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ON

THE PATHOLOGY

OF

FATTY DEGENERATION.

BY

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FATTY accumulation and fatty degeneration, the physiological process and its pathological counterpart, are not to be placed in strong contrast, or regarded as two functions altogether distinct and practically separable from each other. On the contrary, dissimilar as they may be in some of their phases, they shade into each other at so many points that no exact line of demarcation can be drawn between them. They are directed by the same chemical principles, and the results, as measured by the same anatomical rules, are essentially identical.

Not to lengthen these remarks by an enquiry into the laws of fatty accumulation, it is at least necessary, here, at the outset, briefly to indicate the successive steps by which the physiological merges into the pathological process.

Regarding the subject from a chemical point of view :—

1. In a condition of health, where all the organs are as yet sound and the years few, only such alimentary substances as are not available for immediate use are turned into fat. Obesity in this condition generally results from an excessive use of non-nitrogenous food. The physiological problem here is precisely the same as that which a smoky lamp presents, the carbon in both cases being supplied out of due proportion to the oxygen, and being deposited in the one case as fat, in the other as soot. And a properly devised regimen and diet are as surely successful in preventing the formation of fat in the animal, as adjusting the burner and the feeder are in preventing the formation of soot by the lamp.

2. It is a step lower than this when fatty accumulation results from a deficiency of oxygen rather than from an excess of carbon, when the fat is supplied by the carbon which enters into the composition of the nitrogenous as well as of the non-nitrogenous elements of the food. The remedies here are not so obvious nor so easily applicable, for the system may not be able to bear any considerable diminution of the class of aliments which supply the fatty matter in this case. We cannot leave these off as safely as we can suspend the use of non-nitrogenous articles of diet; and, in advancing years, with which this second stage may probably coincide, the organs have lost something of their original integrity and reparative powers, and answer less readily to remedies.

3. The third stage into which this insensibly shades is lower still. Here the source of the fat is removed yet farther from our control; for it is not formed from the food introduced from without, but is a product of the daily waste of the tissues.

This is the lowest condition of suboxidation. The invading substance itself is more widely diffused, and permeates other parts besides the cells of the common adipose tissue. Our remedial measures are now utterly inadequate to meet the difficulty. The principles to be applied are indeed the same, but their practical application is often quite impossible.*

Again, regarding the subject from an anatomical point of view, following the guidance of Virchow,† we find that fatty matter may accumulate under three typical forms:—

1. In the first of these, which common adipose tissue familiarly illustrates, the cells in which the fatty matter is deposited are adapted for its permanent reception. This is a normal condition, the pathological equivalent of which occurs in the form of fatty tumours, and of local fatty accumulations which resist the common physiological influences to which adipose tissue generally is subordinated. The accumulation, except, usually, in the case of fatty tumours, may arise, and be dissipated, and arise again, without any detriment to the integrity of the containing tissue, whose function is to separate and retain fat for the purposes of the system.

2. The second typical form under which fat accumulates is as a temporary infiltration of parts to whose functions it is incidental to be thus temporarily loaded with fat or oil, which is permeating them for transmission onwards. Such parts are the epithelial glands of the intestines and of the liver. When in active operation they are loaded with fatty matter, and when they have discharged their share of the digestive function the fatty matter passes on and they are free. But when, from any cause, this transmission is delayed, and the oil is retained within the gland cells, and the fatty infiltration becomes permanent, then the physiological line is passed, and a morbid condition results, which is most familiarly illustrated by fatty degeneration of the liver.

3. The third form of fatty accumulation is where this substance is infiltrated into parts which do not contain it in any appreciable quantity in the physiological condition, and where the infiltration is accompanied by the disorganisation of the part. The typical normal illustration of this form is supplied by milk, where epithelium cells are produced in great abundance, only to be infiltrated with fatty matter, and then to be thrown off and die, producing milk as the result of this dis-

* See, on all this subject, Dr. H. Bence Jones's 'Lectures on the Applications of Chemistry, &c., to Pathology and Therapeutics,' 8vo. 1867, p. 170.

† 'Cellular Pathologie,' S. 288.

organisation. This form of fatty accumulation is most fully illustrated in pathology. Instance the fatty infiltration of cells which results in the formation of the compound granular cell. Such, again, are the changes in muscular fibre and in the renal epithelium, which will be considered in detail in the further progress of these remarks.

From both these points of view, anatomical and chemical, fatty degeneration seems to stand as one of the last of a series of retrograde changes by which health shades into disease. Anatomically traced, the gland-cells which should transmit fatty matter under these circumstances retain it, till that which should be a store of available nourishment becomes a permanent mechanical burden, and a hindrance to the functions of the part affected. Again, chemically traced, we find that in fatty degeneration the materials of the food and the products of the waste of the tissues are diverted from their usual destination. Their attraction for oxygen is limited by their chemical affinities, rather than measured, as heretofore, by the physiological requirements of the system generally. They are suboxidised, in chemical language, and take the form of fat.

As we descend in the series, from health to disease, the physiological force, which in the first instance rose superior to everything, and made itself felt throughout, attracting to the growing germ all that was required for its perfect development, sensibly fails. Its life-long antagonist, chemical affinity, now asserts its superiority in turn, so that fatty degeneration, in which this growing superiority seems at last to culminate, has even been regarded by some as a purely chemical change independent of all vital influences. I would venture to make a few observations on this, as it seems to me, untenable hypothesis.

First, generally. We may often find substances of fatty origin belonging to the stearic or oleic series, as, for instance, acetic, lactic, or oxalic acid, or the rancid secretions in acute rheumatism or other febrile affections, occurring as the products of disease in the living body, the results of a degradation of the higher members of their respective series. But we cannot imitate Nature's operations directly in the laboratory. We can neither ascend the scale and make fat from the lower members of the series, nor can we suspend the process of degradation at any given point; nor yet can we change a member of one series into another at will. That is quite beyond our power as chemists. The very limited success which we do reach in such experiments is obtained by working, so to say, with Nature's own tools—by putrefaction, for instance, rather than by a less

complex operation. And, practically, the results are as yet rather curious tricks of the perfumer's trade than available applications of scientific chemistry.

It could hardly be otherwise. The powers by which organic substances are formed, converted, and decomposed in the ordinary physiological processes are wholly unlike those which we bring to bear upon them in our chemical experiments; and the results of Nature's operations are wholly unlike ours. To go no further than the instance before us, the strong affinity by which the elements of the hydrocarbons are bound together, their permanence and their resistance to anything short of destructive chemical agencies, contrast strongly with their extreme plasticity under the influences of the living body. By gentle continuous physiological influences results are obtained which violence and direct chemical action cannot procure. There is the same difference between Nature's chemistry and our own as between leading and driving, as between the gentle breaking up of the rocks by frost and the splitting them by gunpowder. Nature does most by the vis a fronte; our operations are mainly applications of the vis a tergo.

When living materials are acted on, one set of changes takes place, which chemistry can interpret but cannot imitate. But when the physiological influence is withdrawn after death, and chemical affinity has full play, we have another set of products quite different to those which appear during life. Taking our illustration, again, from the subject before us, no known chemical process could make wax out of the honey or sugar in the stomach of the honey-bee. The heat indeed, the moisture, the insufficient supply of air in the dark hive while the swarm is making wax, are all more or less direct chemical agencies which tend to the conversion of the honey into wax. But these must act in live bees to produce the result. The whole process ceases with the death of the bee. Chemical affinity is not the ruling power while life lasts, it only becomes so when life has ceased. Then, under its influence the elements of the body take new forms and move in new directions, the bees fall from their curtain, they undergo putrefaction, and the honey in their stomachs is converted, not into wax, but into alcohol and carbonic acid.

Again, more particularly: observations of certain changes in dead animal matter both without and within the living body have been adduced in favour of this opinion. I. The conversion of dead animal substances by gradual decomposition into a matter known by the name of adipocere has been cited as an

instance of the conversion of animal substances not containing fat into fatty matter. II. And the accumulation of fatty matter in and about certain extraneous substances introduced into the cavity of the peritonæum of living animals has been accepted as a proof that the same conversion may take place within the living organism. I think that neither of these conclusions will stand the test of examination.

I. With regard to the adipocerous transformation. Adipocere is a brittle waxy-looking substance, differing in its chemical characters according to the source from whence it has been obtained. This is the substance so familiar to us in our Museums, the eye-sore of anatomists. We may find it, whenever we want some, in the cavities of the long bones, or in the nervous foramina of the skull. The easiest way of making it is by exposing a large mass of animal matter to the action of very slowly running water. There are other methods more available on a small scale, all acting on the same principle of decomposition at a low temperature, under water, with limited access of air; but adipocere, as familiarly known, is generally obtained by this particular means.

A stock of adipocere for examination was procured from the different sources which the macerating jars of the Sussex County Hospital Museum supplied, and from a large specimen in the Museum of the Royal College of Surgeons. For the liberality with which my wishes were met, and a portion of this specimen placed in my hands for analysis, I beg to express my sincere thanks to the Committee of the College Museum, and to their zealous Curator, Mr. Flower, whose kindness on this, as on other occasions, I have much pleasure in acknowledging.

1. Adipocere obtained from the neighbourhood of the bones of the head of a sword-fish was found to be composed of margaric and oleic acids; the latter in excess, combined with lime. There was a small quantity of unaltered fat and of free fatty acids, also some undecomposed nitrogenous matter.

