conditions a markedly less amount of bound carbon dioxide, similar to that of starved yeast. This indicates that the binding dependent on oxygen pressure is intimately connected with the oxidation-reduction processes in the cell. Brewer's bottom yeast showed a behaviour similar to that of starved yeast.

Calculations of *p*H from the maximum values of bound carbon dioxide, considered as bicarbonate, show that the *p*H in the cells in the presence of carbon dioxide must be increased up to *c.* 0·75 *p*H units above that assumed under anaerobic conditions and the same carbon dioxide pressure (25 per cent carbon dioxide). Such a great change in *p*H has not been verified experimentally. Electrometric titrations (glass electrode) were performed on juice from yeast, fixed rapidly by heating. The determinations indicate that in cells pretreated aerobically with carbon dioxide, this is bound in such a way that a decrease in *p*H is prevented. Under anaerobic conditions, however, this is not the case. Fife and Frampton[3] state that in plant material under the influence of carbon dioxide, ammonia will be liberated from acid amides and the *p*H will thus increase. Where yeast is concerned, I have not been able to confirm this, as the amount of ammonia liberated in the yeast was found to be extremely small, although the juice from yeast cells, pretreated aerobically with carbon dioxide, shows an increase in *p*H measured in absence of carbon dioxide in the atmosphere. Nor is it probable that carbon dioxide would be bound as carbamate (*R*.NH.COOH) at the *p*H in question.

The observations recorded here appear to have some connexion with the investigations performed on different material by Ruben and collaborators with radioactive carbon. Recently, Ruben and Kamen[4] have shown that baker's yeast can assimilate carbon dioxide (at present, the original paper is not accessible in Sweden). It appears probable that the carbon dioxide fixation described above might be interpreted as the first stage in the uptake of carbon dioxide and its further 'assimilation' in the yeast cells, corresponding to the dark reaction described by Ruben's school in connexion with experiments on photosynthesis.

KNUT M. BRANDT.

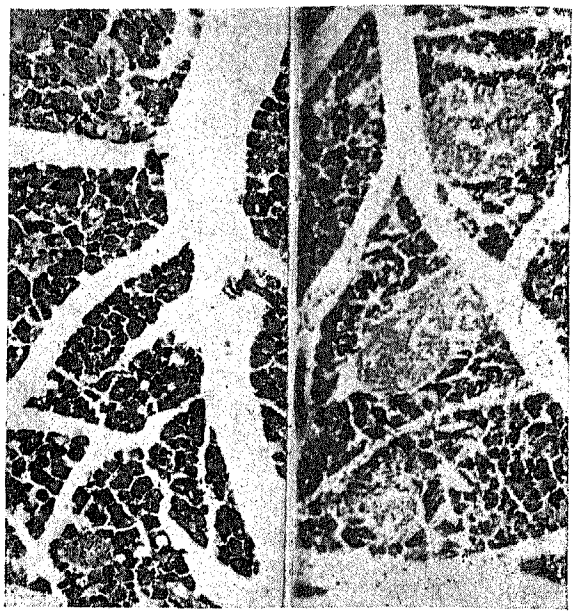
Wenner-Gren's Institute for Experimental Biology, University of Stockholm.
Dec. 8.

[1] Warburg, O., "Ueber den Stoffwechsel der Tumoren" (Berlin, 1926).
[2] Brandt, K., *Naturwiss.*, **30**, 278 (1942).
[3] Fife, J. M., and Frampton, V. L., *J. Biol. Chem.*, **109**, 643 (1935).
[4] Ruben, S., and Kamen, M. D., *Proc. U.S. Nat. Acad. Sci.*, **26**, 418 (1940); cited in *Chem. Abstr.*, **34**, 6953 (1940).

Relation of Scurvy to Histological Changes in the Pancreas

I HAVE shown[1] that the insulin content of the pancreas is markedly diminished in scurvy. In the present investigation attempts have been made to study the histological changes in the pancreas of scorbutic guinea pigs.

Two groups of healthy guinea pigs of weights varying between 163 gm. and 420 gm. were used. One of the groups was placed on a scorbutic diet for 24 days and the other was given normal diet for 15 days[1]. The animals were fasted overnight and killed next morning by a blow on the head. A portion from the tail end of the pancreas was fixed in Zenker-formol solution. Paraffin sections, 7 μ thick, were prepared, and these were stained with Heidenhain's iron hæmatoxylin and Heidenhain's 'azan' stains. In every fourth section from the tail end of each pancreas, stained with iron hæmatoxylin, the number of islets was counted and the size of the individual islets was measured. The results are summarized in Table 1 and the statistical analysis of the individual figures is given in Table 2.



PHOTOMICROGRAPH OF A SECTION OF GUINEA PIG PANCREAS; (*a*) NORMAL; (*b*) SCORBUTIC. × 80.

TABLE 1.

	No. of animals	Number (mean) of the islets in each section	Total (mean) size of the islets in each section (sq. mm.)
Normal guinea pigs	10	7·6	273·52
Scorbutic guinea pigs	10	11·2	1168·25

TABLE 2.

	Size of islets	No. of islets
Difference of the means	894·7	3·6
Standard error of difference	289·16	1·7
t	3·09	2·1
Remarks	Highly significant	Significant

The sections which were stained with 'azan' stain were examined for the different types of cells present in the islets of Langerhans. In the scorbutic guinea pigs, α-cells were found to be increased in number in proportion to the β-cells, and the β-cells were found to be mostly degranulated. There was no degenerative change in the sections studied. Photomicrographs show that the islets are very prominent in the scorbutic condition.

The increase in the size and also the number of islets may be due to Nature's attempt to react against the fall in insulin secretion observed in scurvy. The

absence of any degenerative change seems to be related to the fact that normal recovery takes place when the scorbutic guinea pigs are given supplements of vitamin C.

