority. The ducts were in that opaque condition so common in London dogs, and which renders their course so easy to trace. This depends on the deposit of numerous oily molecules between the nuclei; it is not the minute ducts only that are affected, but the whole extent of the excretory apparatus. The columnar particles of the gall-bladder and larger ducts are filled in their interior with minute oil drops, and the surface in the

fresh state is of a dead white aspect. The effect of colchicum thus appears to be rather that of emulging the excretory passages of bile, than of promoting the formation of yellow matter (perhaps biliary) in the cells.

A cat was dosed twice with half a grain of tartarised antimony: she died of the effects. The liver was rather congested; the gall-bladder was full of bright yellow bile, which was very tenacious, and contained much visible oily matter. Bile had flowed out plentifully into the intestine. The cells of the hepatic parenchyma were very perfect, and contained, especially on the margins of the lobules, much oily matter; they were in no part tinged yellow. The ducts were quite natural. Thus, there was evidence of bile having been emulged by this drug from the excretory passages, but none to show that an increased quantity had been *formed*. The effect produced on the mucous surfaces of the intestine and pulmonary cavities, and on the blood in various parts, was very remarkable, and is detailed elsewhere. (*Vide* 'Med. Times and Gazette,' March 19, 1852.)

To a young dog Aloës, gr. iij, was given twice, once fourteen hours, and again two hours before he was killed. A curious circumstance happened before life was extinct. Strong inspiratory movements were going on, and when one of the large veins was wounded, air rushed in large quantity; immediately after this a loud systolic blowing murmur, audible at some distance from the body, commenced, and continued for some time:—it evidently was occasioned by the frothy condition of the blood expelled by the contraction of the ventricle. The liver was quite natural, moderately full of blood; the gall-bladder was moderately distended with yellowish bile. The whole length of the intestinal tract was tinged yellow by the bile which had flowed out; the mucous membrane was nowhere injected, or showed a trace of irritation; the epithelium remained attached. There was accumulation of oily matter in the central cells of the lobules of the liver; it constituted distinct whitish spots about the size of a pin's head. The cells were generally pale, granular bodies, and did not contain more than a

very little oil, nor had they any decided yellow tint. The ducts were very distinct, being rendered opaque by oily deposit between their nuclei. Aloës in this case certainly acted as an efficient cholagogue, but no yellow matter was produced in the hepatic cells.

Oil of turpentine caused some bile flow, and distension of the gall-bladder with bile, in a dog; no yellow matter was observed in the cells. The lungs were a good deal congested, and in some parts hepatised. The intestinal mucous surface showed traces of irritation; it was injected in parts, especially the large intestine, and covered with more or less of tenacious mucus.

Two doses of rhubarb were given to a kitten, at an interval of about twelve hours; two evacuations followed, the last a copious, solid, dark-green one. The liver was pale, the gall-bladder contained some bile, of a very dark, reddish-yellow tint; the cells were pale, well-formed, containing little oil and no yellow matter; the ducts were slightly opaque, from oily deposit. The whole of the mucous surface of the small intestine was decidedly but not deeply yellow tinged,—that of the large intestine was not, it was pale and white.

Another kitten, of the same age, was treated with the nitro-muriatic acid bath six times, for five minutes at a time, in the course of four days. The blood of the hepatic vein contained well-formed globules, which sometimes formed *rouleaux*, and a moderate number of white corpuscles. The blood of the portal vein presented no visible difference, except that it contained numerous small corpuscles, the germs, probably, of new blood-globules. The liver was extremely pale,—the edges translucent; the bile in the gall-bladder of a very light yellow colour, altogether unlike that of the preceding instance. The cells were perfectly pale, devoid of any yellow tint, and contained very little oil; there was scarce any free oil; the ducts were quite natural. The capillary plexus was most beautifully seen, and the cells lying in its interstices; the meshes were oval or circular, and exactly moulded on the cell, so as to leave no apparent inter-

cellular passages. The small intestine was pale, or but very feebly bile-tinged in its upper three-fourths, in its lower part it contained a good deal of deeply bile-tinged matter; the large intestine was full of ordinary dark-green *faeces*. The stomach was quite healthy, it contained much half-digested food, and gave a distinct acid reaction. The bile-tinged matter in the lower part of the small intestine was chiefly mucus, in this some long muscular fibres were entangled, which were very particularly bile-tinged, very much more than the surrounding mucus.

An adult cat, similarly treated, presented more marked traces of bile-flow, but the bile in the gall-bladder was of the ordinary dark-green colour; the hepatic cells contained numerous concrete, oily molecules, and were devoid of any yellow tint. Thus nitro-muriatic acid does not increase the production of yellow matter in the hepatic cells, but rather seems to tend to diminish it; it also seems to have a cholagogue effect.

A full-grown cat took, during three days, eight grains of taraxacum (the extract) daily, and then for two days longer, twelve grains daily. On examination, the liver was found perfectly natural, the gall-bladder contained bile of the usual dark-green colour. The stomach was empty and pale, except near the pylorus, where it contained some deeply bile-tinged mucous fluid; this extended to the adjacent part of the duodenum, but below this the colour diminished, and the whole surface of the small intestine, except the lower fifth, was barely tinged of a light yellow colour. The lowest part of the ileum was of a dull white, manifestly different from the above, but contained here and there some *faecal* matter, with deeply yellow-coloured mucus; the surface of the large intestine was decidedly tinged yellow, and the canal was full of natural *faeces*. There was considerable accumulation of oily matter in the central parts of the lobules of the liver; the cells in the external parts contained a moderate quantity of oil, and were surrounded also by much free oily matter. No yellow matter was visible in them. The ducts, on being dissected out, were found quite natural.