2. From adipocere which had gathered round human bones, the same general results were obtained; only the margarates preponderated over the oleates, and the saponification was more complete. This last result seemed due to the longer time during which the specimen had been macerating. The adipocere obtained from these sources and from a mass of human muscle burned with a clear flame, leaving a white alkaline ash; but the fat from fatty hearts burned entirely away without any residue.

3. A portion of adipocere from the human thigh (prep. No. 1832*d*, Mus. Coll. Surgeons) was submitted to a most careful analysis, to test in some way the accuracy of the previous observations. It was composed of white stringy fibres powdered over with a dry substance, which lay partly between the bundles of fibres, and partly in distinct masses. This substance had no definite form, and only obstructed the view of the fibres to which it adhered. When it was removed by ether, or, more completely, by cold liquor potassæ, regular fibrous tissue, just such as is seen in muscular fasciæ, came into view. A very little heat sufficed to gelatinise this tissue.

The nature of the different constituents having been determined on separate portions, an exact quantitative analysis was made of ten grains of the specimen, giving:

Free margaric and oleic acids	4·1
Margarate and oleate of lime, with traces of magnesia . .	2·4
A peculiar fibre, containing nitrogen and traces of phosphate of lime	3·4
Water	0·1
	10·0

In the fatty matter here present, margaric acid so predominated, that it was necessary to add olive oil to allow it to crystallise freely in its characteristic form. In this, as in all other respects, this adipocere agreed perfectly with other specimens of adipocere from the human subject, and contrasted strongly with the results of fatty degeneration.*

Briefly to recapitulate. When adipocere occurs in large masses, as in a whole limb which has been submitted to the action of slowly-running water, and where we have the product of the decomposition of various tissues, we find that there has not been a general uniform change of them all. The least destructible of the various tissues—such, for instance, as the fibrous sheaths and fasciæ—are still to be recognised by their microscopic characters. The more perishable, such as the muscular tissue, are represented, after a while, only by a dry amorphous powder, in which the presence of nitrogen may be detected by the usual tests.

But these remains of different tissues are not adipocere. This

* The experiments here referred to were made for me by Mr. James Peel, at that time Dispenser to the Sussex County Hospital. I regret much that I have no longer the advantage of his skill in pursuing this enquiry. The details are reproduced from the Medical Address delivered at Cambridge in 1864. 'Brit. Med. Journal,' 1864, vol. ii. p. 154. To this and to some further observations on the same subject ('Brit. Med. Journal,' 1865, vol. i. p. 475) I shall have again occasion to refer.

is a substance which varies indeed in its composition within certain limits, and which has the special characters of the fat whence it was derived impressed upon it: if, for instance, it has been derived from fish, it consists mainly of oleate of lime; if from the human subject, margarate of lime is in excess. But, otherwise, it is of an uniform and definite composition. It is, in fact, a compound of the particular fatty acid with an alkaline base, perhaps ammonia, or more commonly lime derived from the water used in the process of conversion. If we employ distilled water in our experiments, and withold an alkaline base, no adipocere will be made, but the fat will remain as fat, and will not be saponified.

Further than this. I believe that no fat whatever is made during the adipocerous transformation. Such was the invariable result of all my experiments made, with one exception, on the muscular fibre of the heart. So far from the fatty matter having increased, it was rather diminished in quantity during the process.

For this purpose, however, we must avail ourselves of some of the other processes for the production of adipocere. For however well adapted the process by slowly-running water be for the production of adipocere on a large scale, it is quite inapplicable where great accuracy is required. When the meshes of the net containing the weighed fragments of muscle were fine they became clogged, and prevented the free access of water, and then the muscle putrefied; while coarser meshes allowed fragments of the softened tissue to escape. Notwithstanding all my care, none of the experiments by this method with weighed portions of muscle, of which the fatty constituents had been previously determined by analysis, succeeded. And after varying the apparatus several times, to no purpose, I gave up this mode of proceeding, and made use of the processes by dilute nitric acid or dilute alcohol, with much more satisfactory results, as follows:—

A portion of the muscular substance of a heart which had previously been found to contain 2·14 per cent. of fatty matter, chiefly margarine, was left to soak for twenty months in dilute nitric acid, sp. gr. 1·42 (1 to 16) in a stoppered bottle. At the end of this time the fatty matters were found to amount to no more than 1·1 per cent. of the five hundred grains operated on. The mass had been changed into a substance having the smell and appearance of ointment of nitrate of mercury. The elements of the fat originally existing in the mass had been newly arranged under the influence of the nitric acid, part

having assumed the form of an aromatic ether. Much of the fat had been destroyed; but never at any time during the process was there any evidence of the fat having been increased in quantity.

The muscular fibres generally retained their form, clearly recognisable under the microscope. The fibrils were broken off short into minute fragments; but each of these displayed distinctly either the transverse striæ, or that longitudinal dotting which characterises the stage of granular degeneration already spoken of.

Again, two hundred and fifty grains of pure fibrine from bullock's blood, freed from all fatty matter by ether, were treated in the same way and for the same period. Not a trace of fat, of any of the oily acids, or of the results of the decomposition, could be found on analysis.

A portion of the muscular substance of a heart, which had been previously determined to contain 2 per cent. of fatty matter, was left to soak for eight months in dilute alcohol (1 to 7) in a stoppered bottle. As with the dilute nitric acid, this bottle was nearly filled with the solution, occasionally shaken, but rarely, if ever, opened; and all observations were made on a similar trial solution. At the end of this time the mass was found to contain 1·92 per cent. of fat and fatty salts of whatever kind. The fat seemed to have been destroyed, to this extent, by the process to which the muscular fibre had been submitted.

To the naked eye, the muscle thus acted on appeared as a reddish, flocculent mass, in which the division of the fibres into bundles was indistinctly perceived. Under the microscope, however, all was obscure. A few granular fibrils could be picked out here and there; but the rest was an indistinct, flocculent mass, with something of a linear arrangement. It contained a few white, opaque grains with a radiating structure, apparently composed of a soap of lime. No loose fat appeared anywhere, and ether had very little effect in clearing the field.

I would pass over the effect of slight decomposition on muscular fibre in inducing seeming fatty degeneration, with the remark that, complete as the deception is to the eye, the truth is plain at once on chemical analysis of the suspected structure. In no sense of the word, nor at any step of the process, is adipocerous transformation a conversion into fat.

II. Again: it has been asserted, on the faith of certain experiments, that dead or extraneous animal substances may be converted into fat within the living body. In the absence

of the original records of these observations, I quote from Lehmann,* and from a summary by Mr. Simon.† I am quite sure that everyone conversant with the difficulties of experiments on living animals, and sharing my dislike to witnessing them, will excuse my not having repeated them.

The experiments may be divided into three classes:—

1. Portions of animal substances containing little or no fat, as for instance of the crystalline lens, of coagulated albumen, and such like, were inserted into the peritonæal cavities of living animals. After periods of from four to eight weeks they were removed and examined, when they were found much reduced in size and altered in chemical composition, containing very little protein-substance, but a large quantity of fatty matter (Wagner, Michaelis).

2. Porous substances, such as cancellous bone or elder-pith, inserted in the same way, were found, after a certain time, to contain much fatty matter in their pores, and the coagulable lymph with which they had become invested was also rich in fatty matter (Burdach).

3. The same class of substances as were used bare in the first series of experiments, when covered with collodion, or enclosed in glass bottles, underwent no fatty transformation (Burdach).

These experiments seem to me to prove that if the extraneous substance be protected from contact with the fluids of the living body, no fat is deposited in its interior. But wherever this contact is permitted, fatty deposition takes place, and this whatever the nature of the extraneous body. The substance, animal or vegetable, sponge, elder-pith, pumice-stone, or muscular fibre, is infiltrated with fatty matter simply according to its permeability to the fluids of the living body which contain the fatty matter. And there is no more reason to suppose the fatty matty to have been derived from one than from another class of extraneous substances, from the muscular fibre than from the elder-pith. In all of them alike it is merely an infiltration and deposition, deeper and more abundant according to their porosity, and to the facility with which the living fluids bringing fatty matter from the blood can enter them.

The process of fatty degeneration, if I am correct in these inferences, is not adipocerous transformation, nor does it ensue in dead animal substances—dead as we commonly understand the word. What it is may be more positively stated, after we

* 'Physiologische Chemie,' 2te Auflage, S. 345.

† Holmes's 'System of Surgery,' vol. i. p. 11, article Inflammation.

have carefully examined the mode of its occurrence in some of its well-marked forms.

A complete history of fatty degeneration should be coextensive with physiological histology. It would require an account of how each and every tissue is affected by this morbid process, and a description of their characters severally, under this condition. Instead of following out the subject in such detail, I propose to myself to investigate the general principle which is common to all these manifestations, rather than to recount the varied forms which fatty degeneration may present in different structures. For this purpose it will be necessary to examine thoroughly the process of fatty degeneration as displayed in a few typical instances. And it seems best, on all accounts, to select these instances from the structures which have been made the subject of special study by other observers. In no other way could an equal security against errors, either of observation or of judgment, be obtained.

