statements seem to be quite warranted by the facts observed:

1. That a bacillus, identical with the *B. dysenteriae*, described by Shiga as the specific cause of acute dysentery in Japan, can be isolated from the stools of many cases of asylum dysentery.

2. That the blood serum of some of these cases of asylum dysentery possesses a specific agglutinative action when tested against *B. dysenteriae* isolated from the stools of other similar cases, and also against other strains of *B. dysenteriae* isolated from cases of dysentery in tropical countries.

On the other hand, the experience of an extended series of examinations of the stools of patients suffering from asylum dysentery will permit me to state:

3. That in order to detect the presence of *B. dysenteriae*, the stools must be examined when fresh.

4. That *post-mortem* material must be collected and examined as soon after death as possible, as after a few hours' delay, even in quite acute cases *B. coli* becomes the predominant organism in the intestinal canal.

5. That under these conditions (3 and 4) the isolation of *B. dysenteriae* from the stools of patients suffering from acute asylum dysentery is comparatively easy by the methods I have indicated—when those stools are, naked eye, typically dysenteric.

6. That in cases of chronic asylum dysentery *B. dysenteriae*, if present, is so outnumbered by *B. coli* and other intestinal saprophytes as to render its isolation a matter of extreme difficulty.

DIFFERENTIATION OF *B. TYPHOSUS* AND *B. COLI COMMUNIS* BY MEANS OF THE PHOTOGRAPHIC PLATE.

By WALTER C. STEVENSON, M.D., D.P.H.,
Pathological Laboratory, Trinity College, Dublin.

It does not appear to have been recorded that the gelatino-bromide photographic plate is sensitive to direct application of the products of certain bacterial cultures in a very remarkable manner, and that, further, the effect on the plate is variable with the special nature of the bacteria to a degree which renders easily possible, in at least one important case, a discrimination between bacteria otherwise difficult to differentiate.

My observations having been mainly confined, so far, to the typhoid bacillus and the *B. coli communis*, I will refer at present to these only.

Cultures of these bacilli are made in broth, samples of the same broth being used for each culture. After, say, 24 hours a few drops of each culture are placed upon the sensitive surface of a photographic plate and spread so as to wet an area of any desired extent—say, 1 cm. or 2 cm. in diameter. (In general, 0.2 c.cm. of the culture has been allowed to spread by itself upon the plate, covering an area of about 1 square cm.) This is done in a red light sufficiently faint to avoid sensible fog upon the plate. An opaque cover—an empty developing dish will do—is now turned over the plate, and it is left thus screened for about 40 minutes.

The cover is now lifted and the superfluous fluid upon the wet areas drawn off with a pipette. No change is observed at this stage of the experiment. The plate is then developed in the usual manner, and during development it is best screened from light. It will now be found that the moistened areas develop with very different densities of silver deposit. The *coli* culture produces a full and marked reduction of the salt. There has progressed over the area wetted by this culture an action similar to the formation of a photogenic material in the film. But where the typhoid culture has acted the result is quite different. Only a very faint deposit is, in general, obtained. And if the plate has, in fact, been exposed sufficiently to the red light (either wilfully or incidentally) to produce a general fogging, it will be found that its effect is even inhibitive and its presence marked by an area almost free from reduced silver.

The following points are of interest, but can here only be briefly noted:

(a) The discriminative action is the same, with some variation in degrees of distinctness, when typhoid and *coli* cultures of the same age are compared at very different periods after inoculation. Thus, cultures of these two organisms in broth compared, after 4 hours' growth and after 33 days, react as above.

(b) The activity of each increases with time up to a certain

age which has not been accurately ascertained. This activity possibly varies with the physical conditions attending culture, but may be taken as increasing from shortly after inoculation to 4 days of growth.

(c) A *coli* culture of 24-hours age, when compared with a typhoid culture of any age (tested up to 33 days) gives the more marked reducing effect.

(d) After a few hours' growth the broths may be boiled and thus sterilized, and the differential effect upon the sensitive surface persists.

(e) This discriminative reaction has been obtained with four cultures of *coli* from different sources and with five typhoid cultures from different sources.

(f) It will be found that if the sensitive plate is wetted with tap water and also with sterile broth, and simultaneously applications of the cultures are made—four separate areas being thus prepared for comparison—the typhoid and sterile broth do not differ markedly in their actions upon the silver bromide, whereas the effect of the tap water has been intermediate between that of the *coli* and the typhoid. It is known that water is to some extent a sensitizer.

(g) The time of exposure of the plate to the application of the cultures has varied between 10 and 90 minutes, and the discriminative action of 24-hour cultures found to be best marked with an exposure of 45 minutes. But from at least 10 minutes exposure upwards the difference is obtained with any broths in which there is a visible growth.