A cat, pregnant with four fetuses, which were at about the end of the first third of intra-uterine existence, was dosed with muriate of manganese. Half a drachm dissolved in water was given at mid-day, and again in the evening; she was found dead in the morning. She had not been purged. The lungs and heart were healthy, the former crepitant but rather congested. The stomach was empty, its mucous membrane of a rather dark red; there was no trace of yellow matter throughout the whole length of the intestine, small and large; the only contents were mucus, and some remains of food. The liver was rather full of blood, the gall-bladder very pale, containing very little bile, which was of an orange colour, and mingled with a good deal of mucus; under the microscope it showed nothing but columnar epithelium, a little oily and granular matter. The cells of the liver were very well formed, generally more opaque than usual, many of them contained yellow matter, so that when *in situ*, streaks of yellow matter were seen radiating outwards towards the periphery: the yellow matter did not appear to be in one part more than in another. There were also some masses of free yellow matter. The ducts appeared natural. There was no yellow matter to be seen in the spleen.

The general result of the foregoing details is that of the various cholagogue substances tried. Mercury, muriate of manganese, and colchicum, are the only ones which seem to increase the production of yellow matter in the cells of the liver. I have placed them in the order of their potency. That they also increase the production of glycocholate and taurocholate of soda I think very probable; but unless we were assured that the quantity of these principles is always proportionate to that of the yellow pigment, which does not seem to be the case, the above experiments say nothing as to this point. It is clear that the cholagogue action of a medicine, its emulging effect on the ducts, is distinct from that which it exerts in the *production* of biliary pigment. Jaundice has been known to come on during a mercurial course, and apparently an effect of the medicine. I have at present a patient under my observation (one of Dr. Chambers

in St. Mary's Hospital), who reports her jaundice to have appeared after taking a six grain calomel pill. These statements are in accordance with the experiments I have detailed, —the animals to whom I gave mercury had jaundice of the liver.

One very important effect to be noticed of the administration of mercury on the liver is, that it certainly produces very great congestion of the organ; this is an argument for rather forbearing the use of this remedy in inflammation of the substance of the liver, a practice which would otherwise be recommended by our analogical experience.

The fatty condition of the liver which is so often observed, has been so well described and examined, that it must appear superfluous to offer any remarks upon it. I think, however, there are some points of detail which are worth a short notice. It seems a fair question, What constitutes truly fatty degeneration of the liver? Is it to be regarded as a simple increase of the quantity of oil naturally existing in the hepatic cells, or is it a further and more important change? I am much inclined to think that the latter is the case, and that a real distinction exists between the condition of oily accumulation when there is simply an undue quantity of oil present in the parenchyma, and that of true fatty degeneration when the natural structure is more or less altered and destroyed. To illustrate this I will quote first the instance of a kitten, which had been fed for about a week on food containing much oily matter. The liver was of a dull grayish-yellow tint, in the first stage of hepatic venous congestion. Sections viewed under the microscope were utterly opaque, and showed both the cells and the intercellular substance loaded with oily molecules; the accumulation of oil was equal everywhere. The ultimate ducts were dissected out and found natural. Here all that had occurred was the addition of a quantity of oil to the hepatic parenchyma (not to the ducts), there was *no degeneration* of the cells. In contrast to this instance I will place the notes I made of the condition of two livers taken from the bodies of two persons who died in St. George's Hospital. In one

"the liver was in a complete state of fatty degeneration; the oil drops, however, did not seem to be enclosed in distinct cells, but to lie in an indistinct granular or semi-fibrous stratum; scarce any distinct cells were to be seen." In the second, the liver being also in a state of complete fatty degeneration, I observed that the cells were, for the most part, destroyed, and that only films of granular matter remained; the number of free nuclei also seemed to be fewer than usual. In these two cases it was quite evident that the natural cell structure of the liver was, to a great extent, destroyed, that a real degeneration had taken place; and this I have repeatedly observed in most cases of fatty degeneration of the liver, occurring in persons who have died of various diseases. Whether a liver, whose cells are thus destroyed, can recover its natural condition, is a question of much interest, but one which it seems impossible to answer.

A circumstance of much interest, which seems still further to indicate the degenerative character of the fatty transformation of the human liver, is that in such livers, I have almost invariably been unable to detect the existence of sugar, and this is confirmed also by the experience of my friend Mr. Blyth. This, however, was not the case with the kitten's liver, who had been fed on fatty food,—it yielded on analysis a full proportion of saccharine matter.

Another point which has not been much noticed is the peculiar limitation of fatty degeneration to the margins of the lobules, which is very frequent. I think the change does not consist merely in accumulation of oil in the marginal cells, but that destruction of them actually takes place. A liver affected in this way, presents the lobules most perfectly marked out by a zone of opaque matter, this varies in different cases somewhat in width, but may be said generally to occupy about one fifth or one fourth of the distance from the margin to the centre. I can give no sufficient explanation of the tendency of oil to accumulate in the marginal cells; it may, perhaps, in part depend on the circumstance that the stream of portal blood first passes through them; but this does not at all account for the converse

occurrence, viz., oily accumulation in the central cells, which issometimes very marked in the healthy livers of animals. There is commonly but little yellow matter in the cells of livers deeply affected with fatty degeneration,—sometimes, however, it is sufficiently apparent in a few here and there; the common condition of livers which present more or less of the “nutmeg” aspect, is oily accumulation or fatty degeneration of the margins, with heaping up of yellow molecules in the central cells around the intra-lobular vein.

Fatty degeneration of the liver, when complete, may occur in very different diseases; it is by no means peculiar to phthisis, as is well ascertained. Out of 19 cases which I examined microscopically, four or five only had any connection with phthisis; the others occurred in diseases of various kinds, which, for the most part, but not invariably, had produced great emaciation.

