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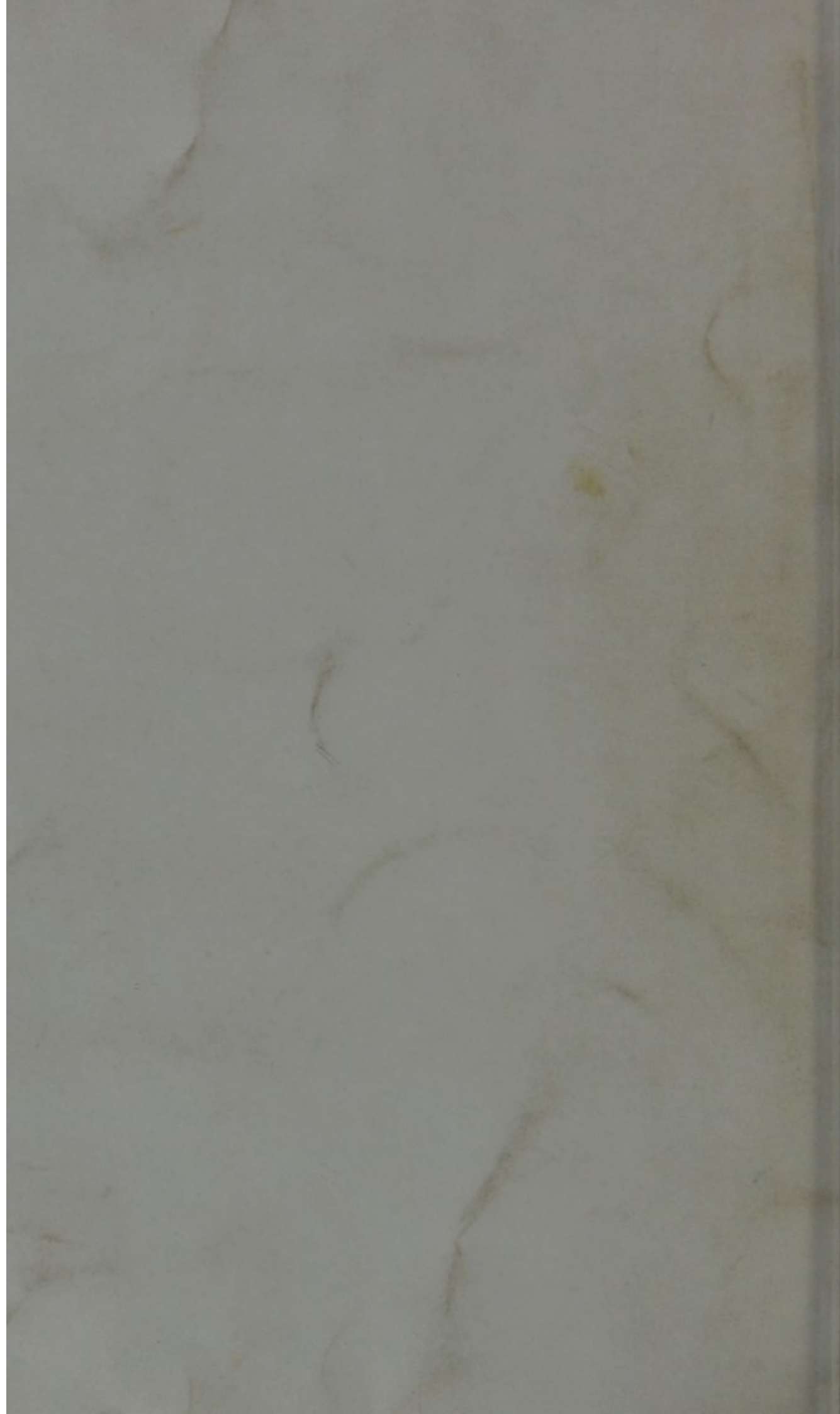
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*W. J. H. Bennett Esq M.D.
with Dr. Houston's Compliments*

ON THE

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MICROSCOPIC

PATHOLOGY OF CANCER,

(WITH A WOODCUT.)

BY

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(From the Dublin Medical Press, vol. xii. p. 5.)

DUBLIN:

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1844.

