

**On the relation of assimilation and secretion to the functions of organic life
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ON THE

RELATION OF ASSIMILATION AND SECRETION TO THE FUNCTIONS OF ORGANIC LIFE.

By J. GEDGE, M.B., Cantab., M.R.C.S.

PHYSIOLOGY suffers much from the want of definite nomenclature. Organic processes specifically identical appear generically distinct, in consequence of the separate terms used in their description.

It is on this account that I would enquire into what is meant by secretion and assimilation, with a view to show that, if our modern notions of physiology are correct, these processes can no longer be described as though they had nothing in common with the ordinary functions of organic life.

Secretion as performed by the gland—the station where this function is somewhat isolated—will be first considered. Cells are the acknowledged agents in this process, as shown by the indiscriminate use of the terms “secreting-cell” and “gland-cell,” and as these histological units when they have arrived at maturity all share alike—all perform a similar office—we may limit our consideration of the function of the gland to that of a cell.

The old notion of cells was that they were vesicles of varying size, having various contents. But now it is allowed, even by those who will go no further, that the vesicle must, during at least part of its existence, be fur-

June 2

nished with a nucleus which has definite chemical and physical characters. In this country, as is well known, we are no longer fettered by the vesicular notion of the histological unit: no longer imprisoned by the constant presence of a cell-wall. That the cell should have been universally considered to be vesicular in the early days of histology is not remarkable, when we consider the comparative ease with which such peculiar cells can be demonstrated: the imperfection of the optical instruments then in use not enabling them to study carefully any but the large histological units met with in the vegetable kingdom. Furthermore, it cannot be regarded as surprising that the cell first described should have been considered the type, and that the attempt should have been made to reduce all other cells to the same formula. Besides, in animal cells where no cell-wall existed, an apparent one could often be made by the action of chemical re-agents. Toy-cells have been constructed by Mr. Rainey and others, having the conventional vesicular character with the indefinite cell-contents simply by mingling certain chemical compounds.

The cell-wall then must be understood to be simply a complication of cell structure, which being always absent in the healthy gland-cell and almost all other animal cells, cannot fairly be regarded as a part of the histological unit. But the discussion of this super-added structure, and its histological homology must be reserved until we have entered in greater detail into cell-physiology.

The term *cell* is here used as a technicality for that elementary part or histological unit, which consists of *nucleus* and *plasm*; the nucleus being always distinguishable by those chemical or physical properties first shown

by Dr. Beale to be possessed by it in common with the germinal matter of the ovum.

Formerly the term nucleus was used very vaguely, size being generally the only diagnostic character. Thus we find even Virchow continually speaking of cells, when correctly (as we now know by the nuclear test) he ought to say nuclei.

When we examine the tissues of the embryo, we find them crowded with nuclei, which have grown from the germinal matter of the ovum, and if this examination takes place when the parts differ from one another in form rather than texture, we find an aggregation of nuclei separated only by a small quantity of interposed plasm. The mass may be broken down into what have been called cells, but there is no true specialisation into these structures; the nuclei bring away the surrounding plasm only in the same way that the stones in a wall that has been thrown down bring away adhering mortar. Soon, however, in the tissues that are to become simply cellular the embryonic plasm is, for a given distance around the nucleus, so acted upon—perhaps by interstitial addition—that a small portion is localised. This localised unit of nucleated plasm is the typical cell, as we find it throughout its active life in the gland. But in many epidermal structures, though best in the coecal extremities of certain glands among the lower animals, we find this same process of cell-formation going on through life. Glancing at such a structure in the deepest layer, we again see the nuclei crowded together, at first hardly separated, but as we ascend, gradually getting more and more spaced by intervening plasm, which as gradually alter in texture until we have specialised histological units. And after the cell

has arrived at maturity, as surely as the relative proportion of the nucleus to the plasm diminishes, so surely does the working power of the cell decrease.