I propose, in this view, to commence with the instance to which I have paid much attention during many years, namely, fatty degeneration of the muscular structure of the heart, connecting with this the fibre of voluntary muscle. Fatty degeneration of the liver and kidneys supplies two well marked and well studied instances of this process in glandular structures. Fatty degeneration of the placenta offers another instance well adapted to our present purpose, both by the peculiar structure of the organ, and by the fact of this change having been closely examined by other observers. To these instances, having long waited in vain for specimens on which to repeat Mr. Canton's observations on arcus senilis, I have added an abstract of his conclusions without any re-examination.

I trust, at some future time, should opportunities allow, to publish the results of the study of fatty degeneration of some other structures. The pathological conditions known as acute yellow atrophy of the brain, rickets, and cirrhosis of the lungs are those which chiefly invite attention as offering the means of testing the correctness of my present conclusions from different points of view. But the appearance of this paper has been so long delayed from various causes, that I prefer to publish it in its present form, rather than to wait for time to carry out another series of observations. The accordance of all the results hitherto obtained, whether from my own observations, or the independent researches of others, gives me confidence that a farther extension of the enquiry will only tend still more to confirm them.

Fatty Degeneration of striated Muscle.

Fatty degeneration of voluntary or transversely striated muscular fibre has a particular claim to our notice as the instance in which this pathological process has been chiefly studied. There are some differences observable in the process as transacted in the heart and in the voluntary muscles respectively, such as to require a separate description in each of these parts. And, first, of fatty degeneration of the heart.

Our knowledge of this disease does not run very far back. Frequent notices, indeed, occur in the older writers of sudden deaths which one can scarcely doubt were due to this change in the structure of the heart; and there are recorded observations of pale soft hearts which one feels sure the microscope would have found to be fatty. But there were no microscopes then available, or they did not stand, as now, at the anatomist's elbow, and fat hearts then arrested the attention which should have been given to the fatty hearts which we have only recently learned to distinguish as such.

A full bibliography of the subject has been compiled by Dr. E. Wagner,* and the labours of British pathologists have not suffered at the hands of their generous fellow-workman. Some later additions to the list may be found in Blachez's† thesis on fatty degeneration in general. The English student will find in Dr. Stokes's valuable work‡ a complete summary of all that has been made out on this subject, and references to the writings of the pathologists of the Dublin school, with whom fatty disease of the heart has long been a favourite study. I need scarcely allude to the classical essay of Dr. R. Quain,§ which perhaps has contributed more than any other paper to spread the knowledge of this disease, nor to Mr. Paget's lectures,‖ where the pathological picture is put before us with all an artist's skill; and if I add a reference to my own writings¶ here, it is as my plea to be heard on a subject which is still a favourite with me, and still, I think, capable of further elucidation by such studies.

Fatty degeneration of the heart, strictly so called, occurs in

* 'Die Fettmetamorphose des Herzfleisches.' Gr. 8vo. Leipzig, 1864.
† 'La Stéatose.' 8vo. Paris, 1866.
‡ 'The Diseases of the Heart and the Aorta.' 8vo. Dublin, 1854, p. 302.
§ On Fatty Diseases of the Heart. 'Med.-Chir. Trans.' vol. xxxiii. p. 121.
‖ 'Lectures on Surgical Pathology.' Second edition, p. 94.
¶ 'London Medical Gazette,' 1849, vol. ii. p. 739; 'British Medical Journal,' 1864, vol. ii. p. 152; and 1865, vol. i. p. 475.

two forms:* viz., a circumscribed and a diffuse form; the first being a chronic, the latter generally an acute form of disease. A third division may conveniently be added, which anatomically might be said to be allied to the circumscribed form, but pathologically takes its place among the most acute affections of the heart.

1. In the first form the disease occurs in minute pale specks chiefly found on and in the substance of the carneæ columnæ of the left ventricle. Sometimes the whole lining of the ventricle may be mottled with little spots of this kind seeming to run in zigzag lines; and sometimes they are observed beneath the pericardium. But their most familiar seat is in the musculi papillares of the left ventricle. They are found in connection with debilitating influences, such as hæmorrhage, long continued cachexia, and habitual intemperance. The circumstances under which they occur allow the disease to go on to produce those further changes which in the more widely diffused forms are necessarily interrupted by an earlier death. Within the narrow limits of these little specks the process may be traced from beginning to end; though, as these changes require time for their development, it is not in the same specks, nor always in the same heart, that the complete history can be followed out. The pale zigzag spots, the appearance most frequently displayed, belong to the later stage of the process where actual fatty infiltration has taken place, and perhaps atrophy of the fibres subsequently ensued. The indications of the early stage, of the actual commencement, are to be sought for in the little purpurous spots which dot the interior of the left ventricle in fever, hæmorrhage, phthisis, and other such-like exhausting diseases. Sometimes these spots are no more than what they appear to the unassisted eye, namely, mere ecchymoses beneath the lining membrane. At other times we may trace within these narrow limits the anatomical history of the lesion. In the muscular structure of the heart of a poor girl who died of pyæmia—to quote a carefully observed instance of this change in its minuter manifestations—were red patches, looking like ecchymoses, of a deep purple mixed with grey in the centre, becoming gradually paler at the edges. In the grey part there was a mixture of pus and blood, with fragments of muscular fibres. Surrounding this was a zone, in which the muscular fasciculi had lost all traces of striæ both transverse and longitudinal, they were simply granular all over. Then, for a space,

* Wagner, op. cit. p. 9.

the fasciculi were longitudinally striated, just as is seen in degeneration of the voluntary muscles. Outside this zone the muscular structure presented its normal appearance.

2. In the second or intermediate form the muscular structure is affected over a much wider extent. It seems to commence deep in the muscular structure, the wall of the left ventricle being affected by preference. As it spreads it approaches nearer the inner than the outer surface, involving whole layers of fibres in its progress, and following the direction of the fasciculi. The muscular fibres thus affected are of a bright yellow colour, so bright as often to give the idea of purulent infiltration. However, there is no purulent infiltration here; there is neither pus nor fatty matter in these discoloured patches, the yellow appearance being entirely due to decoloration of the muscular tissue. After a short exposure to air the bright yellow colour fades, and it is not long distinguishable in preparations preserved in spirits.

These broad patches are separated from the surrounding healthy structure by a deep red zone, the existence of which here, as in the form just described, marks an early active stage in the process of degeneration. We do not find the buff coloured spots in the interior of the carneæ columnæ, where the advanced stage of the disease leads us to infer that it has been long in progress, thus encircled. But it is round the seemingly recent purpurous specks, and round the bright yellow patches where the disease is still in an early stage, that the zones are found. The line of demarcation is not a line of separation like that which surrounds masses of so-called capillary phlebitis in the spleen and kidney. At least I never have found any satisfactory evidence of such separation having been effected. It looks like a sign of the presence of inflammation, which yet, judged by its results, as we understand the term inflammation, we can scarcely call it. Thus much at least, however, we may infer from its presence, namely, that increased vascular action is necessary for the process of complete disorganisation which ensues within the limits circumscribed by this zone.

The causes of this form of the affection are peculiar. It is found in connection with inflammation of the heart, by whatever means this may have been induced. Rheumatic inflammation extending from the pericardium seems, though I have never actually seen this change on dissection under these circumstances, to be a frequent cause of it. Over-training and athletic exercises pushed to foolhardiness do mischief in this way,

and so, more rarely, does overwork accompanied by misery and privation.

3. In the third form we find the affection generally diffused over the whole organ, which is then of a dull fawn colour, soft and rotten, moulding itself on the hand like a wet glove. In connection with this general change we may often find the familiar traces of the first form of this disease dotting the interior of the left ventricle; and habitual intemperance is a condition common to both these forms. This form, as a rule, is the anatomical expression of that peculiar cachexia, whether of old age or of less advanced years, which centres in and is often limited to the heart. It owns no recognised cause, and yields to no known method of treatment. Sometimes it is betrayed by the general signs of pallor and debility and cachexia during life. It is more frequently only discovered after, and as the explanation of sudden death.

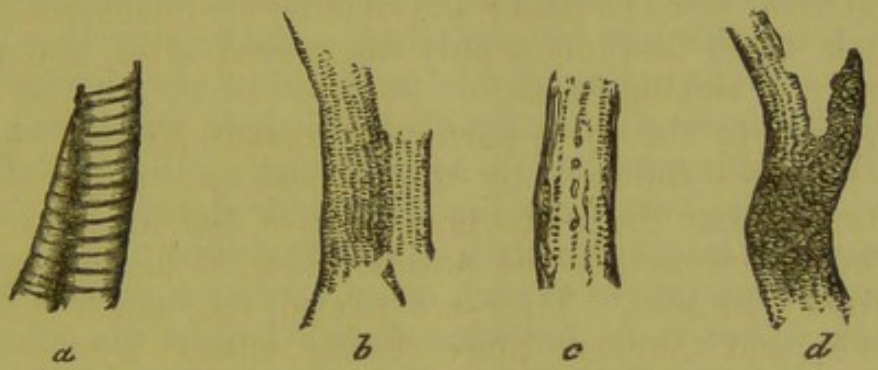
Proceeding to the more particular examination of the anatomical changes induced by the disease, we must observe, at the outset, that the transverse striæ of the muscular fibres of the heart are not, in the normal state, so distinct as those of voluntary muscle. They are placed, too, much nearer to each other, and they are more readily effaced by the use of glycerine in their preparation for the microscope.