OF THE

MICROSCOPE

PATHOLOGY OF CANCER

(WITH A WORDS)

BY

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DUBLIN

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MICROSCOPIC PATHOLOGY OF CANCER.

At a meeting of the Surgical Society of Ireland, held on the 11th of May, 1844, Dr. Houston made the following communication on this subject:—

The principles developed by recent discoveries regarding nucleated cells and their agency in carrying out the phenomena of birth, growth, and decay, in vegetables, have been, most happily, found applicable also to the explanation of similar phenomena in the animal kingdom. The cell-theory of Schleiden, namely—that the functions of absorption, assimilation, respiration, secretion, and reproduction in plants, are all effected by one primitive type of microscopic cell, has been proved by Schwann to be that which holds good equally in regard of analogous functions in animals;—a theory more fruitful, perhaps, in novel results and widely-extended application than any other in modern physiology. The establishment of the cell-theory, as applied to normal textures, naturally led to investigations into the effects of disease on the form and structure of these ultimate elements, in the hope of determining, with accuracy, the principles which regulate the phenomena of diseased action.

Müller led the way in these researches; many other able investigators are also in the field, and astonishing results are daily being brought to light. Being myself possessed of an acromatic microscope of high magnifying power, I have been endeavouring to follow in the wake of these pathologists, and to inform myself as to the accuracy and value of their statements. Up to the date of my resignation of the Curatorship of the museum of this College microscopic pathology was not much appreciated or cultivated, and therefore it is that my published Pathological Catalogue does not embrace this department of investigation. But, since that period, I have taken every opportunity of making myself acquainted with the micros-

copic characters of morbid growths ; and the object of my present communication is to introduce the subject to this society, and to exhibit some preparations from the museum which I regard as illustrative of the several varieties of cancer. As the subject is likely to be new to some of my hearers, I think it right to make a few such general observations regarding the structure and form of primordial cells as may render my observations intelligible, equally, to all.

A *cell* is the ultimate limit of organised structure—an atom, beyond which, subdivision is impracticable. It abruptly assigns the confines of microscopic analysis. The diversities of size in these primitive cells range from dimensions of immeasurable minuteness to the magnitude of a cell visible to the naked eye ; from the 1-376.000th to the 1-20th part of an inch. And a definite scale is assigned to the primary organic cell proper to various structures.

The typical elements of a primordial cell are three. First, an external sac or *cell-membrane* ; then a smaller vesicle or *nucleus* ; and thirdly, a smaller still, the *nucleolus*. [See diagram, fig. 1.]

“By the significant assistance of three small concentric lines, it is thus practicable definitively to express the profound truth, that a slender tripartite cellule is typical of the common germ from which all animal and vegetable existence proceeds. It is the universal focus of parentage to every individual within the confines of organic nature.”—*Dr. Williams*.

Primary cells propagate themselves by the production of cells similar to themselves. When they have attained a certain stage in their existence the cells usually burst, by an act to which the term *dehiscence* is applied, and shed forth their nuclei, which, by the imbibition of nutriment from surrounding appropriate material, grow and multiply like their parents. In its pathological relations this is a very important circumstance. For when the malignant tendency, that of cancer for example, has been once established in a part by the organisation of a cancerous primary cell, in virtue of this extraordinary power, which, from the beginning, inheres in the cell of multiplying its kind, the continuance of the diseased process in the part is certain and inevitable. The whole framework of the body being thus composed of ultimate

