

other correspondent, more able, more industrious, and more likely to continue in life than myself. Dr. Benjamin S. Barton, one of the professors of the College of Philadelphia, is learned in the antiquities of this country, has employed much time and attention on researches into

them, is active and punctual, and will, I think, better fulfil your wishes than any other person in the United States. . . . He will, I am sure, set a just value on the correspondence proposed, for which I shall take care to prepare him.

ABSTRACTS OF PAPERS PRESENTED AT THE AUTUMN MEETING¹

Giant skin growth on mammals of normal size: CHARLES R. STOCKARD. The growth of skin and the skeletal framework of the body are regulated so that they properly fit together. Size regulation in development is accomplished more largely through inhibition of unlimited growth tendencies rather than through a stimulation of resisting tissues, if there be such. Overgrowths or giant reactions in organs and tissues also, more likely, result from disturbance in conditions of growth regulation and growth inhibition than from growth-stimulating stuffs. This is well shown by the continuous growth of tissues when removed from the influences of other body parts. The skin in certain individuals may become greatly thickened and enlarged in area so that it hangs in folds and wrinkles, being too extensive to properly fit the person. Such a condition may result from diseases, and the response is as if the skin had been freed from the influence of the growth-regulating factors which still act to preserve harmonious growths among the other tissues of the body. Recently several investigators have found that the injection of extracts from the pituitary gland into young dogs may bring about an overgrowth of skin along with what appears to be a general increase in body size. This was interpreted as a response to a growth-stimulating hormone. As might be expected, the responses to these injections differed somewhat among different types of dogs. For several years we have been studying, through the hybridization of pure dog-breeds, the differences in growth reactions of various tissues and body regions in giant and dwarf animals and in breeds exhibiting localized growth anomalies. In these experiments striking structural disharmonies have arisen as a result of failure in the regulation of growth coordination and harmonious sizes among the systems of the body. Excessive growth in skin area as related to body size has been a frequent feature arising from a number of different breed crosses. Similar skin growths have arisen from internal chemical disturbances and salt deficiencies in some dogs and also as a result of infection with skin parasites. The English bulldog has a short stocky body with smooth skin but a wrinkled face, since a normal amount of skin is fitted over a much shortened and flat-faced muzzle. When the bulldog is crossed with the German shepherd, police dog, a smooth-skinned animal, the first generation hybrids, F_1 , have fairly close-fitting skin on a stocky mastiff-like body. When this F_1 is bred back to the shepherd parent a shepherd-like dog with close-fitting skin results. However, the F_1 bred back on the bulldog gives an animal with bull type but with more wrinkled and looser skin

than the bull: as though the skin were growing on one pattern and the body on another. The most exaggerated misfits of skin occur in crosses between bulldogs and the short-legged basset-hound. The skin on the basset is loose but not to an excessive degree. The F_1 hybrids in the bull-basset cross have a greatly exaggerated area of skin fully sufficient for a dog of double the size. This skin is not thin but unusually thick, being one quarter to almost one half inch thick on the back of the neck. It hangs in folds from the body and wrinkles along the legs. Among the F_2 hybrids of this cross some individuals have smoothly fitting skin, on others the skin is loose, while on still others there is an excessive extent of skin folding and wrinkling over the anterior parts of the body, head and legs. The looseness of the skin is more marked in some individuals in the F_2 group than in back crosses of the F_1 hybrids on either the bulldog or basset-hound stocks. The St. Bernard dog and the bloodhound as pure breeds have loose wrinkled skin chiefly over the head and front parts of the body. When these are crossed on the smooth-skin Great Dane the F_1 and F_2 hybrids in some cases show excessively loose skin but not more exaggerated than in the wrinkled parent stock. Several other breeds give the same skin reaction on crossing. All breeds with overgrowth of skin have in common other symptoms and characters which indicate that the pituitary gland is functioning in an abnormal manner: in no sense hyper-function. A study of the gross and microscopic structures of these pituitaries reveals frequent cystic conditions and very abnormal cellular proportions and arrangements. The abnormal pituitary in these dogs is further associated with abnormal reproductive processes and modified behavior of the bitch toward her puppies. There is an accumulation of evidence showing the calcium-phosphorus balance to be disturbed. In further line with these interpretations it has been found that puppies with marked rickets of the bones, although from breeds with smooth-fitting skin, may show an exaggerated looseness and folding of the skin accompanying rickets. Dogs on diets low in calcium as well as those developing rickets become most susceptible to infections with sarcoptic mange. On a low calcium diet it is most difficult to eliminate mange from the skin with what is usually an effective external treatment. Also a puppy with severe mange is unusually prone to develop rickets unless careful precautions be taken to prevent it. And many such puppies exhibit an abnormal looseness and folding of the skin. From the evidence at hand we interpret these reactions as being associated with a disturbed calcium metabolism resulting from defective pituitary-parathyroid balance. Bone and skin, having the