In the commencement of fatty degeneration the striæ become less distinct, breaking up into rows of dots or granules, which, transverse in the first instance, in a somewhat more advanced stage affect the longitudinal direction. This appearance of granular disintegration is induced by other influences besides fatty degeneration. It is due to disintegration or disruption of the various elements contained in the primitive fasciculus.* It may be induced in the living body by inflammation, and after death it accompanies commencing decomposition, or attends on the action of certain chemical agents.

Commencing decomposition simulates very closely that change in the heart's muscular structure which is known as the first or granular stage of fatty degeneration. I have been deceived by it myself; and such a mistake is all the more likely to occur, because granular degeneration, like decomposition, may involve the heart uniformly over a very wide extent; much more widely than distinct fatty degeneration ever does, probably because the destruction of the muscular fibres is less complete.

* Todd and Bowman, 'Physiological Anatomy,' vol. i. p. 152. 8vo. London, 1845.

The pathological process is most perfectly imitated by prolonged maceration in dilute alcohol. By this the sarcous elements are disintegrated along the longitudinal lines of cleavage. By prolonged maceration in dilute nitric acid, disintegration is effected in both the longitudinal and transverse directions, and the fasciculus is resolved into small squarish powdery fragments. By varying these processes the results may be modified; and by such means the muscle may be disintegrated at will, in either direction and to any extent, independent of fatty degeneration. But, whether in the living or the dead body, and by whatever means induced, whether real or artificial, there is no increase of fatty matter in the product;



Changes induced in the muscular fibre of the heart in the course of fatty degeneration—

a. Healthy muscular fibre.

b. Granular degeneration, the transverse striation exchanged for longitudinal dotted markings.

c. Commencing fatty infiltration; the granular dots have been partially removed, and the centre of the fibre contains a few drops of oil.

d. Completed fatty infiltration and shrinking of the fibre where it is not distended by retained fatty matters.

All these figures are reduced to a scale of about 300 diameters, from drawings made by the aid of the camera lucida, with a one-eighth object glass.

the optical appearance is due to a mechanical change in the structure of the fibre. It is not a degeneration into fat, but a disintegration into granules—granular disintegration. Chemical analysis tells us distinctly what it is not, and microscopic examination is equally explicit as to what it is.

The granular fasciculi which result from the pathological process, or from any of these chemical reactions pushed only so far as to imitate it, require a high power to display the exact nature of the changes which have taken place. With a magnifying power of about 240 diameters only, it seems as if the transverse

striæ had been replaced by longitudinal rows of dots, divided here and there by other rows of larger and darker dots, and by fine lines. These appearances are explained by the application of a power of 450 diameters or more, which shows that the transverse striæ are not really lost. They are paler indeed than in the normal condition, but they preserve their normal distance from each other. The primitive fasciculus seems to be split into ribbons of unequal width by longitudinal fissures interrupting the transverse striæ. In consequence of these interruptions, such striæ as catch the eye with a lower power seem to run into rows of dots, and this false impression is heightened by the rows of larger and darker dots which occupy some of these longitudinal fissures.

The examination of this altered structure of the heart is much facilitated by the use of glycerine, according to Dr. Beale's directions. Unfortunately, this medium, so very useful in unravelling the fasciculi, greatly obscures their transverse markings. But this is remedied, to some extent, by the application of ether, which dissolves away the large dark dots in the fissures, and brings the transverse striæ again into view, drawing them at the same time nearer to each other, so that eight now occupy the space where only six were found before the ether was applied. Without the use of ether, the transverse striæ may be brought again into view by means of a condenser and a narrow stop. As the various objects in the field come out more distinctly, some longitudinally striated fasciculi may perhaps be recognised among the degenerated fibres; and from the ends of some of these which have been broken during the manipulation, ragged filaments may be seen projecting, just as we shall see presently in degenerated voluntary muscle. These filaments vary in length and breadth, but all have the transverse markings; some are broader; some are so fine that they might be fairly said to represent the old so-called ultimate fibres of muscle, their dimensions scarcely admitting of the presence of more than a single row of the component granules.

In the next stage all traces of transverse marking are lost. The few granules which still affect any regular arrangement are disposed in the longitudinal direction; they are no longer of uniform size, and oil-globules are to be seen mixed with the other molecules. Besides the optical evidence of the presence of minute oil-globules which have, at this stage, infiltrated themselves among the disintegrated sarcous elements, and of larger oil-drops which crowd the field of view, we now have

chemical proof that a new element has been introduced into the mass of tissue, and that the nitrogenous constituents have been replaced to this extent by fat. Not by margarine, the fat which is to a great extent characteristic of the human body, but by oleine, which is the fat of old age, the fat of disease.

The shortness and brittleness of the fibres which have undergone this change are qualities not very obvious under the high powers which are most conveniently employed in the enquiry, but they are nevertheless very important in relation to the connection which exists between rupture of the heart and fatty degeneration. Unnoticed, perhaps, in an ordinary microscopic examination, it is obvious enough, when we attempt to trace a fibre for any considerable distance, that fatty or granular fibres cannot be traced out with the same facility or to the same extent as healthy ones. By this mode of proceeding, we also find that a fibre is not always uniformly affected along its whole course, but that it may be granular in one part and fatty, or perhaps healthy, in another. Sometimes the outer part of the fibre may still display traces of the normal structure, while a row of oil-globules runs up the centre. The fact of the development of muscular fibres proceeding from more than one nucleus would lead one to expect that their decay might also proceed simultaneously from more than one point.

The third stage of this process is, as has been already remarked, more often reached in the circumscribed than in the more diffused forms. At this point the regular arrangement of the internal structure ceases to be distinguishable. At the same time, the fibre loses its symmetrical outline, swelling up in the parts where it is permanently distended with opaque fatty matter; or, where this is not the case, dwindling away. At last, a bundle of irregular threads, or the appearance of a cicatrix, may be all the evidence of the former occurrence of fatty degeneration which has passed through all its stages and gone on to its natural termination in obsolescence of the affected fibres.

We must not confuse this obsolescence, which is the ultimate result of fatty degeneration, and, as such, always of very limited extent, with that general induration of the muscular structure of the heart to which the term fibrous degeneration is, perhaps, more commonly, though less accurately, applied. This is an obsolescence, and betrays, in the irregular shrunken elements of which the resulting structure is composed, the history of its origin. Such a structure is merely

the remnant of the frame which has collapsed on the decay and removal of the parts which it held in connection.

The other process is the substitution of one healthy tissue for another in obedience to the altered requirements of the organ. The fibrous tissue in such indurated hearts replaces a certain proportion of the muscular tissue over a large extent, perhaps over a whole auricle or ventricle. It is found chiefly, but not exclusively, in connection with mixed hypertrophy and dilatation, affecting by preference the thinner portions of the heart's walls. The muscular tissue, under these circumstances, becomes hard and elastic; the cavity retains its shape when cut open; the muscle creaks under the knife; and the cut surface looks paler than natural, but of a white rather than a yellow hue. And under the microscope the explanation of these changes appears in the substitution or the addition of an unusually large amount of fibrous or fibro-cellular tissue.

In the heart this fibrous adventitious structure is employed to resist dilatation; it is the alternative of hypertrophy, the substitution of a mechanical for a vital force. The same substitution is occasionally found in the neck of the pregnant uterus. But the differing functions of the heart and of the uterus lead to different results from the presence of this misplaced tissue in the two organs respectively; and in its occurrence, I believe, lies the explanation of that terrible accident, rupture of the uterus during labour. As far as I have seen, a ruptured uterus does not give way from rupture of fibres which have undergone fatty degeneration; indeed, I am not aware that this form of disease occurs at all in the pregnant uterus. It is ruptured, not at its weakest, but, mechanically speaking, at its strongest point, the torn edges displaying strong fibrous tissue, and not degenerated fibres.* On the other hand, it appears that hearts which have undergone fibrous transformation are not liable to rupture. But, while this change resists dilatation most efficiently, at the same time it limits the contraction of the chamber of the heart thus involved, and reduces it so far to the condition of a mere containing vessel.

Fatty degeneration of the voluntary muscles is essentially the same process as fatty degeneration of the muscular structure of the heart. But there are certain differences, most strikingly shown in the ultimate results, referable to differences in the functions and the anatomical structure of the two fibres

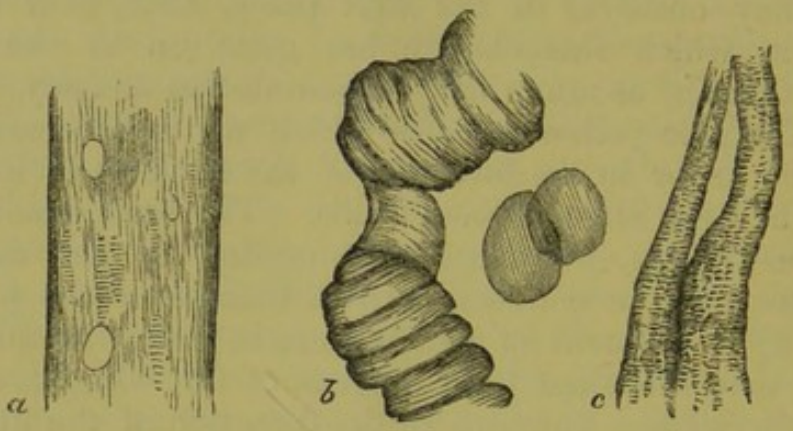
* See some observations on the subject in the 'Lancet' for 1860, vol. ii. p. 306.

respectively. None of the pathological differential characters are absolutely foreign to the muscular tissue of the heart, but some of them are very rarely met with and indistinctly seen there, and can only be thoroughly understood by studying them in their more usual seat, and in their fuller manifestation, in the voluntary fibres. The necessity for a continual action of the heart for the maintenance of life, which affects the process and ultimate results of fatty degeneration of this organ, does not apply to the voluntary muscles, and in these, accordingly, the process more often goes on to its natural termination. In these ultimate results, the anatomical differences of the two kinds of fibre are to be traced.