Now, having completed the anatomical life-history of the cell, it becomes necessary to consider its function, secretion. Formerly this process was regarded merely as separation. The blood was supposed to contain all the complex substances poured out by different glands, and it was simply the duty of the gland-cell to choose from the blood, as it flowed by, the particular substance that it was required to separate. Now, however, the gland-cell is known to fulfil a more important office. Formation rather than separation, would appear to be the function of the gland-cell. It would seem to attract the nutrient material in its vicinity, and with unknown machinery to make use of chemical affinity to construct elaborate compounds. But we cannot gauge the action of a gland by merely analysing the secretion poured out, for there can be little doubt that all glands compound for the blood as well as for their own secretion. This has been shown to be the case in the liver, and we have no right to consider this gland an exception. But besides thus refunding secretions of a complex nature, we must remember that an equivalent debasing action must take place, and as the cell itself must be restored, more fuel than is at first sight apparent is required. In some cases these debased materials are poured out in the gland's secretion; in others they are returned to foul the blood until it has passed through one of the refining glands.

We acknowledge that all this work emanates from the cell. Can we no further localise it? I think we can. In certain cases we are able, from the insolubility of the secre-

tion, to observe the position it occupies when it is first formed. In such cases we see the secretion within the plasm. The exact site it there occupies is not perhaps of much importance, since we are aware of the existence of outward currents in the plasm. Still, certain observations that will be mentioned directly afford evidence of its being formed in actual contact with the nucleus. If this be so, it matters little whether in one case the secretion is seen to be intranuclear, in another adnuclear, or in a third circumnuclear, for it must be remembered that our nuclear matter is shut off from the plasm by no partition wall. In studying the physiological anatomy of the mammary gland during the secretion of milk, I think I have been clearly able to understand how some of the fallacious notions concerning the cell and its function have arisen.

In all cases when lactation first sets in, we find in the milk certain structures known as colostrum-corpuscles. These have been correctly regarded as altered gland-cells, and they can be shown to be vesicular; to consist of cell-walls and cell-contents, with a nucleus or a remnant of one. But if we examine the secretion when the gland is in full working order, we find no colostrum-corpuscles, no cell remains of any kind. On examining the gland itself this may be accounted for. Here, as elsewhere, the more quickly grown the cell, the more fluid the plasm. The plasm of these cells is but little firmer than treacle, and offers but little resistance to the outward passage of the newly-secreted globules; and it is probably in this outward passage that each globule gets its water-proof albuminous coating—the so-called haptogenic membrane. The nature of the colostrum-corpuscles may now be understood. They are the old superficial cells which had long been

dormant, and become rigid with old age. They had set to work to perform their function to the best of their ability, but eagerness would not make up for incapacity, and though choked almost to bursting with their anxiety to succeed, they had to yield their places to their more active juniors. Virchow has jumped to the conclusion that milk is always secreted in colostrum-corpuscles, only that in the acute action of the gland the cell-wall ruptures, and the mass is more rapidly broken up. I should like to ask the learned Berlin Professor whether it is usual in his histological experience to find rapid disintegration of young and active nuclei?

In the embryonic formation of adipose tissue we may with ease observe the adnuclear secretion of oil; the globule continuously enlarging until the plasm is compressed into cell-wall. This latter structure is here, as in the old mammary cell, the remnant of plasm, and wherever it occurs, however far separated from the nucleus, it may still fairly be considered as histologically homologous with plasm. But it is not always due to the outward pressure of cell-contents for, as we see in the vegetable, the plasm may be in part absorbed (*i.e.* metamorphosed), and afterwards thickened by linings. The plant, in fact, has no other means of laying aside such excrementitious secretions as lignin, except by secondary deposit. The cell-wall is, moreover, sometimes altered by interstitial deposit, though it is more usual to find interstitial changes where the plasm has never been altered into cell-wall.

