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STATISTICAL AND PATHOLOGICAL OBSERVATIONS ON SOME ALTERED CONDITIONS OF THE LIVER.

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MARGAROSIS, OR FATTY ALTERATION OF THE LIVER.

This altered condition of the organ, has, of late years, attracted a good deal of attention, especially since Louis had drawn the attention of pathologists to the frequency with which the liver is affected with this change, in cases of phthisis. He detected, by the look and feel alone of the liver, this fatty alteration in forty cases out of one hundred and twenty of phthisis, and its great frequency has been confirmed by many other observers.

The desire to ascertain how far the observations of Louis and others would agree with a series of inspections and analyses of the livers of persons dying with phthisis in the Union Hospital, was the principal inducement with me to enter upon the researches herewith detailed; and though I have not as yet been enabled to extend them as far, numerically, as I have wished, and still propose to myself to pursue, I beg to submit what I have already ascertained to the Society.*

Before, however, we enter upon our statistical and other results, it is necessary to understand what is meant by a fatty liver; for without some *datum* to work from, we shall have no more precise idea of what constitutes a fatty liver than a fatty person, except when their special characters are palpably declared to every observer. In order then that we may start from a definite point in our estimation of this deposit, it is first proper that we should ascertain in what proportion the *oil-fat* or *margarine* exists in a healthy liver, and thence to assign the abnormal ratios in our analysis.

Oil or fat is known to exist in almost all the textures of the human body, and in the healthy liver it is found by Boudet, (as given in "Simon's Animal Chemistry," and translated by Dr. Day for the Sydenham Society,) to amount to 1.3 per cent., while a fatty liver analysed by

the same observer contained 20.8 per cent. Now, if we hold that 1.3 per cent. to be the normal charge of this deposit, and all proportions exceeding this ratio to give the character of fatty to the organ, we shall, I believe, have a greater proportion of this altered condition of the liver in phthisical subjects than even that noted by Louis; and also in deaths from other diseases, we must recognise this alteration more often than would be readily allowed.

Taking, then, 1.5 instead of 1.3 per cent. as the normal maximum of oil-fat in the healthy liver, I find that of thirty one cases, dying with phthisis in the course of our examinations, out of the total fifty autopsies, there were eighteen which were found with livers having various proportions of oil-fat above this normal maximum. Of these thirty-one cases dying with phthisis, fourteen were males, and seventeen females. Of the former there were six instances of fatty liver, and of the latter there were twelve—shewing, so far, a greater preponderance of deaths from phthisis among females, as well as of fatty deposits in their livers. The maximum amount of fat I have met with on analysis, was thirty-two per cent. of what is more properly called *margarine*, and this was in a female, aged 28 years. She had been a practised Cyprian, and likely to be addicted to alcoholic liquors. The next greatest proportion of twenty-two per cent. was also in a female, aged 45. She had been in hospital two months, but her previous history was unknown. On inspection, her right lung, from dense tuberculosis, was found to weigh 3lb. 12½ oz. of averdupois. The highest amount of oil-fat in any of the males was 10.4 per cent. This subject was fifty years of age, had been three months in hospital, and was previously, I learned, a temperate man. Besides these cases of males dying with phthisis, I found two instances in the same sex where there was appreciable *margarosis* of the liver without any tubercles in the lungs. One of these males died of pleural effusion and cirrhosis of the liver, the other of *delirium tremens*—both betraying so far an addiction to alcoholic liquors.

One well-marked exceptional case occurred in a female, aged 29 years, who died of recent engorgement and red hepatization of the lungs, without the least vestige of a tubercle or vomica; she had also chronic peritonitis, and yet her liver, upon analysis, contained 23 per cent. of fatty deposit. The history of this woman was not recorded; for though her liver during life was found enlarged, and it weighed on inspection, 4lb. 8 oz., yet not being suspected to be fatty, enquiries were not made as to her previous habits. The case withal was interesting, as obviously negating the essential and

* As there are upon the average, 75 to 80 cases of declared phthisis in the Union Hospital annually, of which above 70 per cent. terminate fatally in the house, the opportunities afforded to the medical attendants for all statistics relative to this, as well as to other diseases, are frequent and ample.

absolute connection between fatty liver and any species of phthisis.

Though eighteen cases, in which oil-fat was found to exist beyond the normal standard, out of thirty-one persons dying with phthisis, may be held to be a very large proportion, and above what even Louis has stated; yet it must be remembered, that several of these cases containing, we may say, less than five per cent., would probably not have been recognized as fatty by either the sight or feeling. We may easily comprehend how a minor ratio might have been drawn from the same inspections, in the absence of the application of the microscope or chemical analysis. I considered, therefore, that mere tact and inspection would give a very imperfect result in a series of cases undertaken for a correct numerical object, however decided the alteration may have appeared in several of the instances, and, consequently, I submitted a portion of the liver in each instance to both the above tests, where there was any doubt, and in all cases to that of boiling or by ether, to ascertain the quantity; except in a very few, in which cases I was satisfied with the microscope, that the quantity of oil-fat was great from its being so very obvious. The method adopted to afford the most certain result, was to boil one ounce averdupois of the liver, previously cut into very small fragments, for an hour, in a Florence flask, then to measure the supernatant product in a long tube, graduated to two hundred parts of a cubic inch, by which I easily calculated the amount of *margarine* in grains, by simple inspection.