cells, the question arises—How are the normal to be distinguished from the diseased ones? What is the difference between the cells of the breast, for example, in its healthy state, and those found in it when affected with cancer? The cell of cancer has a microscopic figure different from the normal cell: it appears the same in every region in which it is formed; and it propagates itself in a manner and with a force over which the ordinary laws of nutrition have no control. I cannot but stop, here, to draw attention to the resemblance in these views to those of our distinguished countryman, Mr. Carmichael, years since promulgated, regarding the parasitical nature of cancer. Mr. Carmichael did not, it is true, employ the microscope; he did not go the length of portraying the parasite and exhibiting to us its form, size, and mode of connection with the body, but he certainly promulgated the same great truth as that which now directs the investigations of the pathologist. Vague and conflicting notions have hitherto prevailed regarding malignant diseases; and the application of names equally unstable and inappropriate has only added to the confusion; and, what is of still more consequence, the diagnosis between diseases of malignant and those of non-malignant characters is, to this day, as often a matter of guess-work as of certainty. As if in publicity of our ignorance on this very subject, I cannot help alluding to the fact of a society of the most learned and practical surgeons of the day, and in the capital of pathological science, having only just risen from a stormy discussion, of a week's duration, on a point which they have, nevertheless, left just where they found it—namely, the question of malignancy or non-malignancy of certain tumours of the breast, and the mode of distinguishing such as are, from such as are not, malignant. Some light is still wanted on these matters, and, if to be found anywhere, it must be in chemistry and the microscope. Any knowledge regarding the nature and distinguishing tokens of malignant diseases, beyond what we are already possessed of, must be sought in a minute analysis of the ultimate structure of these growths.

Speaking of the chemistry of morbid growths as a means of diagnosis, I may here observe that those

of a carcinomatous nature are essentially albuminous—so much so, that even the soft, gelatiniform cancer of the stomach, when boiled for hours, gives a full precipitate of albumen, without showing gelatine, on any test. Müller states that, in repeated examinations of cancer of the mammary gland, he never detected gelatine, even after boiling for eighteen or twenty-four hours.

Several diseases, which, formerly, were considered to be very unlike each other, as, for example, cancer and fungus hæmatodes, have of late, from the discovery of analogies in their anatomical, chemical, and pathological characters, been brought together and placed under the same class. In further justification of such an alliance, I may here state that the pathological products supposed to characterise, severally, these diseases, are sometimes met combined in the same specimen; and, farther still, that when one has been removed by operation, another of a different kind frequently takes its place.

As the result of these observations, a more uniform and appropriate nomenclature has been adopted. Müller ranges all malignant diseases under the generic head of *carcinoma*, which he subdivides, according to their anatomical characters, as follows:—

1. Carcinoma simplex, or scirrhus.
2. Carcinoma reticulare.
3. Carcinoma alveolare.
4. Carcinoma melanodes.
5. Carcinoma medullare.
6. Carcinoma fasciculatum.

English writers divide the genus carcinoma into three species—*scirrhus*, *encephaloid*, and *colloid*.

The scirrhus embraces the c. simplex and c. reticulare of Müller. The colloid is synonymous with the c. alveolare. And the encephaloid takes in the carcinoma fasciculatum and medullare. The carcinoma melanodes of Müller is not admitted into this classification, as the presence of the melanotic matter with cancer would appear to make rather an accidental than a fundamental combination. The latter classification is more comprehensive, and admits of the introduction of varieties with more readiness than the former; and those who wish to follow it out may consult, with advantage, a very comprehensive and able

article on the subject by Dr. Walsh in Costello's Cyclopædia of Practical Surgery.

The microscopic elements of carcinoma are, capillary vessels, fibres, granules, cells with or without nuclei, caudate, and spindle-shaped bodies.

With respect to *capillary vessels*, they are always present in malignant growths, and come to be a means of assisting in the pathological diagnosis in some cases. Even in scirrhus, the least vascular of all, there can be no difficulty, sometimes with the naked eye, but always, with a magnifying power of twenty diameters, under water, in demonstrating the presence of blood-vessels.

Fibres form a large proportion of the bulk of scirrhus. To them is due the stone-like density of such tumours. They form a very fine areolar network, among the meshes of which the ultimate cells are disposed. By maceration in water the cells can be washed out, leaving the fibrous interlacement distinctly observable.

Granules are small spheroidal bodies without any cavity in their centre, and sometimes clustered into bundles. [Fig. 3.] They are very numerous in the carcinoma reticulare, to which they give the peculiar and distinctive characters.

The *cell* is the most frequent element, and it varies in form and mode of connection in different varieties of cancer. In the carcinoma simplex, c. reticulare, and c. alveolare, the cells are round and about the $\frac{1}{3054}$ th part of an inch in diameter, requiring a magnifying power of 400 or 500 diameters for their exhibition. [Fig. 2.] A lower power may show the cell as a distinct object, but will not demonstrate its cavity.