I wish to express my thanks to Dr. B. B. Sarkar and Mr. P. B. Sen of the Department of Physiology, University of Calcutta, for their kind help.

SACHCHIDANANDA BANERJEE,
(Mitra Research Scholar).

School of Tropical Medicine,
Chittaranjan Avenue,
Calcutta.
Jan. 27.

[1] Banerjee, S., NATURE, 152, 329 (1943).

Growth-Inhibiting Action of Some Pure Substances

THIS preliminary report describes the results obtained with a certain class of growth-inhibitors. Since evidence exists that *H*11 extract contains certain chemical compounds, it was decided to ascertain the inhibitory effects of some pure related substances upon the growth of the Twort carcinoma.

Tumour-bearing mice, averaging 25 gm. weight, were injected intraperitoneally, twice daily, with 0·5 c.c. of the solution to be tested. The surface areas of the tumours were calculated as the products of their diameters, and the group average determined. The inhibitory effect was calculated as the percentage difference between the average increases in size of the treated and the control mice.

Typical results obtained in comparable experiments are summarized in the accompanying table. Mice injected with certain chemicals, for example, anthraquinone, rapidly increased in weight during the course of the experiments, whereas the tumours were inhibited. Tests of substances toxic at higher concentrations, for example, the tannates, showed that, at lower concentrations, tumours were significantly inhibited, the host mice appearing completely unaffected.

Substance tested	Concentration (per cent)	Days of treatment	Percentage inhibition
Sodium tannate	0·25	28	83·3
Calcium tannate	Sat. soln.	8	51·3
1 : 2 : 4-trihydroxy anthraquinone	0·25	14	55·03
1 : 2 : 4 : 5 : 6 : 8-hexahydroxy anthraquinone	0·25	14	81·3
Anthraquinone	0·1	13	46·9
1 : 2-dihydroxy-5 : 8-naphthaquinone	0·25	14	90·6
henanthraquinone	0·1	8	52·1

Badger *et al.*,[1] found that some quinone derivatives of carcinogenic hydrocarbons inhibited the growth of the Walker carcinoma 256, and Berenblum and Schoental[2] came to similar conclusions. Other phenolic, aldehyde and quinone derivatives of cyclic hydrocarbons have been tested; the results will be described later.

All these compounds have the property of combining with proteins. Derivatives of vegetable tannins react with proteins because of their polyphenolic constitution, and quinone compounds through their characteristic radicals. The inhibitory effects of these otherwise dissimilar substances are probably directly due to this reaction. A much greater inhibition of tumour-growth than of body-growth was produced. This greater susceptibility to the action of the inhibitors shown by the malignant cells must presumably reside in their intrinsic differences.

Such differences may be accounted for by a provisional hypothesis concerning a modification of cytoplasmic organization in tumour cells. Needham[3] has discussed the organization and differentiation of cells in terms of a cytoskeleton composed of protein fibrils. Wrinch[4] holds a similar view. The hypothesis is that, in the malignant cell, the cytoskeletal components have lost the power of linking up with one another to form a three-dimensional lattice such as may exist in a normal cell.

Fully differentiated cells are unable to divide, but the 'disarticulated' cytoskeleton of a malignant cell, while providing the morphological basis of dedifferentiation, would not hinder division. As the abnormal fibrils would presumably lose the power of responding to the evocator substances which control differentiation, malignant cells would remain undifferentiated and show unregulated growth.

Mottram[5] holds that malignancy results from cytoplasmic modification. The morphological differences between the cytoplasm of malignant and normal cells described by many workers are reviewed by Ludford[6]. The 'disarticulation' of cytoskeletal fibrils would result in such differences. The similarities between malignant cells and embryonic cells might also be explained in terms of the organization of the cytoskeleton.

On the cytoskeletal hypothesis, the various carcinogenic agents would induce malignancy by directly or indirectly modifying the cytoskeletal fibrils so that they no longer link up with one another. The premalignant period would be occupied by the accumulation of abnormal fibrils until their predominance prevents the formation of a normal 'articulated' cytoskeleton.

The mode of action of inhibitors with the property of tanning proteins would be to link up the discrete fibrils of a tumour cell to form a 'pseudo-cytoskeleton'; treated malignant cells would then become stabilized, 'non-malignant' cells, and would be much less able to reproduce themselves, with the result that the whole tumour would tend to regress. This effect of tanning agents on adult, healthy cells with normal cytoskeletons would be relatively insignificant. There may be a similar effect on the mitotic spindle and nucleus.

The cytoskeletal hypothesis furnishes a possible explanation of the site of action of tumour inhibitors which tan proteins and also of various phenomena associated with malignancy.

I am greatly indebted to Mr. J. H. Thompson, director of research of these Laboratories, for constant help and encouragement. My thanks are also due to Mr. C. R. B. Williamson for valuable technical assistance.

A. K. POWELL.

Department of Pathology,
Hosa Research Laboratories,
Sunbury-on-Thames, Middx.

[1] Badger, G. M., *et al.*, *Proc. Roy. Soc.*, B, 13, 130, 255 (1942).
[2] Berenblum, I., and Schoental, R., *Cancer Res.*, 3, 145 (1943).
[3] Needham, J., "Biochemistry and Morphogenesis" (Cambridge, 1942).
[4] Wrinch, D., NATURE, 150, 270 (1942).
[5] Mottram, J. C., "The Problem of Tumours" (London: H. K. Lewis and Co., 1942)
[6] Ludford, R. J., "Cytology of Cancer", pp. 252–259, in "Cytology and Cell Physiology", ed. G. Bourne (Oxford: Clarendon Press, 1942).