Another kind of degenerative change is present in the much more rare *lardaceous* liver. One specimen of this kind which I examined, had the following characters: it was enlarged, bulky, of solid feel and glossy aspect, having a yellowish tint with some whitish spots, and containing very little blood. Thin sections under the microscope showed some of the lobules in a pretty natural state, the cells perhaps rather enlarged, and arranged very much in a linear manner. In other lobules there was a manifest infiltration between the cells, of an homogeneous, highly refracting substance, much resembling concrete oily matter; this was very abundant in some parts, so much so as to compress the cells and reduce them to mere bands anastomosing together, and producing the appearance of a plexus containing the homogeneous matter in its meshes. In many spots, especially in the vicinity of the deposited substance, the cells were deeply tinged with yellow matter. The refracting matter in another instance consisted of spherical, oval, or irregular shaped masses, which had somewhat the size and figure of the natural cells, but did not, I think, result from a transformation of these. Liquor Potassæ added to thin sections under the microscope reduced the deposited matter to mere filmy

fragments, and diminished considerably the refracting power ; its action upon this substance and the surrounding cells, many of which contained much oil, was very different ; the latter becoming more transparent exhibited their oily contents with great distinctness ; the former, though quite translucent, showed no trace of oily matter. The minute ducts in the latter specimen, as well as in the former, were of natural appearance. I have several times examined spleens from the human subject, which contained a great quantity of matter precisely similar in appearance to that which was here deposited ; its seat in the spleen appears to be chiefly the Malpighian bodies whose natural cell structure it replaces, and then extending outwards, brings about an atrophy of the red pulp, which occurs to such an extent that at last mere red streaks are seen separating the translucent glistening substance, and the natural deep colour of the organ is lost. The term by which Rokitansky designates this peculiar deposit, is the "lardaceous" (speckig), and the pathological relations he assigns to it is with "constitutional disease of the vegetative system, especially with scrofulous and rickety disease, with syphilitic and mercurial cachexia," and occasionally as a sequel of intermittent fever. Dr. Budd recognises this condition as a scrofulous enlargement of the liver ; this I think is so far correct, as intimating its relation to scrofulous disease, but it ought clearly to be understood that the deposit is totally different from tubercle, and is, indeed, so far as I know, *sui generis*.

The minute ducts in the fatty and last-described condition of liver have appeared to me pretty natural ; this fact renders it more easy to understand how, with so considerable alteration of the parenchyma, bile can still be secreted.

Rokitansky, describing cirrhosis, says—"We are not of opinion that granular liver always takes its origin in the same fundamental affection ; we are inclined to adopt two morbid states as the essential and original anomalies which give rise to granulations in the hepatic parenchyma as a secondary affection. In one case there is a morbid development of the capillary gall ducts, (the so-called secreting

tissue,) an accumulation of the secretion, and probably also an hypertrophy of the parietes of those vessels giving rise to the nutmeg liver and to an obliteration of the capillary blood-vessels, the so-called vascular substance."
"In the second case, the original affection of the hepatic parenchyma in granular liver is proved, by the post-mortem appearance of the granulations, to consist in a slow chronic inflammation. This induces a gradual obliteration of the parts attacked, and their conversion into fibro-cellular tissue, the amount of which varies in proportion as the processes of absorption or organisation predominate in the inflammatory product. This secondary metamorphosis, from not occurring uniformly, results in a subdivision of the organ into larger and smaller scattered compartments, which present the characteristic rounded form of the granulations in the same ratio as they correspond to single hepatic lobules."

Dr. Budd, in his chapter on Cirrhosis, describes it as "the consequence of adhesive inflammation in the areolar tissue about the small twigs of the portal vein, by which serum and coagulable lymph are poured out. The serous part of the effusion gets absorbed, and the fibrine contracts and becomes converted into dense fibrous tissue, which divides the lobular substance of the liver into well-defined masses," &c.

I cannot say that I have observed any condition corresponding to the first form of cirrhosis which Rokitansky describes. A morbid development of the capillary gall ducts must mean a morbid enlargement of the hepatic cells of the lobules, and such I have never seen in this disease. Dr. Budd's description expresses the opinion ordinarily received, to which I have but little to add that can be esteemed new. I think, however, that a somewhat different view may be taken of the nature of the morbid change constituting cirrhosis, and that some of its different forms may be more exactly traced.

In some cases, no doubt, the fibrous tissue of the Glissonian sheath is affected with what may be truly called adhesive inflammation, attended with the effusion of coagulable lymph and serum. These cases will be marked by

tolerably distinct symptoms—pain in the side, vomiting, fever, perhaps jaundice, as Dr. Budd enumerates them. The portal canals are the seat of the inflammation,—chiefly, I believe, the larger, and not to any great degree the smaller, canals or the fissures. In other instances, which I believe are more numerous, the same parts may be affected, but the nature of the change is different. The fibrous tissue of the sheaths undergoes thickening and condensation, but not as a consequence of effusion of lymph and serum in an acute attack; the process is much more of the nature of degeneration, more akin to the chronic thickenings which are so often observed in fibro-serous membranes, and which are often coincident with this condition of the liver. The result of the above changes, when they do not extend to the smallest portal canals and interlobular fissures, is, I believe, the common hob-nail condition of the liver. If the thickening and condensation proceed further, and affect the sheaths which surround and invest the lobules, then the condition is different, and corresponds very nearly with that which I described in a communication to the Pathological Society, three years ago, under the name of “nutmeg liver.” This description I subjoin, but would remark, at the same time, that in several of these cases I have no doubt that there takes place also a deposition of unhealthy plasmatic fluid in the substance of the lobules, which solidifies them, and tends to increase still further the atrophy of the cells which the defective supply of blood induces. It is difficult, in examining the *débris* of the parts thus degenerated, to distinguish accurately, in all particulars, between what should be regarded as cause, and what as effect; but, though aware of this, I still am strongly inclined to believe that such a process as I have indicated does actually affect the lobules themselves, and that the unhealthy nutritive process, which is the essence of cirrhosis, may manifest itself chiefly in either of three situations:—1. In the larger and middling-sized portal canals, excluding only the smallest. 2. In these last, and in the fissures. 3. In the smaller canals and fissures, and in the substance of the lobules. The first form

results, as said, in the common hobnail liver; the second and third produce tough, firm, dense livers, which are sometimes termed "brawny."