(h) While in some of the earliest of these observations, and before I had gained experience as to the best methods to employ, a few cases occurred in which the distinctive difference was not well marked, in all my recent observations, twenty-four in number, I have unfailingly obtained the differential effect.

(i) Finally I have observed that if pools of well-grown *coli* and typhoid broth cultures are poured on a photographic plate and exposed to light, a reduction of silver is seen in a few minutes without development. After about 30 minutes the deposit due to the typhoid broth is distinctly darker than that due to the *coli* broth. If the pools be now poured off the sensitive plate the difference reaches its maximum, but as the gelatine dries the distinction is almost completely lost. Tap water has no visible effect, except the swelling of the wetted gelatine of the plate.

I am continuing the experiments, and am not without hopes of more extended applications of the phenomenon.

NOTE UPON THE CAUSATION OF CANCER.

By H. J. CAMPBELL, M.D., F.R.C.P.,
Senior Physician, Bradford Royal Infirmary.

THE observations of Professor Farmer and others with regard to the mode of division of the nucleus in cancer cells render it possible to formulate a theory which seems to me to afford reasonable explanations of many of the difficult points in connexion with cancer.

Briefly stated, my view is that cancerous growth is caused by the degenerative reversion of epithelial cells to a germinal type, in association with a local irritant and in the presence of an abundant blood supply. The post-heterotypic multiplication of the cells having once commenced, as a result of the degenerative reversion to an ancestral type, the local conditions serve to continue and fix the type, with the result that the growth becomes practically a colony of unicellular parasites. These act as one would expect members of such a colony to act; they encroach upon the tissues of the host, preferring to multiply along the lymph channels both on account of the resistance being less in this direction than in any other, and also on account of the favourable nutritional environment there met with; or when they permeate the walls of a vein tend to be washed off from the colony as independent units, which, when they lodge in suitable situations, give rise to new colonies, namely, the metastatic growths.

Just as in animals we find an ascending and a descending stream running along parallel lines, so in cells, with regard to specialization, evolution may be downward as well as upward. Again, just as the individual in his development presents a brief epitome of the history of the race, so, to a certain extent, does the individual cell in its decay tend to approximate to an earlier type of cell similar to that from which it has been evolved, and with similar attributes and powers. However, the more specialized the cell the greater

will be the difficulty in its reverting to an ancestral type. Thus one sees that, with certain exceptions, nerve cells, having once been formed, are incapable of multiplication and in fact just as nerve, muscle, connective tissue, and epithelium may be said to form a descending scale in respect to their specialization or departure from the ancestral type, so do these various tissues differ in their attributes and in their powers of multiplication from the ancestral cell. The epithelial cells may, indeed, be looked upon as those cells which have been left over after the more specialized cells have been budded off, and it follows that it is these cells which will most nearly resemble the ancestral cells in their attributes, and especially in their powers of reproduction, and will most easily revert to the original type. In other words, as this reversion must be in the form of a degeneration, it is in these cells that one may expect a degenerative reversion most readily to occur. It may be objected that the reversion ought to be to an embryonic type, that is to say, to a type which is capable of reproducing the whole organism; but, in the higher animals at least, the power of so complete a reversion has been lost, though in many of the lower animals, and in most of the higher plants, this capacity is retained by the least specialized of the individual cells of which the organism is composed.

If, then, the tendency of degenerating epithelial cells to a reversion to a germinal type be allowed, the next thing to consider is, what the causes are which determine the appearance of the disease at any one time or place. With regard to time, the essential condition is that the epithelial cells should be becoming somewhat inert, that is to say, growing prematurely old, and losing their normal powers of reproduction or multiplication. In other words, that, with regard to them, the decadent period of life should have set in. It has often been said that a man is as old as his vessels, and this is equally true of most of the organs of the body, and of the epithelial cells more especially. A tendency to what may be described as precocious degeneration of the epithelium may be a parental legacy; and just as in some families the vessels tend to develop atheroma early, whilst in others the hair becomes prematurely white or thin, or the nerve cells all soon tend to undergo atrophy, so also with these tissues the liability to the early formation of cancer is not infrequently a pronounced family characteristic. Again, the favourite sites for cancer are those, like the breast or the cervix uteri, where degenerative processes appear most early. Further, with the increased rapidity of living under modern conditions, all the degenerative diseases are tending to increase in frequency, and to appear at earlier ages than was the case with our more slow-living ancestors. I need only instance general paralysis of the insane and degenerative conditions of the heart muscle apart from valvular disease.

Again, with regard to cancer houses, streets, and villages, any external conditions which favour the early onset of degenerative changes in epithelial structures will favour the development of cancer, hence it is not surprising that environment should be effective within somewhat narrow limits in determining the frequency of the disease. The high percentage of stomach cases is further hardly to be wondered at considering the amount of irritation to which this organ is exposed by overcooked, hard, irritating food on the one hand, and nauseous, artificially, semi-digested messes on the other, let alone the worry it suffers from the continous drugging it receives on the wall-poster advice of the quack medicine vendor. It is therefore small cause for surprise that the stomach epithelium tends early to grow old and feeble, and the cells individually to strive to retrace their evolutionary history.