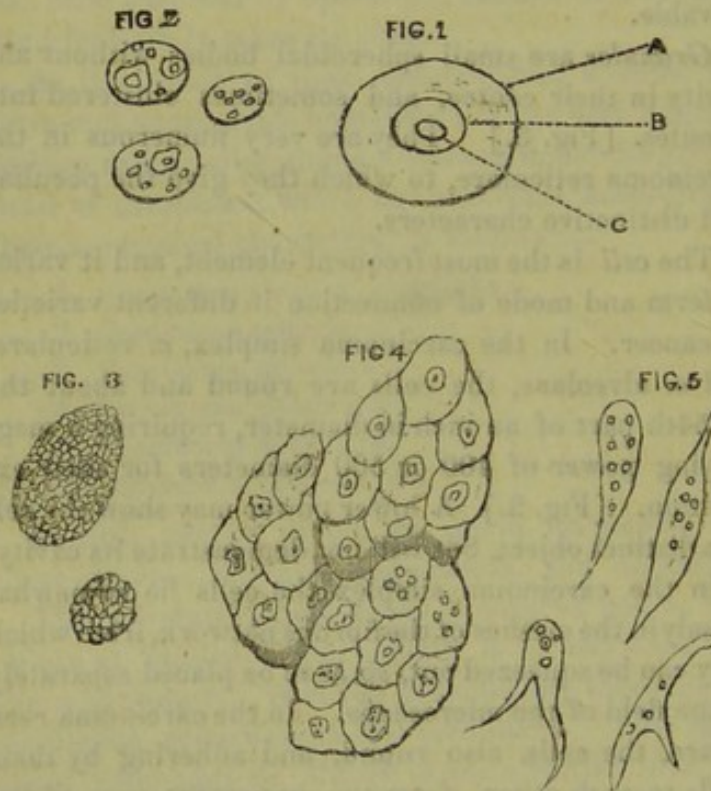
In the carcinoma simplex the cells lie somewhat loosely in the meshes of the fibrous network, from which they can be squeezed out, so as to be placed separately in the field of the microscope. In the carcinoma reticulare, the cells, also round, and adhering by their walls to each other, form the important part of the structure, while fibres of cellular tissue serve only to form membranes, uniting together its several lobuli. In c. medullare (fung. hæmatodes) the cells appear in the form of spindle-shaped or oval bodies, [Fig. 5,] connected either to each other, or to a fibrous basis, as in the other instances. In c. alveolare successive

series of cells are incased, one within the other, the smallest microscopic, the largest being visible to the naked eye. [Fig. 4.] They exist in extraordinary numbers in all these instances, and are the real *seminia morbi*. The corpuscles seen through the microscope in their interior are either young cells, or nuclei from which young cellules are developed.

EXPLANATION OF THE WOODCUT.

(In part after Müller.)

- FIG. 1. Plan of a primitive cell. *a.* The cell-membrane. *b.* The nucleus. *c.* The nucleolus.
2. Cell-globules of carcinoma, magnified 500 diameters.
 3. White granular corpuscles from a carcinoma mamillare.
 4. Cells from a carcinoma areolare of the stomach.
 5. Caudate corpuscles, of different shapes, from a carcinoma medullare.



In the observations which I have to make on the several varieties, I shall adopt the classification and nomenclature of Müller.

Carcinoma simplex.—The tumour of *c.* simplex is irregular in form, but not lobulated. It is hard and resisting to the knife (whence the term stone-cancer,)

and presenting in the section a greyish appearance. The mass is composed of two substances—a containing and a contained part; the former fibrous, the latter grey and granular. The fibrous substance is composed of an irregular network of firm bundles of fibres, and may be seen by maceration, or by scraping away the grey matter for which it serves as a basis. Sir E. Home described these bundles as radiating from a common centre, but they present great varieties in this respect. The grey matter consists of the microscopic formative cells crowded together, although but slightly adherent to each other, or to the fibres among which they lie, and admitting of being squeezed out from the surface of a section, by pressure. The matter thus seen to ooze out is the true “cancerous juice,” the surest evidence of malignancy. The fibres and cells, when looked at together and undisturbed, present a glossy semi-transparent aspect. In the early stages there is often no distinct appearance of septa with interposed grey matter, whilst in the more developed state, and when the cancerous juice is in greater abundance, the grey lobular character becomes more manifest.