The following is the quotation from the Report of the Pathological Society:—"The form of the liver, in the condition referred to, is scarcely at all altered; its edges are not rounded, nor its surface puckered,—or, if these changes have occurred, they are but slight; its capsule is often smooth, and free from false membrane or other traces of chronic inflammation; its consistence, however, is greatly increased, it is much less fragile, and tears much less easily than natural. On the surface of a section, deep red patches of sanguine congestion are observed coalescing irregularly with each other, and leaving in their interspaces pale greyish or slightly yellow spots; the relative size of the congested and non-congested patches may vary somewhat, but the boundary between them is extremely well defined, the deep tint of red ceasing abruptly, and not shading off into the pale hue of the circumscribed grey spots. Under the microscope it is seen that the cells in the central parts of the lobules, which are the chief seat of congestion, are remarkably altered; they are gorged with yellow matter, and appear as round or oval masses of dark yellow or reddish substance; they are much less numerous than in the healthy state, and lie no longer closely in contact with each other. This condition of the secreting structure is coextensive with the congestion of blood; beyond this, towards the exterior of the lobules, a very different condition is found to exist; here the cells are no longer distinct from biliary engorgement; on the contrary, they are pale, stunted, starved, and often scarcely discernible, or appearing as mere *débris* in the midst of an amorpho-granular basis substance. In some cases the fissures are greatly enlarged: instead of having a diameter of $\frac{1}{333}$ inch, or rather less, I have found several to measure as much as $\frac{1}{34}$ or even $\frac{1}{44}$ inch; this increase in width taking place, of course, at the expense of the lobules, which thus become considerably diminished. The investing membrane of the lobules is very greatly increased, and becomes much

more condensed and more distinctly fibrous; it has appeared to me in some instances to be continuous with the amorpho-granular substance which infiltrates the pale external portion of the lobules. It also seems to me very probable that these cases, where the fissures become so greatly enlarged at the expense of the parenchyma, are but further stages of the degenerating process above described; for, as the exterior part of the lobules becomes atrophied from the deposition of an amorpho-granular basis substance, and loses its natural structure, it will tend to become blended with the fibrous tissue of the continually enlarging fissure. The foramina, which are commonly so evident in thin sections existing at the interlobular spaces, are no longer apparent, the pressure of the thickened fibrous tissue having obliterated the corresponding branches of the portal vein.

"The essential circumstance in the changes now described seem to be the effusion of an unhealthy plasma, not only in the canals and fissures, where it induces unnatural increase and condensation of the fibrous sheaths, but also in the external part of the lobules, where it passes into a solid form, and constitutes an amorpho-granular basis substance, compressing the capillaries and stunting the secreting cells. At the same time the thickened fibrous tissue of the canals and fissures still further obstructs the arrival of blood in the lobules, which thus at last are scarcely supplied otherwise than by the reflux of blood into the ultimate twigs of the hepatic vein and the capillaries which immediately surround them; and thus the morbid congestion of the interior of the lobules is accounted for, and the peculiar yellow engorgement of the cells in this situation, as depending on their congestion.

"In two instances that I observed, where the liver had undergone this change, there was contraction of the mitral orifice of the heart, by chronic thickening of the tissue of the valve and of the cordæ tendineæ. This confirms the view I am inclined to take of the pathological nature of this alteration, viz., that it is a fibrous degeneration of the secreting structure from an unhealthy state of the plasma

supplied to it by the blood, and not an inflammatory action producing effusion of lymph. So far as I have observed, this degenerating process does not terminate in the irregularly contracted 'hobnail' condition, which is the result of cirrhosis; nor have I ever seen in such livers so serious and considerable a lesion of the secreting cells."

The view which I have proposed, that the thickening and condensation of the fibrous tissue in the liver is not so much the effect of any inflammatory action as of a slow degenerative process, such as stiffens the valves of the heart and contracts the orifices, is on the whole supported by the results which are exhibited in the appended Table. It contains a list of 30 cases, in which there appeared, on microscopic examination, more or less thickening of the fibrous sheaths derived from the capsule of Glisson. In 13 of these there was certainly coincident fibrous degeneration taking place in other organs; in 14 cases it may be considered doubtful whether there was any such coincident change; and in 3 there was none. I have included among the 14 doubtful cases several of large, firm, infarcted kidneys, with more or less unnaturally adherent capsules. This morbid alteration I believe myself to belong to that state of system which produces cirrhosis and thickening of the fibrous tissue in other parts; but it may not be so considered by others. The 3d, 47th, and 69th cases are particularly interesting, as showing the existence, at a former period, of tubercular disease, which became quiescent, and was superseded by a diathesis and disease of a very different kind, which might, perhaps, be appropriately named the fibrinous. If, indeed, the view should prove correct which is entertained by some eminent pathologists, that fibrine is an excrementitious or effete substance—not, as was formerly supposed, one of the highest importance to the renewal and growth of tissues—then the existence of such a diathesis and morbid state as I have just alluded to would become in a still higher degree probable. We should then recognise the fibrinous as a form of excrementitious plethora, in which a fluid material, characterised by a tendency to spon-

taneous coagulation, and existing in the blood probably in undue quantity, produced injurious effects, by slowly perverting the nutrition and spoiling the texture of various parts: we should perceive a connection between various phenomena which now appear isolated. The deposition of vegetations, so called, on the valves of the heart, or the deposit of fibrinous masses in the spleen or elsewhere, would then appear as instances of tumultuous and excessive formation of fibrine in the blood, which was thus cast out hurriedly in these parts. The presence of fibrinous nodules beneath the capsule of the liver, or on the pulmonary pleura, would indicate a process of a similar but much more gradual nature. All the various thickenings of fibrous or fibro-serous membranes, stiffening of the valves of the heart, contraction of its orifices, shortening of its cordæ tendineæ, many of the common pleural adhesions, white pericardial patches, would be properly ranked as having their origin in a similar morbid condition of the blood. They would appear then as manifestations of a general state, and not as local affections.¹ The common fibrous tumour of the uterus would be a particular localisation of the general diathesis. There would appear reason to consider the large, firm, dense kidney, with its adherent capsule, as another result of such morbid action. The adhesion of the capsule to the surface is evidently the result of a similar change to that which thickens the capsule of the liver, and the increased bulk and coarser condition of the epithelium of the tubes may not improbably be attributed to its having undergone a kindred change, modified, of course, by its own peculiar nature. I cannot help remarking that no term seems to me, in many cases, so exactly to describe the condition of the renal epithelium in this condition of the organ as the word *stiff*; comparing the morbid structure with the healthy, it gives one the idea of being as much incapacitated from undergoing its normal chemico-vital changes as a stiff and rigid aortic valve is from following its