We may observe, in the first place, that, in a voluntary muscle in which this change has gone on to the extreme degree, there is as much fatty accumulation as fatty degeneration. The pale yellow muscles which we find occasionally in sheep's backs or in the forearms of the subjects of lead-palsy, supply the best illustrations of this. The most readily-accessible illustrations, however, are supplied by the muscles of limbs atrophied in connection with disease of the joints. If we tear up a fragment of such a muscle under the microscope, we find that the chief bulk consists of fat, which is deposited in lines or strings running in the direction of the fibres; not replacing them, but lying in their interspaces—lying, in fact, just where fat lies in healthy, well-fed animals. Between these lines of fat, and occupying much less space than they do, we find muscular fibres in all conditions—from perfect health to the most extreme degeneration. And, besides, bands of fibro-cellular tissue occur, which add very much to the difficulty of the dissection. Such, and such general fatty degeneration as we find in the heart occurs very exceptionally in voluntary muscles.

The first stage of fatty degeneration of the voluntary muscles, as far as I have been able to satisfy myself, is characterised by swelling of the affected fasciculi. For a greater or less length they appear uniformly dilated to about twice the size of the healthy fasciculi, smooth on the surface, seemingly wanting the transverse striæ, but streaked longitudinally with fine linear markings running the whole length of the fibre. These may not be very distinct in their even course, but where the fibre has been stretched, or twisted, or broken across, they come out quite clearly. Sometimes they are gathered up into a point like the end of a camel-hair pencil; at other times the broken fibres look like the unravelled ends of a rope with the

strands hanging out, having undergone at these points complete longitudinal disintegration. A higher power shows here, as in the muscular structure of the heart, that the transverse striæ still exist, only they are much paler than natural. They are not interrupted by the longitudinal markings. They are approximated to half the normal distance, sixteen of them occupying the same space as eight do in a healthy fibre. Ether does not cause them to approximate more closely, though it seems to shrink up the fasciculus; and it displays the longitudinal markings very clearly, at the same time that it extracts some fatty matter from its interior.



Changes induced in voluntary muscular fibre in the course of fatty degeneration:—

a. Swelling of the fasciculi with longitudinal streaking. The transverse striæ approximated where still visible.

b. Transverse disruption of the swelled fasciculi. Two fragments have separated entirely from their original connection. The articulated masses are held in connection by an empty string of thickened sarcolemma.

c. Granular disintegration with atrophy of the fasciculus.

These figures were drawn in the same way and to the same scale as those of the changes in the heart's fibres, but they are here represented enlarged only about 150 diameters.

This longitudinal cleavage would seem to hold nearly the same relation to fatty degeneration of voluntary muscle as granular disintegration bears to that of the heart. Nearly, for it passes more directly into fatty degeneration than the corresponding change in the heart does, ether readily extracting oil from the streaked fasciculi. And it is more specifically a pathological process, being much less readily imitable by any artificial reactions. For chemical decomposition and putrefaction do not induce this particular appearance, but seem, as far as I have observed, to pass over it to a further stage, converting the fasciculus at once into a finely granular mass, which

retains only the outline of its former structure. This process of conversion may be traced in some of the transverse striæ which have survived the rest. These appear distinctly granular, broad, and uneven; as if falling to pieces under the action of the dilute nitric acid which has disintegrated the sarcous elements elsewhere. The striæ seem to persist longest just beneath the sarcolemma. Some fasciculi which appear granular owe this deceptive appearance to the striæ on the two opposite apposed sides of the flattened fasciculi crossing each other diagonally, the regular arrangement persisting on the surface for a while after the sarcous elements in the interior have been deranged or have been dissolved entirely away.

Sometimes these large pale waxy-looking fibres occur alone. More commonly, however, we find mixed with them round or oval masses, which seem, from their general appearance and dimensions, to have originated in the breaking up of the longer fibres. These may be either striated longitudinally, or minutely granulated, like the fibres from which they seem to have originated by a transverse fracture of the brittle fibre. This transverse cleavage is displayed most strikingly in fragments of a very peculiar form which are rarely met with. It was from the neighbourhood of an aneurism that I have been supplied with the best specimens of muscle which had undergone this very peculiar form of disintegration. The transverse divisions were in this instance so very regular, and the appearance was so unlike muscle and so like muscular entozoa, that it was only on Dr. Beales's corroboration I ventured to conclude that the masses in question were, or rather had been, really muscular.

These are neither granulated nor streaked longitudinally, but they are cracked and broken transversely, and they are often connected at either end, as if they had but partially escaped, with a string of sarcolemma. They have a singular affinity for the colouring matter of carmine, which tinges them more deeply than any of the other structures which the altered tissue presents. Though they are found under the same circumstances as, and in connection with, the pale waxy-looking fibres already described, yet I am not sure that this transverse splitting is one of the series of pathological changes which lead to fatty degeneration. I am, as yet, uncertain whether these fragments, with the rounded granular masses and the more enigmatical articulated forms, do not melt away without undergoing any further change.

Coincidently with the disintegration of the sarcous elements

the investing membrane of the fibre is thickened. It may be traced in its passage from one wrinkle of the fibre to another, stretching across between two portions which have been displaced, or, perhaps, lying in folds, like a loose stocking, where the fibre has been pressed in at the ends. The thickening of the sarcolemma is accompanied by the appearance of numerous irregular fragments which cloud the field of the microscope. Some few of these are the nuclei of the muscular tissue; others, and these the most numerous, are apparently the rudiments of fibro-cellular structure; others are of uncertain nature; and many are undoubtedly collections of oil-globules, arranged like rows of squarish beads. These last are removed by ether, which clears the field a good deal, while acetic acid has very little effect in this way. And with these are a number of larger loose oil-globules, which have been set free during the manipulation of the tissues.

As in granular disintegration of the fibres of the heart, so in that of voluntary muscle; the longitudinal markings, which have replaced the transverse striæ, are in their turn obliterated. Dots appear, first in regular lines, then without order; and the total disruption of the sarcous elements and all their subsequent changes follow in the order which has already been traced, and might be described in the same words as have been employed to tell the complete history of fatty degeneration of the heart.

As in the muscular fibre of the heart, these preliminary changes occur in connection with other processes besides fatty degeneration, and notably with any local irritation. Like granular disintegration of the heart, they indicate a condition which may terminate in fatty degeneration, but in which, thus far, no fatty degeneration, no change of the chemical composition of the structure has taken place. Here, as in the heart, the results of commencing decomposition are, as far as we can trace them, identical with these organic processes. Here, as in the heart, is a common point from which the two series of changes—the chemical and the pathological—diverge to their respective terminations. And, before dismissing this branch of the subject, it will be of interest to point out some of the various pathological conditions which tend to this common point.

The changes which we have just been considering as preliminary to fatty degeneration are identical with those which Dr. Zenker* has described, and most beautifully delineated, as

* Zenker, 'Veranderungen der willkührlichen Muskeln in Typhus abdominalis.' Leipzig, 1864.

occurring in the voluntary muscles in the course of typhus fever. The pale swelled fibres with linear markings, the rounded granular fragments, the scattered nuclei and embryonic connective tissue, as displayed in his plates, might be taken as exact illustrations of the stages of fatty degeneration. The same familiar forms appear again in Dr. Bennett's* figure of the changes induced by cancerous tumours in the muscles in their immediate neighbourhood. But perhaps the most interesting observations on this subject are those made by Mr. A. Stuart,† of Petersburg, detailing the results of an enquiry into the effects of inflammation on living muscle.

By the application of nitrate of silver to the muscles of frogs, changes were induced in them identical with those which we have just traced in the heart. The parts directly exposed to the chemical action of the caustic swelled or shrunk up, and their texture was destroyed. But those a little further off underwent a regular series of changes, of inflammation in fact, which Mr. Stuart describes with great minuteness. Thus, briefly, first the muscle became pale and more transparent than natural; then the sarcous elements seemed to break up and arrange themselves in longitudinal rows; then these dots became larger, though still remaining sarcous elements. These changes occupied two or three weeks, the process thus far being disintegration rather than degeneration, no fat having as yet appeared in the altered fibres. Then the last stage set in, namely, the conversion of the albuminous substance into fatty matter.

The conclusions which seem fairly deducible from these observations on fatty degeneration of both kinds of striated muscle may be expressed in a few sentences.

Inflammation, anæmia, cachexia, want of nutrition, and all the other causes to which fatty degeneration of the heart has been ascribed, have thus much in common, that they disorganise the fibre and prepare it for ulterior changes. The fibre is functionally destroyed by these means, and the disintegration is a change which ensues in the disorganised tissue.