So far, then, if I have succeeded in establishing that under certain conditions the epithelial tissues, and especially those in certain regions, are in a state ripe, as it were, for reverting to an ancestral germinal type, then it only needs that some exciting cause should appear in order to start the cancerous growth. But even if started, if it is to go on, the nourishment must be abundant, and hence, again, the great liability to cancer of those regions, like the breast and the uterus, where the mechanical arrangements for the supply of blood are far in excess of the needs of a decaying or degenerating organ. The exciting cause may be a mechanical irritant such as a rough tooth or a gall stone, a chemical irritant as occurs when an irritating discharge flows over a granular surface, or a biochemical one as in the case of a simple ulcer becoming malignant, or as in Paget's disease of the nipple. The effect of the exciting cause is probably complex, in that it not only may act as an irritant to the cells, but will also cause dilata-

tion of vessels and excessive blood supply to the part concerned. Thus it seems to me that all the conditions present in cases of cancer can be more readily and satisfactorily explained by this theory than by any other which has so far been advanced.

STRUCTURAL LINKS IN MALIGNANT GROWTHS.

BY
FRANK BUSHNELL, and F. CAVERS,
M.D.Lond., B.Sc.Lond., F.L.S.,
Pathologist, South Devon and East
Cornwall Hospital, Plymouth. Lecturer in Biology, Municipal
Technical School, Plymouth.

It is said that the qualities which constitute malignancy differ in degree rather than in kind from the characteristics of benign growths. Thus, for example, simple adenoma becomes malignant adenoma, fibroma becomes sarcoma, and papilloma becomes carcinoma. Again, it is impossible by clinical or pathological methods to distinguish sharply between certain cases of retained placenta, simple and malignant moles, chorion-epithelioma (deciduoma malignum) and even teratoma. Progressive growth and the formation of metastases, the infiltration of surrounding tissues, their atypical character, and the absence of specific symptoms are most frequently noted in carcinoma and sarcoma. The laws which govern the growth of tumours and the "fecundity" of the cellular constituents are as yet unknown, but a rapid rate of multiplication and also of degeneration—in other words, cellular instability—is usual. The growth is not in proportion to the nutrition of the body as a whole or in part, or to the age of the patient—for example, the "cancer age" is late middle life.

In carcinoma both lymphatics and blood vessels are the channels for the supply of nourishment, but in sarcoma no lymphatics are known. In both cases the cells are bathed in nutrient fluid and must be fed by a process of osmosis, perhaps aided by increase of assimilatory activity. The purpose of new growths is, of course, unknown. A parallel is perhaps suggested between cancerous growths and the rank vegetative activity often observed in herbaceous plants and in the larger fungi.

Various irregularities in the divisions of the nucleus have been observed in malignant growths—for example, multipolar spindles, increase in the number of chromosomes or in the amount of stainable substance (chromatin) in the nucleus, direct or simple division, etc. Professor Farmer and his colleagues have recently shown that heterotype nuclear divisions, characterized by a reduced number of chromosomes which are annular or "bunched" in appearance, are attached to the long axis of the spindle, and divide transversely, are present in malignant growths in man. Drs. E. F. Bashford and J. A. Murray have reported the same in other mammals and in fishes.

During the study of a large number of sections made by one of us (F. B.) it was noted that the mitoses were very readily observed in a glandular carcinoma of the rectum, less so in a sarcoma, and least in a scirrhus mammae. The appearance of the mitotic figures, as sketched from microscopical preparations with high magnification, is of interest to all pathologists, and the difference between the slender V-shaped somatic chromosomes and the thick irregularly-shaped heterotypic ones, is especially well shown in Fig. 1. In Fig. 2 the somatic mitosis shown in A stands in sharp contrast with the heterotypic ones, B to G; these sketches are all from a glandular carcinoma of the rectum, and were made with uniform magnification. A similar contrast is shown in the sketches H (somatic) and I (heterotypic), which are from a sarcoma. It was observed that the cells undergoing heterotypic mitosis were frequently enlarged and of a spherical or ovoid form. Another feature noticed in the glandular carcinoma was the occurrence of both somatic and heterotypic mitoses in the glands of Lieberkühn adjacent to the growth, and their tendency to be situated nearer to the lumen than to the basement membrane.

Observations are being made with a view to mapping out the topography of cancer cells by this method and to ascertaining their distribution, as described by Professor Farmer, in various growths and in "heterologous" neoplasms. No evidence was obtained of conjugation of resting nuclei, or of conjugation of cells in pairs ("gametes"), or of appearances resembling the formation of "swarm-spores."