¹ Rokitsansky says, "The bases for fibroid new formations are solid, most probably always fibrinous blastemata."

natural easy movement. Again, under the head of fibrinous disease, we should range various forms of so-called chronic pneumonia, in which, with little appearance of acute inflammation, there has taken place exudation into the cavities of the air-cells, and complete condensation of the tissue. Some of these cases, by the nature of the exuded material, would form a connecting link between chronic pneumonia (the fibrinous) and the recognised tubercular infiltration. The above are all instances of extra-vascular change produced by the fibrinous disease; one, however, we may refer to as originating in the interior of the vessels, and occasioning, by its arrest of the circulation, irremediable gangrene of the parts thus deprived of their supply of blood. I allude to the spontaneous coagulation of the blood within the vessels, of which several instances have lately been recorded, and which can be ascribed with no kind of probability to any other cause than such a state of the blood as we are now considering.¹

The preceding is rather a long discussion, but may be excused, I trust, from its intimate connection with the pathology of cirrhosis.

The form of cirrhosis which produces the "brawny" liver often coexists with dilatation and hypertrophy of the heart, the former predominating more or less. The retardation of the circulation thus occasioned throws the blood back upon the large veins; and the hepatic veins in particular, with their radicles in the centre of the lobules, are in consequence much congested. I am strongly inclined to think that this congestion of the central part of the lobules has much to do with the peculiar alteration of the cells which there takes place, and which is almost exactly co-terminous with the congestion. The bile-pigment is in all probability derived from the colouring matter of the blood, and it is worth noticing that this yellow matter is especially collected in those parts which are especially the seat of sanguine con-

¹ When the above was written I was quite unacquainted with Rokitansky's doctrine of fibrinous crases of the blood, contained in vol. I of his work. The coincidence of opinion of independent observers is not without value.

gestion. Hepatic venous congestion of the first degree is far the most common; and it is in the same part which this occupies, viz., in the centre of the lobules, that we find almost invariably yellow matter present in the cells.

Cirrhosis is sometimes combined with fatty transformation; a section then presents opaque inlets, the lobules gorged with fatty matter separated by wide, more transparent spaces, which are the enlarged fissures and spaces occupied by new-formed fibroid tissue.

The ultimate ducts in cirrhosis are of course involved in the dense fibroid tissue, and are more or less atrophied by its pressure; their nuclei appear stunted and starved, and the structure is sometimes altogether lost, at least the ducts can no longer be discovered. Usually, however, by the aid of acetic acid they can be seen pretty readily in the widened fissures and canals.

Jaundice manifestly results from the conveyance into the blood of biliary pigment, that constituent of the bile which is certainly excrementitious and intended to be cast out with the *faecal* matter. In most cases there is retention of the yellow matter in the liver, from a mechanical obstacle to its flow into the intestine, or from inaction of the excretory ducts; the retained matter, which, however, is not in excess, being absorbed into the blood instead of passing out with the secretion. In other cases it seems to be formed in excessive and unnatural quantity, as in the acute yellow atrophy of the liver, and perhaps in diseases of the heart, producing great congestion of the veins. It is extremely common to find yellow matter in the cells of the central parts of the lobules in cases of different description quite unattended with any jaundice: this is so frequently the case that it really seems probable that it results from the congestion of the intra-lobular veins and surrounding capillaries which takes place during the last hours of life. Great dilatation of the cavities of the heart, with consequent retardation of the circulation, produces most remarkable yellow engorgement of the central cells of the lobules, and this condition is, I think, not unfrequently accompanied

with marked jaundice. In this case, however, I believe there is no cessation of the flow of bile into the intestine; the function of the ultimate ducts and of the exterior cells is still performed; and there seems only to be increased production of yellow pigment in the central cells. It must be borne in mind that this yellow pigment as it exists in the cells does not evidence the presence of biliary matter, of cholic acid, or its conjugates. The yellow matter can be extracted by alcohol, and gives the characteristic reaction of bile-pigment with nitric acid; but Pettenkoffer's test decides against the presence of the organic biliary acid. The deep colour of the urine in jaundice also seems to depend solely on the presence of the pigment; no trace of cholic acid is often discoverable. I conclude, therefore, that in most cases jaundice results from the absorption into the blood not of completely formed bile, but of one of its constituents only, viz., the yellow pigment. This takes place, (1,) when a mechanical obstacle prevents the flow of bile into the intestine through the duct. com. choled.; the bile then accumulates in the larger ducts and distends them: it continues to be secreted for some time, but afterwards, accumulation of yellow matter takes place in the cells, from which it is no longer freely extracted by the elaborating ducts; (2,) when inaction of the elaborating ducts occurs. This is the commonest case; the cells become filled with yellow matter, as before, because it is not withdrawn from them; (3,) when, with or without impairment of the action of the excretory ducts, an increased quantity of yellow pigment is formed in the parenchyma of the liver.

I may quote here some remarks from Prof. Lehmann's work on Physiological Chemistry, which seem to me not only to bear out the opinion he adopts, that the components of the bile are not formed in the blood, but also to support the view I have maintained, that the bile is not completely formed in and by the hepatic cells, but that this is effected by the action of the ultimate ducts. Lehmann says, "It is just in disease of the parenchyma of the liver that jaundice very seldom occurs; in fatty liver, bacony liver, and the rare tuberculosis of the liver, certainly never; even in

granular liver and inflammation of its substance but seldom. Jaundice only presents itself constantly in diseases of the gall passages, and in acute yellow atrophy."