In the pathological condition known as fatty degeneration we may often study the secretion of oil with great ease. Lately I met with a case of this disease in the liver, where instead of each cell containing a multitude of

small oil-globules shut off from one another by plasm, the oil was secreted in each cell in one drop.* So that in different cells the different stages in the formation of adipose tissue were exactly imitated. In some of these cells no plasm existed except in the form of cell-membrane, and as the nucleus was driven to the surface of the cell, the resemblance to the adipose vesicle was complete. I have observed too in the early stages of fatty degeneration of muscle that the oil globules are disposed around the nuclei, whence they spread so as soon to occupy an inter-nuclear position in the axial canal, which is often as distinct in the fibres of the heart as it is in the muscles of insects.

These cells which thus retain their secretion ought no longer to be spoken of simply as cells. They are glands and reservoirs all in one, and I would propose to distinguish them from other histological elements by calling them *store-cells*. Structureless membrane or cell-wall is often formed out of the original plasm of a cell during the process of free-cell-formation and such structures as long as they remain entire are known as *cell-capsules*. These bodies get more and more common as we descend in the animal and vegetable kingdom, but among the higher forms they will probably be found to be far more common than is at present believed, particularly in connection with the development of those glands which at present are so daringly described by a class of stratification-physiologists who evolve diagrams with a levity approaching to the imponderability of their consciousness.

Homogeneous or structureless membrane is also found investing the muscular fibre, and here, too, it must be regarded

* I have since met with this variation again, and I am inclined to think that it is caused in part by rapid, continuous secretion, and in part by a difference in the proportion of the mixed fats secreted.

as a remnant of plasm. Anyone who has carefully studied the formation of muscle in the nucleated plasm of the embryo cannot have failed to observe that the sarcous matter is stored much in the same way as oil in adipose tissue. In a very similar manner is elastic tissue formed. At a comparatively late period no trace of this tissue can be found. Then, within the plasm beside the nuclei we recognise its first formation. Soon the fibres increase in size and the nuclei get further apart. At length the nuclei dwindle, and many disappear, though some are left among the sheathing to perform the very slight office required of them in so very permanent a tissue. These observations lead me to conclude that sarcous matter and elastic substance are as much secretions as the oil of adipose tissue or the calcareous matter of shell.

But let us return to the cell. At present we have only treated of secretions insoluble in the fluids of the body, and we have been obliged to give such prominence to this class in consequence of the obvious difficulty in getting evidence of the whereabouts of other cell-secretion. Still, we occasionally get an opportunity of seeing bile in the plasm of the liver-cell, and sometimes we observe other secretions exuding from the plasm of cells.

From what I have seen of the so-called "diaphanous corpuscles" or "colloid bodies," as well as from carefully-recorded observations, I think there can be but little doubt that these bodies are globules of albuminous secretion, and from having seen them around a naked nucleus and at other times exuding from plasm, I think we may fairly consider that here we have evidence again of intranuclear secretion.

It is by a process similar to that of secretion that nutri-

ment is first received into the system. It is through the spongiolo of the rootlet, and the villus of the intestine, that the highest plants and animals gain means of adding to their tissues. In each position we find the same process going on. Cells, arranged to filter and secrete, invest these structures, and are from time to time renewed as they become clogged and inefficient. In the spongiolo the old and useless cells are left to coat the rootlet as it lengthens. But such an arrangement would obviously be ill-adapted to alimentation in animals, and consequently the inefficient cells are shed, and no elongation of the villus takes place. But this first process of elaboration is not alone sufficient in the higher animals; much more remains to be done. A great tubular gland, having its distal extremities stretching into these villi, receives this secretion and retains it for further elaboration. This gland is furnished with free and naked nuclei, which elaborate the secretion in which they live, and at the same time reproduce their kind, growing and dividing, by likening to themselves the surrounding fluid. This is assimilation.

These nuclei, however, though so long as they remain in this gland they never invest themselves with plasm, still perform the function of secretion by ~~joining~~ new products *forming* in the surrounding liquid. Some of these nuclei pass out with the fluid they have elaborated into another tubular gland, and now no longer as lymph-corpuscles, but as white blood-corpuscles in a different medium, they commence a new life, and form another secretion. Whether this secretion invests them as it does in the lower vertebrates, or whether it is detached as soon as formed, depends perhaps more on rapidity of secretion than on the nature

of the substance secreted. This second secretion is the formation of the red blood-corpuscle.

