SPECIAL ARTICLES

THE ACTION OF THE PARENTERAL ADMINISTRATION OF SUGARS ON THE HYDROGEN-ION CONCENTRATION OF NORMAL AND MALIGNANT TISSUES IN LIVING ANIMALS[1]

THE principal factors—biochemical and physiological—which control the acid-base equilibrium of the blood of animals are well known. Very little is known, however, concerning the regulation of the acid-base balance in the tissues. Even in the case of the voluntary muscle, which has been subjected to intensive investigation during the last twenty years, it has so far been impossible to gain an adequate picture of the factors which may control the hydrogen-ion concentration of muscle tissue in living animals. Data obtained on isolated tissue have only limited value, inasmuch as the conditions prevailing in the body can not be duplicated accurately. Attempts to apply the customary colorimetric and electrometric methods to extracts or macerations of tissues have yielded figures differing by as much as one pH unit for one and the same tissue. This is due to serious technical errors, such as acid production during the preparation of the material, loss of CO_2, interference of oxidation-reduction systems in electrometric estimations by means of metal electrodes, etc. More satisfactory results were obtained by Rous, who applied pH indicators to exposed tissues of living animals and, by noting the color change, obtained an approximate estimate of the hydrogen-ion concentration.

About a year ago we described a technique for the continuous measurement of the pH of the tissues in living animals, which makes use of a specially constructed capillary glass electrode in conjunction with a quadrant electrometer and potentiometer.[2] Further improvements in this method have been made since. A great advantage of the glass electrode over other electrodes is that it permits pH measurements in the presence of the oxidation-reduction systems which occur in all tissues. However, there is one objection to the method in that the electrode makes contact not with a single morphological tissue unit, but with the different cells comprising the tissue as well as tissue lymph. Direct contact with blood can be avoided by careful insertion of the electrode into the tissue.

Recognizing this limitation we believe from our extensive experience that the method is of real value in the study of various problems. We have applied it to the study of the nature of cancerous growth. The work is based on the fact that certain tissues are known to ferment glucose with the formation of lactic acid. As a normal tissue we chose the voluntary muscle of rats, because of the ease with which it produces acid upon slight injury, a fact which from a technical standpoint furnished a severe test of the reliability of the method. On the other hand it was shown by Warburg and coworkers by experiments *in vitro* that lactic acid production is especially pronounced in malignant tissues, even in the presence of oxygen. Furthermore, Cori and Warburg have found that venous blood coming from a malignant tumor has a lower glucose and a higher lactic acid content than normal venous blood. The same investigators have also shown that the lactic acid formation in tumor tissue *in vitro* and *in vivo* can be increased by increasing the glucose supply.

We were therefore interested to ascertain whether it is possible to force the lactic acid production in voluntary muscle or malignant tissue by means of injection of glucose to such a degree as to cause an increase in the hydrogen-ion concentration. Having found that this was easily possible with malignant tumors, we decided to study also the action of other natural sugars obtained in pure form through the kindness of Dr. C. S. Hudson and his collaborators. The sugars were injected mostly intraperitoneally but sometimes subcutaneously as a 20 per cent. solution in doses of 600 mg per 100 g body weight. The animals—rats and mice—were deprived of food for 24 hours before the beginning of the experiments. They received pentobarbital in doses to produce a light anesthesia. The following tissues were studied: voluntary muscle of rats, Jensen rat sarcoma, Flexner-Jobling rat carcinoma, Walker rat sarcoma 325 and the spontaneous mammary mouse carcinoma of the New York State Institute for Malignant Disease.

In order to ascertain whether the observed increase in hydrogen-ion concentration is accompanied by increased lactic acid retention, Dr. J. M. Johnson, after the last pH measurement, analyzed the tissues for lactic acid by the method of Friedemann, Cotonio and Shaffer. The results indicate that there was always more acid present when the tissue had shown an acid drift as measured electrometrically. This means that there is an increased acid production throughout the tissue and not just locally at the electrode. In view of the relatively high dissociation constant of lactic acid it is not surprising that the tissue buffers are unable to prevent an increase in the acidity of the tissue. Whether or not other organic acids besides lactic are concerned in the production of the observed acid drift can not be decided on the basis of the present evidence.

[1] Read before the National Academy of Sciences, April 24, 1933.

[2] Carl Voegtlin and Herbert Kahler: SCIENCE, 75: 362, 1932.