Now, if with these various alterations of the parenchyma of the liver bile can still be formed, as we know it often is, it seems highly probable that some other apparatus besides the cells has a large share in the formation of this secretion, or at least is capable of taking such.

I will conclude these very imperfect remarks on the subject of jaundice by the detail of two instances of acute degeneration of the liver, which I have recently had the opportunity of examining through the kindness of my friend Dr. Ogle. The first is an instance of acute yellow atrophy, as it is termed by Rokitsansky.

A. B—, a lad, admitted into St. George's Hospital, Sept. 24th. He stated his illness to have lasted only one week, having had sickness and pain at epigastrium, and being jaundiced. His urine, however, had been darker than natural for a fortnight. He had taken balsam copaibæ for gonorrhœa the last two months. On admission his pulse was 64, rather weak; bowels said to be relaxed, and motions of a light colour; had severe headache and pain of stomach. Fomentations: Hyd. c. Cretâ and Ol. Ricini. Motion next morning very offensive, of pale yellow colour; some tenderness in the right hypochondrium. Jaundice, in spite of Calomel, gr. j, ter. die, became considerably deeper, and he suffered from sickness. Bowels rather costive; motions very pale, but vomited matter coloured by bile. He began in about nine days to be mercurialised; pills omitted; but jaundice deepened. Nitro-muriatic acid was given. There was now no pain, but sickness very distressing; no food whatever retained. Latterly he became very drowsy; pupils dilated. On October 10th there was stupor, occasional delirium, and succeeding coma. He died on October 12th.

Post-mortem examination, 57 hours after death.—General jaundice; lungs and heart healthy; yellow serum in pericardium; endocardium tinged yellow; some yellow serum in peritoneum. Intestines healthy; dark olive-coloured fluid in duodenum and stomach. Liver weighed 2 lbs.; the

cut surface was of a bright gamboge colour, the ducts quite pervious. Gall-bladder contained much thinnish fluid, barely tinged by bile-pigment. Lymphatic glands of mesentery and about the lesser curvature of the stomach much enlarged; kidneys much congested, but healthy, weight 13 oz.; spleen healthy, weighed 6 oz.

Microscopic examination.—Liver flabby, apparently bloodless, of deep yellow colour. The parenchyma consists of a mass of broken-up granular matter, tinged deeply yellow and mingled with oil drops; here and there some large deep-yellow masses or globules are seen, which refract rather highly. Scarce a single cell, or even nucleus, is to be seen. Along the margins of the lobules and in the portal canals there is a considerable quantity of free oily matter. The addition of liquor potassæ produces an abundant formation everywhere of small rod-shaped crystals, which tend to form crosslets; often, however, the limbs of the cross are more nearly parallel than at right angles: these are probably margarine or margaric acid. The ducts were dissected out: only one is seen terminating apparently by a closed extremity, which is pretty evenly rounded; it consists of obscurely visible nuclei, lying in a sub-granular basis, which also contains very many opaque rather large globules, resisting acetic acid, and whitish by direct light. Similar globules are strewed about in the canal or fissure, *i. e.*, in the surrounding material. A blood-vessel accompanying a large duct is covered with network of streaks, formed by rows of similar globules; these are spread over the vessel and in the neighbourhood, and also along the sides of a translucent canal accompanying a branch of the vessel; they are doubtless lymphatics. Some of the ducts are remarkably bulged at their sides, and infarcted; their nuclei are generally somewhat altered from their natural aspect, and the intervening substance is tinted yellow. This liver contained no sugar, by Trommer's test.

I regret very much that this specimen was not examined for cholic acid; it would have been very interesting to know whether any of the special organic constituents of the bile could be discovered amid all the prodigious quantity of accu-

mulated pigmentary matter. The alteration which the ducts had undergone was very remarkable, and showed that their elaborating action must have been almost, if not entirely, arrested. The engorged state of the lymphatics seems to indicate that they had been taking upon themselves the function of the ducts, or endeavouring, at least, to do so. The globules, which rendered them so unwontedly distinct, consisted, I believe, of some concrete oily matter.

The second case was that of a person who died with diseased kidneys, peritonitis, and slight pericarditis, with diseased aortic valves. The urine had been albuminous, and pleurisy, with effusion, had occurred on the right side. There was no jaundice; the bile in the gall-bladder was dark and thin; the capsule of the liver was thickened in patches. There was some old cretaceous tubercle in the upper lobe of the right lung. There were one or two white patches on the pericardium, which contained some fluid and shreds of lymph.

The liver was very soft and flabby, the capsule perhaps a little thickened; it was very full of blood. All the cells were more or less altered; some, I think the central ones, were mere masses of yellow matter, others were quite broken up into a granular detritus, mingled with very numerous oil drops. The *déperissement* of the cells was by far the most striking circumstance, and had certainly occasioned the lax and flabby state of the organ. The fibroid tissue was not materially increased. I could find no trace of the minute ducts,—they seemed to have perished.

This case cannot, I think, be regarded in any other light than as an instance of rapid degeneration taking place in the liver. The remote cause of this was probably the dyscrasia of the blood induced by the renal disease; the immediate cause must be mere matter of conjecture.

List of Cases in which more or less of thickening and condensation of the Glissonian sheaths or capsule of the liver was observed, and in which the presence or absence of similar changes in other parts is noted. The number of

cases analysed amounted to 74, out of these 30 were the subjects of the change in question.