The first step which we can recognise in the process of, or towards, fatty degeneration of muscular tissue, is longitudinal or transverse disintegration of the sarcous elements into filaments, or discs, as the case may be. Circumstances will determine which of these forms the disintegration shall take, and, probably, the exciting cause of the disease has a certain

* 'On Cancerous and Cancroid Growths,' p. 105, fig. 121.
† Schultz's 'Archiv für microscop. Anatomie,' i. S. 415.

influence in this particular. But, although the exciting cause may have a modifying influence, the general course of the degenerative process is guided and transacted by the ordinary agency of the living body, irrespective of these partial influences.

The actual fatty degeneration is secondary in every sense to this disintegration. Its occurrence depends on the existence of fatty matter in the blood available for this purpose. And it is conceivable that, for want of an available supply of fatty matter, disintegration should not be followed by fatty degeneration at all. If this be true, a question suggests itself, whether this explanation be limited to fatty degeneration of muscular tissue, or whether it has a wider bearing. The answer to this question must be sought in the examination of fatty degeneration of other tissues.

Fatty Degeneration of the Liver.

Fatty degeneration of the liver supplies at once the most familiar and convenient illustration of this form of disease as it affects glands. There are difficulties in the investigation, arising partly from the complexity of the organ, and partly from the fact that fatty infiltration is, to a certain extent, a normal condition of the hepatic glandular structure. But we have nothing to do with these sources of difficulty just now. For, in the first place, we are, from the present point of view, only concerned with the proper secreting structure. When fatty degeneration of the liver is spoken of, unless some other structure is specially named, it is generally understood to denote fatty degeneration of the glandular epithelium which fills, in whatever way, the lobules of this organ. Again, we have not here to determine the precise point at which fatty infiltration of the hepatic cells passes the physiological limits and constitutes a morbid change. For it is only when the nature and degree of the change is quite unequivocal that it comes within our present scope. These questions, all-important in considering the history of fatty degeneration of the liver in itself, have but a secondary importance in relation to the subject of our present enquiry, namely, the general pathology of this affection.

As in the heart, so here in the liver, fatty degeneration may pursue its course in different ways, and with different degrees of rapidity. We may find general fatty infiltration pervading the whole organ, in a form whose progress we measure by

months or weeks, and which we connect with excessive absorption of fat from the alimentary canal or with its defective elimination from the lungs. Or we may find the results of a more chronic change, where we date by years or months, and where the history of the disease may be traced in the successive stages of its progress, as displayed in different parts of the organ. And yet again, though more rarely, we may find in a very unusual form of disease, known as acute yellow atrophy of the liver, a clue to the general pathology of fatty degeneration of this as well as of other organs. The diffused form of fatty degeneration of the heart finds a parallel in the changes which occur in the liver. And so, too, though the total amount of the changes which the heart displays, under the circumstances, falls far short of those which cirrhosis induces in the liver, does that circumscribed form which runs on uninterrupted to its termination in the carneæ columnæ of the left ventricle. Nor, as we shall presently see, is acute yellow atrophy of the liver a change so entirely sui generis. The mode of its extension and its results are strictly comparable to those of what we have already described* as a special form of affection of the muscular structure of the heart.

Fatty degeneration of the liver, as familiarly known, appears, in the first instance, to be merely an increase of the amount of oily matter which is found in the physiological state in nearly all the hepatic cells. The gland-cells at the outer edge of the lobule are chiefly thus affected. The oil-globules may be larger as well as more numerous than those which occur in health, but this does not seem to impair the functional activity of the cells which contain them. For these cells still retain their nuclei, and still, mostly, contain bile; and, doubtless, many a liver advances thus far in the appearance of disease, and then returns within the physiological limits.

When the change is more widely extended, involving the lobules more deeply, as in some cases of pulmonary phthisis and in the cachexia of drunkards, we cannot doubt that we have to deal with something more than a temporary infiltration of fat. We find now a large number of loose oil-globules, which have been set free by rupture of the hepatic cells that had contained them. And in a large proportion of cells no nuclei are to be seen. These cases, however, illustrate only one stage of fatty degeneration, and give less insight into its anatomical history than do those where the affection has been more

* Page 42.

partial and less rapid in its progress, such in fact as cirrhosis supplies.

In the next stage, so abundantly illustrated in the dissecting room of every hospital, the fatty infiltration may seem to have changed its situation. It no longer appears in zones corresponding to the capillaries of the portal circulation, but in the form of little opaque ochrey spots, surrounded by rings of clearer pale tissue. The microscope tells us that these opaque yellowish specks owe their peculiar appearance to the presence of numerous hepatic cells which are loaded with fatty matter and stained with bile. These cells are unusually coherent, and the fatty matter which they contain is not, I think, so easily soluble in ether as that which is found nearer the edges of the lobules in an earlier stage of the affection. The proportion of cells which have no visible nuclei is constantly on the increase, with the advance of the disease. The pale somewhat transparent tissue which surrounds these opaque yellow specks seems to be composed of a fibro-cellular substance containing the vessels, now shrunken and obsolete, but no trace of the glandular epithelium of the original structure.

The history of the process seems complete, as gathered from different specimens representing these successive stages. Apparently the process of degeneration has travelled from the circumference of the lobules to the centre. First the cells became permanently infiltrated with fatty matter; then they were shed, and none were produced in their places; while the space which they had occupied—the cavities, if I may assume thus much, in which they grew—collapsed. And a tough fibro-cellular tissue resulted, traversed by shrunken vessels suggestive of the cause of the portal obstruction and of the dropsy by which the last stage of fatty degeneration of the liver is so commonly attended.

The mutual connection of these changes is very distinctly shown in the form of disease already alluded to as acute yellow atrophy of the liver.* For the most part this is an acute form of disease effecting the disorganisation of the liver in a few days, accompanied by fever and delirium, and characterised by the brightest yellow jaundice. In such cases few or no hepatic cells are to be found in the parts of the liver which the disease has invaded—perhaps the whole of the organ—only loose oil-globules and particles of bile. These cases, however, are less intelligible, and less applicable to our present purpose than those where the progress of the disease has been slower. For, under

* Rokitansky, 'Path. Anat.' ii. S. 313, 2te Aufl

such circumstances, as the longer period allows, the line of demarcation between healthy and diseased tissue is more strongly drawn, and the successive stages by which the final disorganisation is reached are more clearly to be traced. To this less common form of the disease I wish particularly to call attention.

The healthy tissue, in this form, is represented by bright yellow round nodules easily separable from the rest of the organ, some appearing even to be encysted, on account of the consolidation of the interlobular connective tissue which surrounds them. If the yellow colour is not apparent at first it is brought out on exposure to the air, when the whole surface appears mottled with bright yellow and deep purple in the strangest manner. These yellow nodules contain hepatic cells, which are altered more or less according to their distance from the centre of the lobule. As in the commoner forms of fatty degeneration, the disease advances from without inwards. As we follow the steps of the pathological change we notice first that the cells become granular. They contain a little oil, but certainly in no excessive quantity; there is perhaps even less than in the normal condition. The biliary matter, on the contrary, seems to accumulate within the affected cells. The cells lose all tendency to cohesion to each other, and, where the disease has advanced farthest, they part from the basement membrane also; for in the circumference of the lobules no cells whatever are visible—they seem to have dropped off, and to have been dissolved or discharged.

The present seat of the disease, the tract within which these changes are proceeding, is indicated by a deep purple stain, while the parts which have not as yet been involved are in a state of biliary congestion indicated by a bright yellow colour. This congestion, however, means no more than puerile respiration does under parallel conditions of the lungs, namely, that a part is undertaking the duty of a whole organ. The purple stains are wider in proportion as the disease is more active and its progress more rapid. In the chronic forms these are narrowed down to thin lines and rings, which separate the parts still capable of performing their functions from those which have been disorganised. The microscope finds in these purple patches few or no oil-globules; a few hepatic cells which may possibly belong to the yellow part; and a few small granular masses of very variable size; but no pus corpuscles or large compound granular cells. The line which, as it were, separates the living from the dead is, in the liver, as in the heart, the seat of excessive vascular congestion. Inflammation may ensue, as a secondary

consequence of the local action, showing itself by the formation of adhesions along those lines where they happen to crop out on the surface of the organ. But there is no reason to consider the disorganising process as essentially inflammatory.

The parts where the process has gone on to complete disorganisation differ in appearance according to the length of time that may have subsequently elapsed. In recent acute cases they are dark, much below the level of the surrounding tissues, and of a soft yielding texture. In chronic cases, where the history gives us reason to believe that a longer time has intervened since the invasion of the disease, they are collapsed and pale, and, though flexible, they resist the knife like the tissue of a cicatrix. The microscope here, as in the results of ordinary cirrhosis, shows nothing but a fibrous structure in which the course of the different vessels can still be traced, the epithelium cells having been all shed, leaving nothing to indicate that we have under examination what was once glandular tissue. In one case of several months' duration, where death had been preceded by all the usual signs of portal obstruction, the small bloodvessels in the interlobular spaces were convoluted like the vessels in the spermatic cord. A few oil-globules lay in this disorganised tissue here and there, but no hepatic cells could be seen anywhere in it.