I have now attempted to show that nuclear growth is the true process of assimilation, and I have brought evidence to show that the cell-secretion is intra-nuclear, and that many tissues are mainly composed of stored secretions, histologically homologous with the secretion poured out by glands. In doing this I have foreshadowed what it is now necessary for the completion of my scheme to state distinctly, viz., that I consider the formation of plasm as distinctly a process of secretion, as the storing up of oil. The formation of plasm is surely as much a secretion as the formation of fibrin. Just as the nucleus assimilates nutrient material and proliferates, so does the lymph-corpuscle; just as the nucleus secretes embryonic plasm, so does the lymph-corpuscle secrete fibrin; just as the nucleus secretes oil, so does the lymph-corpuscle secrete the red blood-corpuscle.

Certain minds will feel a repugnance to these notions, because substances of small chemical complexity are associated as histologically homologous to substances of great chemical complexity. But who can draw the line between silica, calcium carbonate, urea, oil, sugar, albumen, and other protein compounds? Some again may object on the grounds of physical complexity. But surely we may see a certain gradation from slime to silk, to byssus, to elastic fibre, to muscular fibre.

I have persistently marked out two groups of secretions—two broad classes, but as they go on in many cases synchronously a difficulty in nomenclature arises, for so little is known of the directive agency manifested in secretion by means of which one secretion passes out at one side of a

cell to go back into the blood, and another exudes from the other side to leave the gland, while at the same time plasm continues to be secreted, and the nucleus to grow. If my scheme of reconciliation be a natural one, it should be of the same value to the pathologist as to the physiologist. But the morbid variations of physiological functions require for their explanation a far more extensive knowledge of physiological chemistry than we at present possess. Still, in cases where we have only an exaggeration of healthy processes, we may, at least, expect to find fresh machinery. Prominent in this class are the abnormalities of assimilation manifested by nuclear growth. If any living tissue be torn, or otherwise injured, local congestion results. Assimilation, under these circumstances, goes on with unusual rapidity, in consequence of the increased supply of nutriment. The healthy nuclei surfeit themselves on the nearly stagnant blood, and suddenly grow and multiply. Soon we find a swarm of nuclei on the spot. These set to work like navvies after an accident to clear away obstacles, or fill up chasms, as the necessities of the case may require. These navvies, it is said, are brought by vessels, and disembarked on the spot, by orders emanating from a nerve-station; but with this view I am not disposed to agree. The nuclei are, however, there, and they may be seen working away at the removal of a piece of dead bone in necrosis, or excavating through elastic tissue in phthisis, or filling up a wound by granulation, reconstructing gradually a healthy tissue. When a large number are thus congregated together, the nutriment being handed on from the rear, we might expect, if the phalanx were thick, that those in the front would come badly off, and such actually seems to be the case, for we find the front rank of

ill-fed nuclei falling away as pus-corpuscles. During this rapid nuclear growth, we have, as a correlate of assimilation, abundant heat, whence the name inflammation. But under certain conditions, this nuclear growth is arrested. The material that would have continued to form nuclei, and kept up the outward flow of pus, is now formed, by the nuclei there assembled, into a poisonous secretion, which passes into the blood. The presence of this blood-poison is known to the surgeon by the effect it produces as it flows through the nervous centres, causing rigors which remind us of malarious fever. The poison passes on, but not often without affecting the white blood corpuscles—the fibrin-secreting nuclei. It is not generally, however, until it reaches the refining glands, that its effects become very serious. Then, if the dose be strong, the gland strikes work. The nuclei cease to pour out their normal secretions, and abnormal nuclear growth commences. At the same time a change takes place in the plasm, producing the appearance known as “cloudy swelling.” This is soon seen to be due to the presence of fatty particles, and indicates an acute form of fatty degeneration, which may be caused by the nucleus preying upon the surrounding plasm, using a part for assimilation, and secreting the remainder as a less complex chemical compound. The degeneration, or metamorphosis proceeds, until at length the proliferating nucleus is free, nothing being left of the plasm except a little fatty detritus. This is the diffuse suppuration of pyæmia.