- CASE 2.** Glissonian sheaths thickened, capsule of liver opaque. Valves of heart rather opaque, kidneys granular, fibrous tumour in uterus.
- „ 3. Liver firm and tough. Glissonian sheaths extremely dense and semi-fibrous, encroaching on the obules in some parts. Valves of heart (aortic) thickened, one adherent to side of aorta. Kidneys heavy, capsules adherent, texture firm. Spleen firm. Tubercular cavities contracted.
- „ 5. Glissonian sheaths thickened, liver fatty. Uterine cancer.
- „ 8. Liver in an early stage of cirrhosis. Glissonian sheaths condensed, patches of thickening in the capsule. Renal capsules adherent.
- „ 11. Liver dense, Glissonian sheaths thickened. Mitral valve thickened. Kidneys remarkably dense and hard. White spot on pericardium. Apices of lungs puckered.
- „ 17. Capsule of liver considerably thickened in patches. Kidneys cysted, everted, granular.
- „ 18. Capsule of liver a good deal thickened in parts, and sprinkled over with minute fibrinous nodules. Kidneys infarcted, some of their inner tufts compressed. Old universal adhesions of right pleura.
- „ 19. Capsule of liver and Glissonian sheaths somewhat thickened. Kidneys small, dwindled, granular.
- „ 21. Liver fatty, with incipient cirrhosis. Kidneys large, infarcted, mottled. Vomicæ and tubercles in lungs.
- „ 22. Liver enlarged, surface puckered, Glissonian sheaths increased, encroaching on the lobules. Kidneys somewhat granular. Spleen firm.
- „ 24. Glissonian sheaths rather thickened. Kidneys infarcted with much oily matter. Capsules of spleen thickened.
- „ 27. Glissonian sheaths somewhat thickened, liver unusually dense. Kidneys dense in texture, rather shrunken, capsules adherent. Visceral pericardium rather opaque, and dotted over by fibrinous granules.
- „ 32. Liver unnaturally dense, slight increase of Glissonian fibroid tissue. Kidneys firm, tubes infarcted, pleurisy with false membranes.
- „ 40. Liver contained two or three fibrinous nodules, adhered to diaphragm. Kidney not healthy, capsule adherent. Tracheal, bronchial, and lumbar glands greatly enlarged, their substance was of an homogeneous granular aspect, not tuberculous, more like fibrinous matter. Lungs contained masses of crude tuberculous matter, yet not quite resembling ordinary tubercle; I should consider it of an intermediate nature between tubercle and plastic effusion. A white patch on the pericardium.

- CASE 44.** Glissonian sheaths thickened, capsule of liver thickened, its edges rounded. Kidneys shrunk, granular, cysted. Both pleurae thickened, or covered by false membranes. Pericardium thickened. Capsule of spleen considerably thickened. Parietal peritoneum thickened in parts.
- „ 45. Glissonian sheath rather thickened. Kidneys infarcted, tubes containing moulds.
- „ 47. Glissonian sheaths thickened, capsule puckered at one part. Aortic valves thickened. Chronic thickening of right pleura. Left pleura obliterated. Induration of pulmonary apices around tubercles, some masses of these enclosed in a fibroid cyst. Tricuspid valve a little thickened. Kidneys not healthy, containing cysts.
- „ 48. Glissonian sheath thickened, liver fatty. Kidneys rather infarcted, capsules somewhat adherent.
- „ 49. Liver rather large, its capsule considerably thickened. Glissonian sheaths of pericardial canals thickened. Kidneys coarse, tubes infarcted, capsules unduly adherent. Capsules of spleen thickened. Chronic thickening of pericardium. Peritoneum thickened generally. Mitral and tricuspid valves thickened in spots.
- „ 51. Liver nutmeg, fibroid tissue of pericardial canals thickened. Valves a little thickened. Kidneys large, coarse, capsules unduly adherent.
- „ 54. Liver nutmeg, fibroid tissue in portal canals and fissures thickened and condensed. Kidneys coarse, tubes infarcted. Mitral and tricuspid valves a little thickened. A little sub-pleural fibrinous exudation with condensation around a small cretaceous mass.
- „ 55. Glissonian sheaths thickened. Kidneys coarse, cortical tubes infarcted.
- „ 57. Glissonian sheaths greatly thickened, encroaching on lobules, which themselves seem to be invaded by a solidified substance. Kidneys certainly degenerating, capsules very adherent. Pericardial white patch, some recent pericarditis. Mitral orifice greatly contracted. Aortic and tricuspid valves slightly thickened. Capsule of spleen somewhat thickened.
- „ 58. Glissonian sheaths rather thickened. Died of scarlatinal dropsy.
- „ 59. Liver covered with old and recent false membranes. Glissonian sheaths thickened in parts. Lobules seem penetrated by a fibrous basis substance. Kidneys not healthy, structure confused. Right pleura obliterated. Slight recent peritonitis.
- „ 60. Glissonian sheaths slightly thickened. Kidneys coarse, tube infarcted.

CASE 67. Glissonian sheaths somewhat thickened and condensed. Aortic and mitral valves thickened, condensed, and stiffened; mitral orifice somewhat contracted. Fibrinous deposits in spleen and kidneys. A fibrous tumour in fundus of uterus. Pericardium adherent.

„ **69.** Glissonian sheaths much thickened, capsules thickened considerably in two or three patches. Kidneys coarse, large, surface markedly granular. Surface of lungs puckered from induration around tubercles. Mitral and tricuspid valves thickened. Spleen enlarged, firm, its capsule thickened.

„ **73.** Glissonian sheaths thickened, capsule slightly rough. Kidneys large, tubes infarcted.

„ **74.** Glissonian sheaths much thickened, capsule thickened by a white patch in one part, in another the surface drawn in deeply. Considerable chronic thickening of the arachnoid. Granular disease of the kidneys.

One important deduction which may be drawn from this Table is the very great frequency, almost constancy, with which thickening or condensation of the fibrous structures in the liver is associated with actual degeneration of the kidney, or some approach to it. Out of the 30 cases, 26 exhibit this association.

The following list contains a summary of the various diseased conditions, coincident with which fatty degeneration, partial or complete, occurred :

1. Fatty degeneration complete; margins of lobules most affected. Fæcal abscess of cæcum; extreme emaciation.
2. Ditto incomplete. Phthisis; cavities; granular kidney; albuminuria.
3. Ditto far advanced. Ascites; false membranes covering peritoneum and liver; pneumonia.
4. Ditto partial, affecting margins of lobules. Fever, symptoms resembling those of delirium tremens; pneumonia; hepatisation.
5. Ditto complete. Pneumonia; hepatisation.
6. Ditto partial, margins affected. Sudden death; heart's tissue degenerated.
7. Ditto partial, marginal. Hypertrophied heart; granular kidney, containing some cysts.
8. Ditto partial, marginal. Fever; pneumonia; kidney degenerated.