Fatty Degeneration of the Kidney.

The analogy between fatty degeneration of the kidney in its different forms and fatty degeneration of the liver is very close. The different mode of arrangement of the glandular tissue in the two organs respectively involves certain differences in the disposal of the effete products of the disease. The secondary constitutional results, too, vary, of course, according as urea or bile is retained in the system. But where these do not interfere, the identity of the disease in the two organs is almost absolute.

We owe our knowledge of this subject to the labours of Dr. G. Johnson.* Venturing to draw from his observations conclusions somewhat different to his own, I feel that I could have no greater security from being led astray by my preconceived notions than to adopt his classification and his excellent descriptions in detail, and I have reproduced them accordingly. Further, never having made this class of diseases of the kidney

* 'On Diseases of the Kidney' and 'Med.-Chir. Trans.' vols. xxix., xxx., xxxiii.

the subject of particular examination, I gladly avail myself of the opportunity of testing the correctness of my views by his independent observations.

Fatty degeneration of the kidneys occurs in two forms. In one the kidneys are large, smooth, soft, and mottled. 'The convoluted tubes are found to be everywhere greatly distended with oil, which has accumulated in their epithelial cells. The detached epithelial cells, when filled with their oily contents, have often a remarkable resemblance to the cells of the liver in the same condition. The fatty accumulation occurs in the epithelial lining of those portions of the tubes whose office is the secretion of the solid constituents of the urine. In some of the tubes the epithelial cells cannot be seen; they appear to have undergone a process of atrophy, and the tubes are occupied only by their oily contents.'* 'It is this form of fatty degeneration of the kidney which occurs in animals, as a consequence of confinement in a dark room.'†

In the other form, also, the kidney is generally large and soft. As time goes on it may shrink, and in such case become harder. But the character which marks this form of the disease is the uneven granular surface of the organ. 'In the granular kidney, many of the tubes contain a number of detached oily cells, which are readily washed out by the stream of urine passing through the tube; while in the mottled kidney there is commonly only a single layer of epithelium, which still remains adherent to the basement membrane.'‡ 'The greater part of the oil is contained in distinct cells; and these can readily be traced through a gradual series of transitions up to the gland cells of which they are, evidently, a degenerated offspring.'§ 'The convoluted tubes are found filled in different degrees with oil, some tubes being quite free, while others are ruptured by the great accumulation in their interior. The opaque yellow spots scattered throughout the kidney are convoluted tubes distended, and many of them ruptured by their accumulated fatty contents; just as the red spots are convoluted tubes filled with blood. In parts of the same kidney, there may commonly be seen some of the appearances already described as indicative of desquamative nephritis.'‖

The analogy of these two pathological conditions of the kidney to general fatty infiltration and cirrhosis of the liver

* 'On Diseases of the Kidney,' p. 388.
† 'Med.-Chir. Trans.' vol. xxx. p. 183.
‡ Op. cit. p. 391. § Page 384.
‖ 'Med.-Chir. Trans.' xxx. p. 183.

respectively are sufficiently obvious. I am not aware of any affection of the kidney which could be strictly compared to acute yellow atrophy of the liver. For, although the acute desquamative nephritis which sometimes follows scarlatina presents some points of comparison, yet the power of repair which the kidney possesses affects the resemblance in a most important point. In the kidney the glandular epithelium is reproduced, and the organ is restored to perfect integrity; while in the liver, as we have seen, the secreting structure is not restored, and the organ collapses. Stripping of the glandular lining of the renal tubes and subsequent—consequent—collapse of the organ does, however, occur, as a result of what Dr. Johnson calls chronic desquamative nephritis, in the small contracted kidney. In the cortex of one of these kidneys the appearances described as occurring in the portal zones of a cirrhous liver are reproduced. The framework is there, the vessels and tubes and the hard connective tissue, but the gland tissue is gone, and the empty tubes lie collapsed where they are not distended by effete epithelial cells.

I believe that these independent observations on the kidney confirm in every particular my own conclusions from the examination of the liver. Though, in the absence of such a test as acute yellow atrophy supplies, the renal could scarcely be made the basis of such a general inference as the hepatic changes. Both alike seem to show that fatty degeneration is not the first step, but a secondary affection of disorganised cells. If the cells are thrown off simultaneously with their disorganisation, and pass away, there will be no evidence of fatty degeneration at all. But if retained, whether free in the cavities of the gland, as in the granular, or still adherent to the basement membrane, as in the mottled kidney, they will be infiltrated with oil. Lastly, these observations on the kidney show that, after the cells are shed, the cavities which contained them collapse, and the organ, to this extent, undergoes the same retrograde changes as obsolete structures display everywhere else.

Fatty Degeneration of the Placenta.

Fatty degeneration of the placenta has been so fully described* that it might seem almost superfluous to open the subject anew. But, after a careful anatomical examination of

* Barnes and Hassall On Fatty Degeneration of the Placenta, 'Med.-Chir. Trans.' vols. xxxiv. and xxxvi.; Druitt, 'Med.-Chir. Trans.' vol. xxxvi.; Kilian, 'Brit. and For. Med.-Chir. Rev.' vol. vii. p. 272; Handfield Jones, 'Path. Trans.' vol. iv. p. 238.

the whole subject, I must venture to express my dissent from some of the conclusions which are generally received with regard to this pathological condition. I would suggest, as the result of my observations, a somewhat different arrangement of the description of the various anatomical changes, and certain qualifications of the inferences which have been deduced from them.

Few human placentæ are entirely free from a peculiar local change, which shows itself in the form of hard white lobular patches, chiefly affecting the edge of the organ and its maternal aspect. In the collapsed state in which we find this organ after delivery, they are sensibly elevated above the surface. A vertical section of one of these patches shows the change of colour and consistency to extend from the surface into the substance of the placenta, to a greater or less depth, sometimes through the whole thickness of the organ. As we trace its lateral extension, we find the lobules of the placenta to coalesce into broad hard white tracts where few or no pervious blood-vessels are to be seen, and in which the proper functions of the organ must have been entirely suspended. Sometimes the change seems to have begun on the fœtal surface, and occasionally it would appear as if the fœtal and the maternal surfaces had been affected simultaneously, a line of comparatively healthy structure separating the confines of the two tracts of disease. In these white patches the evidences of fatty degeneration of the placenta are to be sought for.

Not every white placenta, however, is fatty, for the organ may be blanched throughout its entire extent, merely from the fact of its having been drained of blood, in the course of, or as the cause of, a miscarriage. Not even every placenta which displays to the unassisted eye the familiar broad white patches just described is fatty. For the disorganisation which is indicated by these obvious characters may be of more than one kind, to only one of which the name of fatty can be properly applied. Two of these I propose to describe as the typical forms of placental degeneration, the fatty and the fibrous, as chiefly displayed in the villi of the chorion.

In the first form, these patches are of a loose texture; they are separated from the healthy tissue by no very distinct line of demarcation, and on pressure they give issue to a creamy fluid. By the action of ether, we may obtain unequivocal chemical proof of the existence of a fatty matter in abundance in the disorganised tissue, rather soft, but solid at ordinary temperatures. And, by the help of the microscope, we may

trace in these patches all the morbid appearances which have been so well described by the authors already alluded to.

These patches want the smooth hard surface which characterises the other form, to be described presently. On tearing them up with the dissecting needles, we find them to consist of villi closely packed together, so closely, indeed, that it is difficult to unravel any considerable length of tube continuously from the friable mass. The tubes are granular and opaque in parts: the glandular epithelium is indistinct, little oil-globules appear here and there, and the extremities and lateral diverticula of the tubes are, many of them, filled with opaque yellow granular matter. This may be cleared by a solution of caustic potash, but the colour and opacity reappear on neutralisation by acetic acid. It is a granular-fibrinous rather than a fatty matter. Little oil-globules are, however, distinctly visible on the walls of the tubes, and in a more advanced stage of the degeneration, larger drops may be seen lying within the cavity of the tubes, or loose among the tissues. As we recede farther from the maternal surface of the placenta, which is the apparent starting-point and chief seat of the change, the tubes gradually resume their normal characters; the ends and diverticula become clear, and the epithelial glandular edging—as it appears—of the canal is again visible.

In the other form, the change does not seem always so closely connected with the maternal surface of the organ as in that just described. The white patches, too, have characters of their own. They are hard and compact, and are separated from the healthy tissue by well-defined abrupt boundaries. They are smooth, almost polished, on the free surface. When they have been cut or torn, no creamy fluid exudes on pressure; and the microscope finds no fatty matter in them. The action of ether gives the same negative results. By agitating equal portions of one of the hard and one of the softer white patches in separate test-tubes with ether, and evaporating the solution, the fact may be placed beyond a doubt that the soft patch contains fatty matter in large quantity, and the hard one little or none at all. With pains and patience the villi of the chorion of a fatty placenta may be unravelled almost up to the maternal surface. We cannot, indeed, follow a single tube so far, but we may disentangle the soft friable mass, in some fashion, to this depth. In a typical specimen of the fibrous form under consideration, however, this is quite impracticable. Up to the edge of the hard white mass, as seen on a vertical section, the villi are quite healthy and of their normal size. But there they

suddenly shrink into threads, which can only be followed separately for a very short way. By the help of acetic acid, which clears, and somewhat softens, the hard opaque mass, the course of some of the tubes may be traced a little farther, rather by the eye than the dissecting needle, the arrangement of their nuclei, and the points where the section has crossed their direction, showing the lines of obsolete tubes. Near the maternal surface minute oil-globules are scattered here and there; and deeper in the centre of the mass a few may be seen, not scattered, but gathered into clusters, as if within some vessel. But the fatty matter forms no appreciable proportion of the bulk of the substance, whether examined by the microscope or by chemical reagents. The mass is almost wholly made up of obsolete tissue, apparently of collapsed, contracted, and mutually adherent villi. And its texture and appearance strongly resemble those of the tissue which we find in the interlobular spaces of the liver after the destruction of its glandular elements. Limiting the application of the term fatty degeneration to the form already described, I would designate this as cirrhosis of the placenta.