¹ Charlottesville, Va., November 18, 19 and 20, 1935.

highest calcium requirements of all tissues, are interrelated in these disturbances. The excessive increase in skin area, giving looseness with folds and wrinkles, is a growth reaction correlated with defective states of the pituitary gland and in most cases accompanied by modification of skeletal growth, but not necessarily with gigantism or overgrowth of the bones. Coordination in the development and growth of the body organs and parts to insure harmonious size relations is dependent upon a normal pituitary secretion. The so-called growth hormone of the pituitary is probably not simply a growth-promotive hormone but the hormone having most to do with the regulation and coordination of the growths among the many body parts. When this hormone is lacking or changed, structural disharmonies and distorted misfits of the body parts are exhibited to varying degrees.

The rôle of the lymphocyte in blood formation: H. E. JORDAN. Pigeons and chickens lack lymph nodes but possess relatively very large amounts of lymphoid tissue in bone marrow, liver and rectal ceca, much in the form of nodules with germ centers. This material is exceptionally favorable for study of the problem of the function of the small lymphocyte. These lymphocytes are identical in marrow, spleen, liver and ceca. They are daughter cells of hemocytoblasts and retain the capacity to differentiate after a certain amount of growth into erythrocytes and granulocytes. In the liver and ceca they normally develop into granulocytes. In bone marrow the lymphoid nodules constitute a stage in erythropoiesis. These nodules consist typically of a germ center of proliferating hemocytoblasts and a mantle of small lymphocytes. The lymphocytes migrate both into the adjacent venous sinuses and into the intervacular stroma, meanwhile growing in size and acquiring features similar to those of the original hemocytoblasts. Within the vascular sinuses the larger lymphocytes develop into erythrocytes, the smaller into thrombocytes; in the intervacular stroma larger lymphocytes develop into granulocytes.

The production of blood-platelets in the lungs: W. H. HOWELL. The paper describes a new technique by means of which counts may be made of the blood-platelets and the red corpuscles in the same specimen of blood. The application of this method to various arteries and veins disclosed the fact that in the arteries the number of platelets per cubic millimeter of blood is constantly higher than in the veins. This difference is accentuated after the use of experimental methods which cause a diminution in the normal platelet-count, such as defibrination of the blood or the intravenous injection of saponin or peptone. Comparisons of this kind between the artery and vein of various organs indicate that the blood in passing through the systemic capillaries loses in plates, whereas in traversing the lung capillaries the number is increased. This indication that platelets are produced in the lungs was corroborated by perfusion experiments with a platelet preserving solution. In the case of the lungs irrigation with such a medium is followed by a marked increase in the relative number of platelets. The ratio of platelets to

erythrocytes increases from a ratio of about one to twenty to four or eight to one. Since similar increases were not obtained from other organs this result is interpreted to mean that a supply or storage of platelets exists in the lungs. Histological examination of the lungs of the experimental animals demonstrated for the normal animal, and to a more marked extent for those in which platelet production had been stimulated, that platelets are formed in the lungs from the cytoplasm of megacaryocytes. With the fixation and staining methods used megacaryocytes were found with cytoplasmic processes branching in the capillaries and composed entirely of the characteristic platelet material. The sections show many detached processes of platelet material in addition to numbers of normal platelets.

On the significance of the numerical relations of the fibers in the spinal nerves of the mouse, rat, dog and man: HENRY H. DONALDSON.