The *c. simplex* is usually a solitary tumour, slow in its growth, and rarely attaining a large size. A most important consideration regarding it is the fact, that of all the varieties of carcinoma it is that from which there are most hopes of benefit by operation, as being that, the removal of which is least often followed by relapse.

I have lately had opportunities of examining three recent specimens of carcinoma simplex of the mamma, furnished to me by Mr. Cusack, Mr. Adams, and Mr. Smyly, in which the general pathological, as well as the microscopic characters, were such as I have described them above. In Mr. Adams’s case, two or three lymphatic glands were implicated, and in them the degeneration, although less advanced, was of the same kind as that in the primary tumour. They had been all slow in their growth, and had reached some size before producing any painful sensations. Here (showing them) are drawings of the cancer cells in these cases, as seen in the field of the microscope; and the resemblance which they bear, in all the three, to each other, as well as to the representations given

of such cells by Müller, sufficiently stamps their true diagnostic character. In the instance of a chronic, mammary, or fibrous tumour removed by Mr. Adams, and which we submitted to microscopic analysis, cells, such as existed in the foregoing instances in great abundance, were not discoverable at all—a point of great interest and importance, as determining the absence of malignancy in the latter; and the more so, because some of the rational diagnostic symptoms—the lancinating pain, for instance, were present in a distressing degree in this very tumour, whilst in another, which was truly cancerous, there was a complete absence of all such painful sensations. Dr. Fleming has this day brought me for inspection this small wart-like tumour, extirpated from the back of the hand of an elderly man under an apprehension of its being cancerous; and the more particularly so as a similar operation had been performed on this patient's lip for cancer some years previously, without the occurrence of any relapse. In this tumour I could not discover with the microscope either blood-vessels or nucleated cells. It resembled more a piece of concrete albumen than an organised product. I am, therefore, of opinion that, at the time of removal, it had not taken on the cancerous degeneration.

Here is a preparation from the museum, of open cancer of the breast in a woman of seventy, which I removed by operation, and from which there had not been any relapse, five years subsequently, when the woman died of bronchitis. The pathological characters are those of carcinoma simplex. [See Pathological Catalogue, F. c. 805, p. 521.] Here are also several other specimens of this form of disease, and particularly one removed by Dr. Fleming, F. c. 811, after the removal of which there had not been, at the expiration of twelve years, any return of the disease.

The *carcinoma reticulare*, described first by Müller as a variety of the disease, occurs in the breast, even more frequently than the c. simplex. It grows to a large size, and is apt to acquire a lobulated form. Its consistence is variable, but usually it is softer than the c. simplex. It derives its name from a white reticular appearance which it presents in the section, and which is visible to the naked eye. The c. reti-

culare presents the same microscopic cells and fibrous basis that are found in the *c. simplex*; but contains, in addition, a vast number of peculiar white corpuscles, the disposition of which among the grey mass is such as to produce the net-like appearance above spoken of. These corpuscles are formed by the agglomeration of small granules. They are usually oblong in shape, although sometimes rounded, [Fig. 3,] and two or three times as large as the red globules of the blood. As the disease advances, the reticular figures readily become confluent, and then appear like irregular white spots. When this occurs, the white mass, as observed by Müller, presents some resemblance to the first appearance of white tubercle in a grey tissue. *C. reticulare* is sometimes very rapid in its growth; and, in by far the greater number of cases, it returns after being extirpated. Here is a specimen and drawing of this disease from a patient who died in the South Dublin Union Workhouse, presented to me by Mr. Shannon. The tumour is very large and lobulated, and the lymphatic glands, both in the direction of the axilla and clavicle, are implicated. Delineations of the cells and corpuscles, magnified, are also here shown. This woman had been visited by Mr. Wilmot and Mr. Cusack two years previously, and while the tumour was of the size of a hen-egg, and these gentlemen had disapproved of any operation, under the conviction that the woman would live longer if let alone. She died of bronchitis, but had acquired a true cancerous aspect, and had suffered much pain in the tumour before death. Notwithstanding the great size of this tumour, and the extensive contamination of lymphatic glands, it is remarkable that it had not contracted adhesions either to the pectoral muscle, or the integuments, except in the situation of the nipple, which was much retracted.