To show how expedient it is to submit some equivocal looking livers to either the microscope or other tests, before pronouncing absolutely on any alteration of this kind, I may mention the case of a female, aged 27, who died with phthisis, and whose liver was found to weigh 7 lb. 10 oz. It was of an ashy-buff colour, consistence moderate, but yielding like soft cheese to pressure of the finger; it had little vascularity, but was of a uniform plastic texture. It was at sight declared to be a large fatty liver of some exceptional kind, but the microscope showed no true oil-ovules nor stellar globules, but a mass of little cells and granules. On submitting it, moreover, to boiling and ether, no fat was detected; though on treating a portion with liquor potassæ and hydrochloric acid, an abundance of pure albumen was discovered. It was, therefore, a case of what is called waxy liver—a true albuminosis, not the result of inflammation, but a vito-chemical deposit.

The mode in which this oil-fat exists normally, and in slightly augmented proportions, is in small ovules in the cells, having a highly refractive power, and these ovules are well depicted by Mr. Bowman, in his plates on this subject. In this normal and primary condition, this deposit seems to consist entirely of what is called *elaine*, which is a liquid oil, till its temperature is reduced to twenty-five degrees; but when the deposit proceeds to any characteristic extent, this liquid oil becomes intermixed with, or holds in solution, a fatty matter of much more consistence, which has a crystalline or stellar appearance under the microscope. This other fatty element does not become fluid till its temperature is raised to 116°, by my trials on several specimens from the liver; and Simon states its melting point at 118°. This modified form of fatty matter is

called *margarine* by writers on animal chemistry, and it exists in combination with *olein* in human fat, and in that of the carnivora; while in the ruminantia, the fat called *stearine*, which only melts at about 144°, resides in this class, in combination with *olein*. The different appearance and consistence between beef or mutton suet and human fat or that of the carnivora, or even the hog, sufficiently declare the specialities of the two kinds, chemically as well as economically.

For the reason then that *margarine* constitutes the great bulk of livers that are fatty, I would designate this alteration, as an object in pathology, *margarosis* of the organ; though simple *olein* forms the normal deposit, and may be the solvent medium by which the other principle is conveyed to and deposited in a firmer state in the liver.

There is every reason to think that the relative proportions of these two elements vary in the human liver, giving more or less firmness or softness to the affected organ, both during life and after death; but as far as any consistence exists, where this fatty alteration is of any prominence, it is entirely owing to the firmer material, and therefore the alteration may be appropriately styled a *margarosis*.

In the primary stage of this alteration the oil-ovules seem confined to the hepatic cells, but as it advances they may be observed in the interlobular tissues, while the *margarine* seems to be deposited in masses of round or stellar globules, which encroach upon and usurp the interlobular spaces—the tissues becoming atrophied, and, consequently, the biliary apparatus and function restricted and diminished. Two most important questions about this alteration remain to be shortly considered, and these relate to its physiological causes and pathological effects.

These questions, I am sorry to say, have not advanced further than hypothetical solution. Andral supposed that a sufficient quantity of hydrogen ceases, in phthisis, to be eliminated from the bronchial membrane in the form of aqueous vapour, and hence it is separated in excess from the blood in the liver, and so produces a deposit of fatty matter in that organ.

Liebig's hypothesis, as is well known, is nearly allied to this, only he makes the carbon to be the accumulated and metamorphosed element, and to be deposited in the liver—it becoming increased in amount in the blood from its insufficient oxidation in the lungs in cases of phthisis, in which disease the vito-chemical action of these organs is either long or seriously restricted or impaired. Others again have attributed the accumulation of fat in the liver, in the wasting varieties of phthisis, to the absorption of oil-fat from the other textures and organs of the body, and to its being currently precipitated on the liver, owing to the portal capillaries being relatively of so small a calibre as to arrest the fat-ovules: while some have referred this fatty accumulation to an undetermined catalysis of the liver itself.

The hypothesis of Liebig is very ingenious, and may well be appreciated by the chemical pathologist, but I greatly doubt, whether there is any diminished consumption of oxygen in the lungs, in the majority of cases of ulcerous phthisis, though there may be in the stage of occult tuberculization. In cases where the tubercles have become softened, with subsequent ulcerations and vomica, there is every reason to infer,

that the tissues are consuming a great quantity of oxygen; in fact, their solution and puriform decomposition are chiefly, if not entirely, owing to the metamorphic action of oxygen. At any rate we have evidence so far that *margarosis* of the liver is not essentially connected with phthisis, as we have already noticed a well-marked case, containing 23 per cent. of *margarine*, where there were no tubercles nor purulency in the lungs. This was in a female; and in two males, whom we have noted, there was to the amount of 3 per cent., and no phthisical results were detected in the lungs of either. I need not here recall, how the converse exhibits itself in the thirteen cases of phthisis, that presented, on inspection and from the usual tests, no abnormal deposit of oil-fat in the liver.*

