THE TYPING OF MALIGNANCY*

(A CLINICO-PATHOLOGICAL STUDY)

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WHILE it is realized by some authorities on cancer that the term "cancer" comprises a number of distinct diseases, in actual practice this distinction is imperfectly acted on. Naturally, treatment is urgent and resolves itself into one of surgery or radiation or both; and even as to prognosis, in spite of some broad variations, the ultimate outlook appears to be much the same wherever the growth arises or whatever its histology. Despite this inevitable issue, a close observation of material from the operating room and the bedside actually reveals distinct differences through which a wider range of attack on the disease might become manifest. It seems clear, for instance, that the different grades of blood-findings denote differences in the type of malignancy peculiar to the given patient,—in that the morphological features found at one time are still recognizable at other times, so that the case might almost be identified from the blood-film alone. It has also been noticed that a case may show a three or four grade blood-change at a time when the surgical indications are those of an early lesion, and only one or two grade change when the case is clinically an advanced one. When, however, a search is made for special clinical details to correlate with the microscopic findings in blood and tissue it is the rule to find no record of signs and symptoms suggestive of a specific behaviour of the neoplasm, though actually that behaviour exists. There are often peculiarities in the mode of dissemination through the body, apart from the ordinary pathology. This may be accounted for in part by anatomical considerations, but there still remain possibilities of individuality, so that a search for specific differences in the tissues of neoplasms apart from their histological nomenclature seems desirable.

The present communication necessarily provides only an outline of the thesis that there are types of malignancy over and above the classical clinical and pathological forms. In venturing upon the conception of malignancy as in many instances a virus process, one uses the term "virus" for any type of living exogenic agent which is not already ruled out by bacteriology, so that one is open to apply that term either to one single agent common to all forms of malignancy, or to a class of many different agents (as, for instance, Borrel would do). In other words, malignancy is in the first place of two types: one in which the existence of a virus is excluded, and another in which there is the possibility of a virus (*i.e.*, an exogenic agent) at work. The second group is divided into seven types on the basis of microscopical studies; and one of these is again subdivided into five more.

The basis of grouping is not the form of the tumour cells themselves but the types of granulation and the so-called "inclusion bodies". There is of course no doubt about the existence of these structures, the only dispute is as to their being intimately related to the malignant process, to the same extent that almost precisely similar bodies in admittedly virus diseases are related to those. Their abundance in some cancerous tissues suggests that they are more significant than the cancer cells themselves, so that instead of reporting on a neoplasm as this or that form of carcinoma the types and numbers of inclusions would be taken as the essentially significant feature.

Following the method adopted when discussing inclusion bodies in the blood-cells in malignant disease,[1] it is useful to list the kinds of inclusions to which attention is being drawn, leaving aside for the moment any discussion as to their precise nature (degeneration-products, artefacts, non-specificity or specificity). Most of them appear as granulations of varying sizes from ultramicroscopic size up to 2.5 or 3 μ and

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then there is a gap till we reach the classical Plimmer-body of 12-14 μ. The types of malignancy are provisionally taken as follows:

A. Cases without evident cell-inclusions.
B. Cases with inclusion-bodies of these various forms:
I. Granular forms ("the granulation of neoplastic tissue").

	Frequency Percentage
(*a*) Extremely minute (submicroscopic).	2
(*b*) Micro-granules, usually in small vacuoles	22
(*c*) Macro-granules (1-2.5, or 3 μ) usually taken to be pycnosed nuclei, or lymphocytic fragments, etc.	14
(*d*) Both *a* and *b* present in the same specimen	18
(*e*) Packets of (usually) eight particles, sometimes within an oval deeply oxyphile sharp contoured "cell". The particles take up nuclear stain intensely (trachy and pachy-chromatic)	5
II. Blastomycetic forms (*e.g.*, the classical Plimmer bodies)	31
III. Torular forms	2
IV. Mycelial forms	1
V. Cases associated with antecedent septic infections	1
VI. Coccidial forms: (benign neoplasms)	1
VII. Protozoan forms, where plasmodial masses occur in the tumour cells	3

RELATION OF TYPE TO SITE OF PRIMARY 92 CASES

Type	*Buccal*	*Gastro-intestinal*	*Breast*	*Uterus*	*Skin*	*Sarcoma*	*Total*
I	3	5	5	9	0	3	25
I	4	0	6	2	1	1	14
I	4	5	6	1	1	3	20
II	5	11	14	2	1	0	33

To determine to which of the types a given case belongs one makes use of fresh operation material. Preparations of the tissue "milk" are made within as few minutes as possible. Some of this is examined by the dark-field method, with and without colour filters; some is used for making films. Of these some are placed immediately (before drying) into Schaudinn or Bouin fixative, and some are air-dried for Leishman staining.

Histological sections are also analyzed in due course, using both frozen and routine preparations. The granulations are then orientated upon the tumour-cell background, which itself is specially interpreted — the cells being (*a*) proper, (*b*) trophic, (*c*) exogenic—which mimic the host cells closely,[2] (*d*) free-swimming or naked "nuclei".

The blood-grade is worked out as an additional factor,[3] after which the clinical behaviour of the disease in the individual case can be taken up. This combined clinico-pathological approach explains the wide discrepancies shown in the literature in regard to laboratory data on "cancer" (*e.g.*, pH readings, glucose tolerance tests, cholesterol analyses, lactic acid determinations, etc.). It also shows how much more detailed a clinical study is to be desired, *e.g.*, make-up of patient, oxidation-reduction potential, degree of maleness or femaleness, etc. By this combined study one may seek to explain why some cases develop slowly, others in a "galloping" manner; why some cause hardly any clinical effects, while others produce marked changes; why some growths apparently identical in structure should disseminate in different directions; why the blood should show inclusion bodies at an extremely early stage as well as long after the growth has been excised.

To sum up, the study of tumour-juice by special cytological methods immediately after excision provides important information, especially if combined with intensive study of the blood-cell reactions. The cases may be divided up into seven or more types according to the form of the granulation present. The studies indicate (1) that this granulation is vitally significant, even more than the cancer cells *per se;* (2) that the degree of malignancy is in some sort proportional to the abundance of granulation and its type; (3) therefore the danger to the patient lies ultimately in the granulation, that is, in particles very much smaller than cells, rather than in a given histological variety of neoplasm. (This is in line with the conclusions of Besredka and Gross that the tumour tissue itself is a reaction to a virus); (4) that some of the cells in a histological preparation are not body cells at all, but foreign exogenic cells; (5) that closer study of the clinical features, after making some such typing as here suggested, may tend to give a lead towards a more exact and individual mode of therapy.

A detailed analysis of the inclusion bodies is expected to be published shortly.

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