This preparation, of which a drawing likewise shows the recent appearances, may serve as a good specimen of the *c. reticulare*. It is a breast which I removed from a woman in the City of Dublin Hospital some years since. The tumour had grown rapidly, and although so large as to weigh five pounds, was but little adherent to the pectoral muscle, and not at all to the integuments. A cluster of diseased lymphatic glands, which were removed from the axilla at the same

time, are also depicted in the drawing. The operation was performed at the woman's own solicitation, and I ascertained that she lived for about three years after, having died finally of some affection of the chest, which, from what I could learn, was most probably carcinoma of the lungs. [See Pathological Catalogue, F. c. 806, p. 522.]

A large cancerous growth of the anterior mediastinum, exhibited lately by Dr. O'Ferrall at the Pathological Society, and of which he politely sent me a portion for microscopic examination, I found to belong to this species. The quantity of white corpuscles was very abundant in some of the central portions of the tumour, where the disease appeared soft and cream-like, resembling somewhat in this respect tubercular infiltration; whilst in the lymphatic glands of the neck, which appeared to have only lately taken on the cancerous action, the corpuscles were so free, and the fibres so dense as to give to the tumours the appearance rather of *c. simplex* than of *c. reticulare*.

The *carcinoma alveolare* (the "cancer gelatiniforme" of Laennec, and the "cancer areolaire" of Cruveilhier,) is most often met with in the stomach. It is easily distinguished from all the others. The basis of the tumour is fibrous, with laminæ crossing in all directions, and having the interspaces occupied by cells, varying in size from that of a grain of sand to that of a large pea—all, containing a viscous, transparent jelly. In the stomach, the diseased growth is covered with peritoneum, through which the half projecting sacculi and cells are seen. By the microscope, these cells are found to contain, within them, many smaller cellules, which, in their turn, include others of still more diminutive size, forming compound cells; and thus the process of development goes on until the larger cells in the interior wall of the stomach burst and pour their jelly-like contents into its cavity. Preparations A. b. 125, 126, and 137, are well-marked specimens of the disease in the stomach. Of No. 125, it is written, in my published Catalogue, "All the tunics appear to be involved in the disease, the mass of which is so thick as almost completely to obstruct the passage. The tumour consists of semi-transparent, gelatinous matter enclosed in fine cells,

having the appearance inside the stomach of a concrete jelly, and on the outside that of a mass of hydatids, varying in size from a mustard seed to a cherry. There were no adhesions to the parts around"; and of No. 126, it is said that "The interior is soft and gelatinous like frog's spawn; the exterior, which is free from any unnatural adhesions, may be aptly compared to the ovary of some fish in which the turgid ova shine through their transparent investment; with this difference, that in the disease the corpuscles vary much in size, whilst in the ovarium they are uniform." Preparations A. c. 403, 404, 405, and 405, are examples of this disease engaging the peritoneum. Delineations of it may also be seen in Cruveilhier's *Anatomie Pathologique*, liv. 10, tab. 4; and in Carswell's *Pathological Anatomy*, fasc. 3, plate 1, fig. 8.

We have, in our museum, a series of preparations comprising nearly all the bones of an individual affected with carcinoma alveolare. The bones are perforated with numerous holes, which, in the recent state, were filled with the soft gelatiniform cells of the cancer. [See E. a. 345, et seq.] My friend, Mr. Smith, exhibited to this society, on a former occasion, an interesting series of the same kind, now deposited in the museum of the Richmond School of Medicine.

Carcinoma medullare (one of the varieties of encephaloid, and better known by the name of fungus hæmatodes,) like the foregoing, consists of two elements, a contained part, the cancerous matter, which gives the medullary or cerebriiform appearance to the whole, and a containing part, consisting of denser septa which divide the mass into lobes and lobules. These septa are usually of delicate texture, and rarely fibrous as in scirrhus. There is much difference in the consistence of different parts of the tumour. The mass, generally, is usually of a pink tint, and is marked by the presence of numerous blood-vessels. Patches of effused blood are likewise often observable. Cruveilhier affirms that all the vessels visible in such tumours are veins; but, from the bright red colour of the blood which they contain, other pathologists are disposed to regard them as arteries. This variety of the disease is usually lobulated and irregular, forming tumours which increase in number and size with great

