

ning of the action potential. The total amplitude of this deflection averages 100 millivolts as compared to a maximum QRS in normal human precordial electrocardiograms of about 5 and in standard limb leads of about 3 millivolts.

"Depolarization" is followed by a process of recovery (repolarization) which slowly restores the potential across the cell membrane to its previous resting value. It consists of a rapid, a slow, and a second rapid phase, which may change independently of each other. The last phase of the recovery process coincides with the T wave of surface records.

Changes in ionic concentration of the extracellular space modify shape, voltage and duration of the action potential. As expected, voltage and length of the excitatory process of closely adjacent cells may differ significantly.

Surface electrocardiograms in the frog may be interpreted in terms of the components of these monophasic action potentials. The theoretical concept which views an electrocardiogram as a distant representation of changes in depolarization and in various phases of recovery of single cells and of cell groups is supported by these observations.

✓ *Modifying Effect of Steroid Hormone Therapy of Human Neoplastic Disease as Judged by Radioactive Phosphorus ( $P^{32}$ ) Studies.* SAUL HERTZ,\* Boston, Mass.

The encouraging results obtained in the application of  $P^{32}$  to the therapy of leukemia and polycythemia aroused the hope of utilizing this isotope in the treatment of cancer of other organs. Unfortunately, the few attempts which have been made in this direction have been limited by the failure of sufficiently selective concentration by the cancerous tissues to take place. With exception of certain brain and breast cancers the differential uptake has been of such small order as to discourage any wide application of  $P^{32}$  in this connection.

We have, therefore, set out to attempt to modify the  $P^{32}$  uptake by tumors. We selected hopeless cases of advanced metastatic cancer of several types for our experiments.  $P^{32}$  was administered as sodium acid-phosphate; carrier free as separated by the Atomic Energy Commission laboratories at Oak Ridge, Tennessee. Dosage varied from 1-10 millicuries of  $P^{32}$  and was given orally to 12 patients of this type. Radioassay of excreta, biopsy and post-mortem material were carried out. External Geiger-Mueller counts utilizing a single thin-walled G-M tube (Victoreen) gave rough estimates of the distribution of  $P^{32}$  in vivo.

Radioautographic studies will be presented in correlation with the above tracer data to indicate that pretreatment of patients by testosterone and oestrogens promotes positive balance of  $PO_4$  in the body of these subjects; and provides concentration factors of  $P^{32}$  = 15 to 20 times by neoplastic tissues as compared with 2 to 3 times by normal control tissues.

Preliminary therapeutic experiences encountered in these subjects utilizing this principle of hormonal modi-

fication of tumor metabolism of  $P^{32}$  will be discussed. The direction of our projected and current work utilizing ACTH for this purpose will be indicated.

*The Regulation of Breathing During Severe Exercise.*

J. B. HICKAM, W. W. PRYOR, E. B. PAGE and R. J. ATWELL, Durham, N. C.

It is generally agreed that the stimuli which produce hyperpnea during exercise are of both reflex and chemical origin, but the relative importance of the two is debated.

An investigation has been made of the nature and relative importance of some of the factors controlling respiration during severe treadmill exercise. Before, during, and after exercise, observations have been made of the respiratory rate and volume, the arterial blood oxygen and carbon dioxide contents, the arterial pH, the  $CO_2$  tension (calculated), and of the effect of inhaling tank oxygen, 15 per cent oxygen, and a 5 per cent  $CO_2$ -21 per cent  $O_2$  mixture.

The results show much variation among individuals in the importance of different respiratory stimuli during exercise. Inspiration of 15 per cent oxygen during severe exercise causes a definite, sometimes great increase in ventilation. Conversely, tank oxygen, as reported elsewhere, causes a fall in ventilation. This effect increases with severity of exercise. During severe exercise, there is a slight fall in arterial oxygen saturation. Apparently arterial oxygen is often more important in the regulation of breathing during exercise than at rest. In most subjects, inhalation of 5 per cent  $CO_2$  causes a marked increase in ventilation, but the effect is variable. In general, subjects most sensitive to oxygen changes are also most sensitive to  $CO_2$ . A few subjects are quite insensitive to these chemical stimuli and allow large changes in arterial oxygen and  $CO_2$  with little response in ventilation. The reflex ventilation increase of beginning exercise is usually followed 40-50 seconds later by a further sharp increase, apparently chemical in origin. When work stops, ventilation falls abruptly. This fall is small or absent in subjects sensitive to  $O_2$  and  $CO_2$ . It may also be small in insensitive subjects. This suggests the presence of a factor other than arterial  $O_2$ ,  $CO_2$  tension, and the reflex effects of moving muscles.

*Life Stress and Water Balance in Diabetes Mellitus.*

LAWRENCE E. HINKLE, JR., CLIFFORD J. EDWARDS and STEWART WOLF,\* New York, N. Y.

Earlier studies on diabetic and non-diabetic subjects have established that a significant rise in blood ketones and major changes in blood glucose concentration may occur in association with serious conflicts in the life situation. The present study is concerned with the effect of such conflicts on water, glucose and electrolyte excretion.

Experiments were carried out on 17 diabetic and 14 non-diabetic subjects who had undergone detailed psy-