We conclude, first, that the new method yields reliable data; second, that the buffer action of the tissues studied, particularly the malignant tumors, can be overcome by injection of relatively large doses of certain natural sugars and that the acid-base equilibrium is therefore a function of carbohydrate metabolism.

As to the possible significance of these results, it may be pointed out that the pH controls many important biochemical reactions, such as the action of proteolytic, glycolytic and other enzymes; oxidation-reduction; the state of tissue colloids, etc. The work of Jacobs and others, furthermore, suggests that lactic acid, being an organic acid, may have a peculiar action owing to its ease of penetration into cells. We have found that there is an acidity gradient: tumor-surrounding tissue-normal tissue. We therefore may well ask the question whether the excessive local production and accumulation of lactic acid represents an important factor in the destructive action of malignant tumors upon the surrounding normal tissue and upon the tumor cells themselves. Work along this line is under way.

CARL VOEGTLIN
H. KAHLER
R. H. FITCH

U. S. PUBLIC HEALTH SERVICE

SOLAR VARIATIONS AND ATMOSPHERIC PRESSURE[1]

THE Smithsonian Institution has been measuring for 20 years, or more, the amount of solar radiation reaching the earth and computing from the observed data the value outside the atmosphere. These values prove to be variable, and it was deemed worth while to compare these variations with variations of atmospheric pressure on the earth in order to ascertain what relationships, if any, might be disclosed. For this purpose the formulas of correlation were used such as is now the custom to use in the comparison of variables.

The Smithsonian Astrophysical Observatory recently published a table giving the monthly means of the preferred solar values from three widely separated observatories for the interval 1921–1930. The monthly means for the 120 months included were compared with the monthly means of pressure for the same interval at 162 stations scattered over the earth's surface. These data were obtained from the various weather services of the world for publication in "World Weather Records" and were supplemented by means derived from daily charts of pressure for the North Pacific and North Atlantic Oceans.

[1] Read before the National Academy of Sciences, Washington, D. C., April, 1933.

The computed correlations disclosed the following relationships:

(1) With an increase of solar radiation the pressure increases in regions of the earth where the pressure is normally high and decreases in regions where it is normally low. In other words, the normal pressure gradients are increased and the normal circulation speeded up. It has been shown by previous investigations that with high solar radiation the low pressure band at the equator widens and the high pressure belts and centers in middle latitudes move nearer the pole, this displacement being proportional to the intensity of the solar radiation increase.

(2) The centers of greatest minus correlation are in regions of high vapor content and plus correlations in regions of low vapor content, indicating that the absorption of solar heat by water vapor plays an important part in determining the effect of increased solar radiation on the atmosphere.

(3) The centers of greatest minus and plus correlations change positions with the seasons, following the change in position of the areas of high and low water vapor; thus further proving the intimate relation between these conditions.

(4) In the regions of greatest minus correlation of pressure with increased solar radiation, the temperature and rainfall show plus correlations at least for solar radiation changes of short period.

(5) The computed amount of change of pressure and of temperature agree with expectancy.

(6) In considering the effect of solar radiation changes on the atmosphere there are evidently three factors to be considered, namely, intensity of the solar change, the seasonal changes in the atmosphere and progressive movements similar to atmospheric waves. It is possible also that temporary shifts in ocean currents and changes in water temperatures influence the results.

H. H. CLAYTON

BOOKS RECEIVED

ADAMS, LEVERETT A. *An Introduction to the Vertebrates.* Pp. v + 414. 290 figures. Wiley. $3.50.

BARNES, ERNEST W. *Scientific Theory and Religion.* Pp. xxiv + 685. Macmillan. $4.00.

DILLAVOU, E. R. *Business and Law.* Pp. xv + 494. McGraw-Hill. $1.40.

FOLEY, ARTHUR L. *College Physics.* Pp. viii + 759. 453 figures. Blakiston. $3.75.

ROMER, ALFRED S. *Vertebrate Paleontology.* Pp. vii + 491. University of Chicago Press. $5.00.

SCHAUINSLAND, HUGO H. *The Great Enigma.* Pp. 93. Dutton. $1.25.

WASHBURNE, CARLETON and HELUIZ WASHBURNE. *The Story of Earth and Sky.* Pp. x + 368. Illustrated. Century. $3.50.

WHEELER, WILLIAM M. and THOMAS BARBOUR. *The Lamarck Manuscripts at Harvard.* Pp. xxi + 202. Harvard University Press. $2.50.