9. Fatty degeneration partial, affecting exterior half of lobules. Kidney granular, cysted; heart's tissue in a state of fatty degeneration; blood fluid.
10. Ditto partial, marginal. Chronic empyema.
11. Ditto complete. Scrofulous disease of hip; extreme marasmus.
12. Ditto partial, slight marginal, rather oily accumulation. Menorrhagia; extreme anæmia.
13. Ditto partial, marginal. Fever, with head symptoms.
14. Ditto partial, marginal. Suppuration in sub-mucous tissue about epiglottis.
15. Ditto partial, slight marginal. Kidney granular and cysted. Death from injuries from a horse.
16. Ditto advanced state. Encephaloid disease of liver, testicle, lungs, &c.
17. Ditto advanced condition, combined with incipient cirrhosis. Phthisis; renal tubuli infarcted.
18. Ditto partial, slight marginal. Fatty degeneration of kidneys; cerebral affection, with dropsy after scarlatina; tuberculated bronchial glands; miliary tubercles in lungs.
19. Ditto partial, marginal. Maculated fever; kidney not healthy.
20. Ditto advanced stage, margins most affected. Psoas abscess; scrofulous caries of vertebræ; kidney to some extent degenerated.
21. Ditto very advanced stage, associated with partial cirrhosis. Tuberculisation of lungs, not far advanced; fatty condition of kidney; urine albuminous. Died comatose.
22. Ditto partial, slight marginal. Ovarian tumour; hydrothorax.
23. Ditto complete. Circumscribed abscess in peritonæum; cretaceous tubercles in lungs; emaciation.
24. Ditto marginal, slight. Abscess in pelvis; peritonitis.
25. Ditto not quite complete in exterior two thirds of lobules; cells gorged with oil, and breaking up. Bed-sores and abscesses, sequelæ of rheumatic fever; great emaciation.
26. Ditto far advanced, but cells not much broken up; those on margins most affected. Sores and secondary abscesses, after fever; pleural effusion; great emaciation.

27. Fatty degeneration partial, marginal. Acute tuberculisation of lungs; vomicæ; stupor aspect.
28. Ditto partial, marginal. Dropsy after scarlet fever; sub-arachnoid and ventricular effusion; recent pleuritis; anæmia marked.
29. Ditto partial, marginal. Extreme dilatation of bronchi.
30. Ditto partial, marginal. Ovarian tumour, multilocular and solid; emaciation.
31. Ditto general, advanced stage; margins most affected. Incipient granular kidney; dilatation of heart; dropsy.
32. Ditto general and advanced; margins most affected. Acute tuberculosis; pneumonia; prostration.
33. Ditto morbid oily *accumulation* in central half of lobules. Continued fever 16 days; intestine ulcerated.
34. Ditto partial, marginal. Meningitis; pleuritis; abscesses in lungs and liver; injury to head.
35. Ditto partial, marginal, advanced, associated with cirrhosis. Heart enlarged, dilated, flabby; general dropsy.
36. Ditto advanced, but not quite general; associated with cirrhosis. Albuminuria; toxæmia.
37. Ditto partial, marginal. Recent acute pericarditis; diseased kidney; enlarged heart; pleurisy; pneumonia.
38. Ditto very advanced, without breaking up of cells; associated with some cirrhosis. Cerebral affection; meningitis, from inflammation of bones of cranium.
39. Ditto central, oily accumulation. Diseased kidneys; bronchitis; hypertrophied heart; pulmonary apoplexy.
40. Ditto marginal, or more general. Died with cerebral symptoms; lungs full of miliary tubercles.
41. Ditto marginal, very advanced. Died with some congestion of pia mater and hæmorrhagic effusion at base of brain; kidneys granular and cysted; heart enlarged; dropsy.
42. Ditto marginal, with some cirrhosis. Incipient granular kidney; diseased valves of heart; blood fluid; dropsy.
43. Ditto marginal; a broad zone of oily accumulation. Phthisis; large vomicæ; extreme anæmia.
44. Ditto complete, yellow stained. Died with fracture of pelvis, shock to system proving fatal.

45.	Fatty degeneration	complete. Long-standing peritonitis; pneumonia; fatty heart; long suffered from debility and diarrhoea.
46.	Ditto	complete. Phthisis; kidneys healthy.
47.	Ditto	complete. Phthisis; kidneys healthy.
48.	Ditto	complete, universal; associated with slight cirrhosis. Kidneys not healthy; death from unhealthy sup-
puration after removal of scirrhus tumour from breast. The abscess formed in left thigh.
49.	Ditto	complete. Paralysis from non-inflammatory softening of spinal cord; no other disease.
50.	Ditto	marginal. Tuberculosis of lungs and other organs in a boy.

The conclusions which may be deduced from the foregoing Table are—

1. That partial marginal fatty transformation of the lobules of the liver is peculiar to no pathological state, and can hardly be considered morbid.

2. That out of 20 cases of very advanced or complete fatty degeneration, 15 had no connection with pulmonary phthisis.

3. That in about 8 of the 20 advanced cases there was, in all probability, great emaciation; but that in the majority this had not taken place to any great extent.

4. That out of 20 cases of completely fatty liver, only 3 were associated with granular kidney; and in 1 only was there the coincidence with fatty kidney.

5. That of 30 cases of partial fatty transformation, there were 7 associated with granular kidney; but this seems only an accidental coincidence.

Postscript, August 14th.—In one or two instances since the above was written, I have not found the administration of calomel produce any marked quantity of yellow matter in the liver cells. This cannot invalidate the positive results of the above experiments, but only shows that the action of the drug is not always identical, which is not more than might have been expected when various disturbing causes are taken into consideration.