There are two forms of fatty degeneration, which I have not met with in the placenta, wanting to complete the series, so as to render the history of the disease here parallel to what we find in other organs.

I have not met with an instance of fatty degeneration of the placenta parallel to that form of the disease when a whole organ seems to be infiltrated with oil. Dr. Barnes* cites a case where fatty degeneration of the placenta occurred in a fat woman; and, as no disease appeared in the child, the change in the placenta was referred to some affection of the mother. I have myself seen just such another case. But it cannot be said that these differ in any essential point from other cases, except so far as the probable excess of fatty matter in the blood of the mother allowed the fatty infiltration of the placenta to proceed with greater rapidity than it would have done had fatty matter been less easily available. And it seems to me that a fatty infiltration of the placenta, strictly comparable to the fatty infiltration of the liver—to take this instance—which occurs in connection with tuberculous cachexia, would not take the form of local disease. It would probably have its seat in the cells of the decidua, as well as of the chorion generally, and not in certain parts only which had been prepared by previous changes to receive the fatty deposit. The physiological peculiarities of

* Op. cit. vol. xxxvi. p. 167.

the placenta render such an occurrence exceedingly improbable. Like general fatty degeneration of the heart, it could not go on far without involving the death of all that depended on the particular organ, and so cutting short the pathological process. And I do not find any evidence of the occurrence of this form of disease, in any of the cases recorded by Dr. Barnes or Dr. Druitt.

Another condition which I have also, as yet, failed to notice, is a change in the placenta parallel to that which accompanies acute yellow atrophy of the liver. Such a condition might perhaps be found in connection with abortion in fever, and be traced in the cells of the decidua and chorion.

The physiological peculiarities of the placenta are reflected in its pathology, and we cannot rightly interpret its morbid appearances without a full consideration of the normal relations of the different elements which enter into its composition. The chorion is not merely a frame on which the bloodvessels are extended, a means of adhesion between the ovum and the uterus: it is as truly a glandular structure as the liver or the kidneys. Not only is the fœtal blood depurated in its radicles by apposition to the mother's blood, but a supply of new material is constantly being elaborated by the layer of glandular epithelium which is spread over the decidua, as well as the chorion at the surface of contact. The placenta discharges the functions of the stomach as well as of the lungs.*

For this purpose, two separate systems of vessels are brought into mutual apposition during a certain portion of their course. From this point the umbilical veins bring back the blood depurated, oxygenated, and, as from other ductless glands, carrying in it the secretions of the placenta. If the maternal circulation fails at any single point, or if, as from a shock over the whole surface, the decidual glands fail to that extent in consequence, the fœtal elements of the placenta repeating the failure, the blood returns from that point, or that surface, as it came, neither depurated nor enriched with nourishment for the embryo; and then the corresponding fœtal portion of the placenta fails and shrinks up with the abolition of its functions. Conversely, the failure of the fœtal circulation at any point will be followed by the obsolescence of the corresponding maternal structures of that portion of the placenta.

On these grounds, the explanation of fatty degeneration of the placenta seems quite clear, and coherent in its analogy to that of fatty degeneration and its allied changes in other

* See Goodsir, 'Anatomical and Pathological Observations,' p. 50.

organs. An effete gland-cell exposed to the influence of passing blood containing oil will become infiltrated with oil. But if the interruption of the circulation be sudden, and with it the access of oil be cut off, there will be no fatty infiltration. The tissue will collapse, and cirrhosis, or fibrous degeneration, will ensue. This was well shown in a placenta which had been separated suddenly by hæmorrhage along a line a few weeks before delivery. It might seem as if the alternative between fatty and fibrous degeneration of the placenta were merely a question of the sudden or gradual interruption of the circulation in its vessels.

In relation to the general pathology of fatty degeneration, an argument may be derived from this part of the subject, which has been strangely overlooked by those who insist on the direct convertibility of animal tissues into fatty matter. And, perhaps, the same fact might be adduced as support of the opinion that fatty degeneration proceeds from the maternal, and fibrous from the fœtal, vessels. Merely this: that the tissues of a dead fœtus are not liable to fatty degeneration under any circumstances. The products of extra-uterine fœtation may remain enclosed in the living body for years without undergoing this change. The little embryo which is found in a mass of so-called uterine hydatids has undergone no fatty degeneration. And the fœtus which has lain for months and years in the uterus of a cow is found shrunk and blackened, but not converted into fat. This is quite in accordance with what has been previously stated. The dead fœtal tissues are removed from any supply of oil by which they could be infiltrated. There must be molecular apposition if not absolute continuity between the disorganised tissue which is to receive the oil and the living tissue whose moving blood is to supply it; though, as in the case of fatty degeneration of the cornea, an actual capillary continuity is not required.

If these inferences be correct, fatty degeneration of the placenta, such as has just been described, can scarcely be regarded as a change of any importance with regard to the condition of the fœtus. And, as a rule, large healthy children are born in connection with extensive degeneration of the placenta, having derived their nourishment from the portions which were not involved in the local change. Nor, again, can it be looked upon as having anything to do with one of the great perils of childbirth—adherent placenta. For the edge of the organ, where these patches chiefly occur, is just the part where adhesion of the placenta to the uterus is least frequently found.

On the contrary, from recorded cases, it might seem that these hard unyielding masses, already in such loose connection with the uterus, were more likely to induce a still farther separation of the placenta, and consequent hæmorrhage. Nor, lastly, can we regard it as the natural termination of the life of the placenta, for, certainly, this organ is not least active at the completion of the period of gestation. It is a local, not a general disease, a consequence, not a cause, and, interesting in the highest degree as a pathological study, is, I believe, devoid of all clinical importance.

I have had no opportunity of studying the changes induced in the cornea by fatty degeneration, as displayed in the arcus senilis, so well described by Mr. Canton.* So I will merely extract from his pages an account of this morbid appearance.

In the first instance, the corneal cells are the seat of the affection. These cells, in form comparable to the lacunæ and canaliculi of bone, lie between the lamellæ of the cornea. They are so numerous that their opacity imparts a cloudiness to the whole structure, though the lamellæ may not be affected. The superficial laminæ are first involved, and thence the change extends deeper into the substance of the cornea. Presently, the lamellæ themselves are changed, infiltrated by myriads of minute oil-globules, which, as they coalesce into larger drops and collect between the lamellæ, add notably to the thickness of the cornea. The opacity due to changes coincident with old age has much in common with that which results from injury and inflammation of this part.† They both consist essentially of infiltration of the corneal cells with oily matter, but, in the former the change is permanent; in the latter it is—that is, as far as it depends on oily infiltration of the corneal cells—remediable.

The term atrophy does not seem to me to express the correct pathology of this affection. Dr. His,† as cited by Mr. Canton, has put this very pointedly. Demurring to the opinion that the arcus is the result of simple atrophy, he asks, 'How is it that it is just in the margin of the cornea (which is in the most favourable position for nutrition) that such atrophy should occur; and how does it happen, in connection with such an atrophied margin, that the centre of the cornea can preserve its complete integrity through years? These are questions which at present appear to be quite insoluble.' I believe that

* Canton, 'On the Arcus Senilis.' 8vo. London, 1863.
† Canton, op. cit. pp. 30, 32. Virchow 'Cellular Pathology,' transl. p. 301-306.
‡ 'Histologie der Cornea,' p. 138. Basel, 1856.

the solution of the problem is to be found in the close parallel to be traced between arcus senilis and the other instances of fatty degeneration which have been described in this paper.

The pathology of fatty degeneration may be summed up in a few lines. And, as a preliminary, I must confess that a very attentive study of fatty degeneration continued through many years has much diminished, in my eyes, the importance of the specific character from which the process takes its name. Grave as are the diseases with which it is connected and on which it ensues, the fatty change itself is comparatively of little moment, and quite secondary to the degeneration, in date as well as in importance.

It is an infiltration of fatty matter which is derived immediately from the passing blood, or is made on the spot under its influence. And, as far as concerns the human subject, it is not the physiological form of fat, margarine, which is thus infiltrated, but oleine.

The structures which are infiltrated in this manner must be previously disorganised, the infiltration being a consequence, not a cause, of the disorganisation. Structures in healthy vital activity either do not admit of such infiltration ; or, where their physiological constitution allows of this, they have the power of clearing themselves of the oil. They must be disorganised, but they must not be dead, as far as death implies liability to chemical decomposition or disconnection with the current of the circulation. For, experiments show that, under such circumstances, fatty degeneration, as expressed by the formal replacement of healthy structure by fatty matter, never ensues.