The physiological views that I have been advocating appear to advantage when we consider the life-history of cancer. These malignant growths I would arrange in three divisions. First, the gelatinous form, consisting simply of nucleated plasm, which may be an offshoot

from any tissue, since it represents the primal condition of all tissues. Next, those groups composed of specialised elements, bearing no definite relationship to any normal structure. Here we have a complete remodelling of tissue on a new design. The remaining division includes those growths which bear a recognisable resemblance to the tissues whence they spring—a resemblance to the tissue in its rudimental state, but still at a stage after differentiation has commenced. From this last group, which is the least malignant, we pass by an easy gradation to simple hypertrophy.

The order in which I have arranged my divisions, like all arrangements in straight lines, is unnatural; but the groups seem to me to include all those growths known as cancers. But in neither of the three classes, speaking broadly, do we find any structure histologically in advance of gland-structure. And as these masses do not occupy themselves with storing oil or sarcous matter, or elastic tissue, we are led to believe that as they grow they pour out a large quantity of fluid secretion into the blood, the effect of which we have some means of judging.

A growth of this nature makes its appearance in a healthy man; it may create no interference from its position, and its size may be inconsiderable; still we see disturbances in the nutrition—or rather assimilation and secretion—of every part of that man's body, and he wastes and dies. Are we to believe that death results from the drain on the system? I think not. The malignancy is not in proportion to the size of the tumour, and in chronic suppuration we have a far greater drain on the system, and yet life is not so quickly destroyed. Yet in this exaggerated nuclear growth there must be activity. Can one

help suspecting that we are dealing with a poison-gland specially provided for elaborating and letting loose into the blood a secretion which produces mal-assimilation throughout the body?

Let us invert the picture and imagine instead of a cancer an ovary or testicle. The blood flows through these glands, bearing with it secretions from every tissue of the body. Is it difficult to understand how the resulting product of the ovum and spermatozoon may inherit the peculiarities of both parents? The notion is, I think, preferable to Mr. Darwin's modern theory of Pangenesis.

It will be seen that I think it fair to suppose that every tissue has, in different degree, the function which we have assigned to the ductless glands. These vascular secreting-stations, I consider, ought to take a position physiologically (not histologically) by the side of adipose tissue. Fat, we know, is ordinarily of little use; but each store-cell of which it is composed has a permanent nucleus, and in times of dearth we find it unlading and furnishing fuel for further correlation. The ductless glands are principally remarkable for having the machinery for doing a vast amount of work; yet it has been shown we can get on without them. They are stations less necessary to the vascular system than ganglia are to the nervous system, but more necessary than lymphatic glands are to the absorbent system; they might to some extent be compared to London fire-engines standing ready for use in case of emergency, only requiring the order to get up steam. I should be curious to know how a patient without a spleen would fare—say in typhus fever.

I have more than once spoken of machinery, always using the phrase for nuclear matter; each nucleus would

seem to be a battery, the construction of which we have at present no means of finding out. We see how forces can be correlated with its force, and we are thus able to study its affections; but we know no more of its construction than of that combination of matter which sustains chemical action, furnishing heat and magnetism in the earth's centre. Thermo electricity, and the hypothesis of Grot-huss, start us with ideas of what goes on during the incubation of an egg, but fall short of furnishing us with a parallel phenomenon. Physicists boast of our being able to construct such organic secretions as alcohol, oil, and urea, but this is quite beside the question. The day may come when the chemist in his laboratory may out of stones make bread; but I see no reason to think that he will even in that day do it with other than the comparatively clumsy apparatus with which he has constructed his alcohol and urea.