rapidity. The relation between it and scirrhus is shown in the fact that relapses after amputation of a tumour of the latter character very often exhibit themselves in the form of fungus medullaris. This form of carcinoma contains, like the foregoing, formative cells or globules, but differing from them in number and shape. The greater softness of the mass is due to the larger proportion of the globules as compared with the fineness and rarity of the reticular basis. The cell-globules sometimes resemble those of scirrhus; sometimes they are oval or elliptic; and, at others, they are prolonged into caudate or spindle-shaped corpuscles. [Fig. 5.] These several differences are supposed by some pathologists to be of sufficient importance to serve as foundations for the establishment of distinct varieties. As regards fatality, the encephaloid tends with greater certainty and rapidity to the destruction of life than any of the other kinds of cancer.

The last of Müller's varieties is the *carcinoma fasciculatum vel hyalinum*. The tumour is formed of soft jelly-like lobules of various sizes connected by a fine reticular basis. These lobules, when examined with a microscope, are found to consist of transparent fibres, from whence its name, and which cause it to tear, and not to crumble, under pressure with the finger. Granules like those which characterise the carcinoma reticulare [Fig. 3.] exist in considerable numbers among its fibres, but neither cell-globules, nor caudate corpuscles can be detected in its structure. This is a rare disease; but I have here, to show, a preparation and drawing from a case in my own practice, which I regard as a genuine specimen of it. The woman was only twenty-eight. She lived without relapse for two years after the operation, when she was carried off by acute pleuritis. The tumour weighed $2\frac{1}{2}$ pounds. The case is described in the Catalogue, vol. ii., F. c. 800, p. 519.

Investigations of this nature have opened a new door in the science of pathology, and will lead, it is to be hoped, to an accurate knowledge both of the nature of malignant diseases, and of the diagnostic differences between them and affections of a benign character. Most important remedial improvements may be expected to arise out of such a consummation.

So far as these investigations have gone, they appear to warrant the inference that the peculiarities observable in a malignant growth are the results of a perversion of nutrition ; or, in other words, that the cells seen in a cancer are only monstrosities of the normal cells. The amount of deviation in these cells from the natural condition would appear, also, to indicate the amount of degeneracy in the tumour, and its consequent distance from under the healthy controlling influence of the system, as illustrated by a comparison of carcinoma medullare with carcinoma simplex, in respect of their organisation and results. To the question, whether primary cancer be originally a local or a constitutional affection, no positive answer has yet been given. But circumstances, as they stand, would appear to favour the opinion that there is a stage, in many cases of cancer in which the disease is strictly confined to the part, and in which it may be removed effectually by operation ; but that when once, from a continuance of the affection, the system becomes influenced by it, a cure by such means is hopeless.

" Microscopic and chemical analyses can never, perhaps, be employed in general practice as a means of surgical diagnosis ; but if these analyses make us acquainted with the most important integral differences of diseased products, these differences, thus ascertained, will easily lead to some outward distinguishing characteristics for the purposes of practical diagnosis."—*Müller*.

So far as these investigations have gone, they have not yet warranted the inference that the proliferation of cells in a malignant growth and the results of a proliferation of cells, or, in other words, that the cells seen to a cancer are only manifestations of the normal cells. The amount of differentiation cells from the normal condition would appear, also, to indicate the amount of degeneracy in the tumor, and its consequent distance from the healthy controlling influence of the system, as illustrated by a comparison of carcinoma metastases with carcinoma simplex; in respect of their organization and growth. To the question, whether primary cancer is originally a local or a constitutional affection, no positive answer has yet been given. This is illustrated as they stand, would appear to favor the opinion that there is a stage in the progress of cancer in which the disease is entirely confined to the part, and in which it may be removed effectively by operation; but that when once from a continuance of the affecting the system becomes influenced by it, a cure by such means is impossible. "Microscopic and chemical analyses can never, perhaps, be employed in general practice as a means of accurate diagnosis; but if these analyses make us acquainted with the most important internal differences of several products, these differences, that are raised, will easily lead to some sound and practical diagnostic characteristics for the purpose of practical diagnosis."—Müller.