Without attempting a satisfactory solution of the important chemical pathology of this question, it may perhaps be some aid in our future investigations and attempts to solve it, if we advert to the amount of fatty ingredients that have been ascertained to exist in healthy blood,—in the blood of phthisical patients,—and also in the respective vessels of the liver. Now, the quantity of both *olein* and *margarine* in healthy blood, according to Lecanu, one of the first accredited analysts, does not exceed 6.57 parts in 1000 of blood, and is generally less; while the blood in persons affected with phthisis, according to Andral and Gavarret, contains, at the maximum of three analyses, only 4.2 in 1000 parts; and according to Becquerel and Rodier's analysis of the blood in nine affected with phthisis, the same quantity was found to contain only 1.554 parts at a maximum. Taking the above analyses as generally representing the relative charges of fatty matter in health and in phthisis, there is little support for the view that there is in this disease a surcharge of oily or fatty matters in the blood for to be deposited in the liver. The elements, however, of oil-fat, viz., carbon and hydrogen, may be said to exist in excess in the blood in phthisis, and to undergo their catalytic deposition in the liver. To this we can only say, that as no analysis has yet verified this supposition, it can form no ground for pathological reasoning. Confining our research to the proximate element, it appears from the analysis of the blood both from the *vena portæ* and *hepatic* vein, as compared with the general venous and arterial blood, as given in "Simon's Animal Chemistry," vol. 1, (Sydenham Society,) that the blood of the *vena portæ* contains about double the amount of fat that arterial blood does, and even above a fourth part more than is carried off from the liver by the hepatic vein. In the normal function of the liver, the excess of fat in the afferent vessel is very probably disposed of in the cell-elaboration of the bile—a metamorphosis of carbon. In the healthy tension of the liver and system at large, this secretion is as freely per-

formed, as it is regularly demanded for the wants of primary assimilation; but when these demands become limited or impaired, as in phthisis, the tension of the cell-life will also become reduced, so that the fat of the portal blood, instead of being metamorphosed to its normal amount, as bile, will be simply retained, by some molecular attraction, in the cells and tissues of the liver.

Without further enlarging upon this view of a very recondite process, and wishing it to be taken only for what it is worth, I shall conclude with the few remarks which I have simply been enabled to deduce from a survey of the cases under the last head of the paper, viz., that *margarosis*, is chiefly observed in cases of phthisis, and in women more than in men. My observations also lead me to infer that it occurs oftener in chronic cases than in those more acute, or of short duration; and that it is more frequently observed in cases where, during life, the digestive organs and assimilating functions have been in a fair state of integrity and force, notwithstanding ulcerations have been found in the lower ilea after death. I am inclined to coincide with some others, that this abnormal deposit is more peculiar to phthisical females who have been addicted to spirit-drinking; but my observations on this point have as yet not been so ample or correct, as to induce me to hold the connection absolute or even general.

As to the symptoms of *margarosis* of the liver, they by no means declare themselves in the great majority of cases by either pain or uneasiness in the seat of the organ; it is only when the liver becomes much enlarged from the deposit, that a sensation of fulness or of a slight weight is complained of. It is indeed surprising to find the bulk of such fatty livers giving so little uneasiness; but when we consider that they are very light relatively to their size, we may account for the rare complaints that are made of their presence. The biliary function also seems to be neither impeded nor altered, but only in degree, by the deposit—owing probably to the little interference with, or pressure on, the vascular and biliary capillaries, from the gradual deposition of the soft oil-fat among their tissues and in the hepatic cells. As the process proceeds, the amount of secreted bile diminishes, though it may be quite normal in quality, and its amount is likely to be, in general, equal to the demands of the assimilating functions; while, *pari passu*, the anatomical tissues of the organ become atrophied and supplanted by the deposit.

The *physical diagnosis* is not well declared, till the organ becomes much enlarged, and sometimes not even then, except by careful percussion, for the fatty liver during life is softer and more yielding than one that is not so, and more especially if the *olein* element should more than usually prevail in the deposit. This difficulty of easy or early diagnosis is less to be regretted, as the affection seems not to present nor call for any therapeutic indication. It is one of the most innocent alterations which the organ undergoes; and perhaps, for anything that can be appreciated by science or observation, it may be one of those vicarious and compensating secretions that tend rather to protract than shorten existence, in those afflicted with serious diseases of the lungs or other organs.

* Still further to show the want of an absolute pathological connection between phthisis and fatty liver, M. Catteloup, in his "Report of the Diseases of Algeria," observes, "In the course of our researches we have remarked the frequency of a change of structure in subjects, who, offering every appearance of phthisis, yet were quite exempt from tubercle—I mean the yellow-looking and fatty liver." "In France the coincidence of the fatty liver and phthisis is frequently observed; in Algeria, this morbid condition (fatty liver,) is observed alone, no disease existing in the lung."—*Medico-Chirurgical Review*, January, 1846.