Cortico-adrenal influences on salt and carbohydrate metabolism: S. W. BRITTON and H. SILVETTE. Conflicting data on which various theories of cortico-adrenal function depend are possibly due to the use by different investigators of only one animal type. To obtain a broader view of the subject which might be valid for mammals in general and not alone for one form, the comparative physiological approach has been utilized. Sodium chloride and carbohydrate metabolism have been studied in a marsupial animal (the opossum, *Didelphys virginiana*) and a hibernating type (the marmot, *Arctomys monax*), the former definitely and the latter probably an ancient mammal. Carbohydrate and electrolyte studies have also been made on other animals under various experimental conditions. Opossums and marmots have been found to succumb following adrenal removal with general symptoms of insufficiency similar to those observed in higher mammalian forms. Sodium, chloride and water concentrations are, however, strikingly different: in blood serum and muscle the sodium chloride levels are increased over the normal, and muscle water is concomitantly decreased. Daily urinary output of sodium chloride is correlatively subnormal. The commoner laboratory animals (dogs, cats, etc.) show reverse effects from adrenal excision. All the mammalian types which have been examined show similar shifts in carbohydrate values after adrenalectomy: blood glucose and hepatic glycogen are reduced to levels incompatible with life, and muscle glycogen is notably decreased. Serum sodium and chloride values in different animal types suffering from adrenal insufficiency may be either increased or decreased or practically unaffected. The significance of sodium chloride and carbohydrate changes under many different experimental conditions is discussed. Hormones usually act similarly in all animal types. The life-maintaining factor in the adrenal cortex seems to affect only indirectly sodium chloride balance; it appears to be concerned directly in the regulation of carbohydrate metabolism in the organism.

On the incidence of tuberculosis in the offspring of tuberculous parents: RAYMOND PEARL. In a total of 564

matings producing 2,480 offspring the proportionate incidence of tuberculosis among the offspring was found to be in the following ratios by mating types, the incidence in the offspring from matings in which neither parent was tuberculous being taken as 1: Both parents tuberculous, 4.3; father tuberculous, mother not, 1.7; mother tuberculous, father not, 1.6; neither parent tuberculous, 1. These results suggest the inference that a person is, on the average, about four times as likely to have tuberculosis if both his parents had it than if neither parent did. Such analysis of the material as it has so far been possible to make fails to disclose any factor other than heredity playing any significant rôle in producing the observed *differential* distribution of offspring incidence of tuberculosis by mating types, in the present material.

An experimental and clinical study of cobra venom as an analgesic: DAVID I. MACHT. Reptiles and their secretions were used empirically in the primitive medicine of the ancients. Recently, in France, the venom of the cobra was introduced in therapeutics on somewhat more rational grounds. Calmette, Taguet and Monaelesser, Laignel-Lavastine and Koressios, and others have reported some remarkable effects that they observed after injecting cobra venom in cases of malignant tumor, particularly for relief of the severe pain common among patients affected with such disease. Their interesting findings prompted the present investigation. The fourfold objective of the writer's work was (1) to study the general pharmacology and toxicology of cobra venom, (2) to prepare and accurately assay biologically a sterile solution of cobra venom for therapeutic use, (3) to carry out a carefully controlled clinical investigation concerning the influence of cobra venom injections on a series of selected patients affected with malignant tumors causing severe pain; and (4) to analyze the pharmacodynamics of cobra venom action in order to ascertain its more intimate mechanism as an analgesic. Solutions of the drug in physiological saline were prepared; and its toxicity for living plants, as well as for lower and higher animals, was established. The pharmacological effect of cobra venom on the circulation, respiration, kidney function, movements of intestinal muscle, activity of enzymes and on other physiological functions was then carefully investigated. The margin of safety for higher animals having been determined, a solution of the venom in physiological saline was prepared, sterilized by a special method to avoid decomposition of the drug, and assayed biologically to furnish a preparation suitable for therapeutic administration to human beings. In collaboration with several distinguished surgeons, the writer studied a series of one hundred clinical cases affected with advanced and inoperable cancer and other malignant tumors, and suffering from such intense pain as to require the use of the most powerful narcotics and analgesics. In this series of cases, the effect of intramuscular injections of the specially prepared cobra venom was compared with that of other pain-relieving drugs. Favorable results in relieving the symptoms were obtained in seventy-five of these cases. The control of pain and improvement in general condition of some of the

patients were very striking; and the cobra venom was found to be therapeutically more effective and satisfactory than morphine or other opiates, or any other drug. Pharmacodynamic studies revealed that the cobra venom, in the therapeutic doses employed, was neither a local anesthetic for ascending or descending nerve fibers, nor for sensory nerve endings; but pointed to the higher nerve centers in the cerebrum as the seat of the analgesia. This impression was confirmed and established by psychopharmacological experiments on rats trained in the circular maze, by studies on the sedative effect of cobra venom on convulsions of cerebral origin produced in animals by special pharmacological agents and by measurements of the pain threshold before and after injection of the venom in guinea pigs and in human subjects. The pharmacological data in hand indicate that the mechanism of cobra venom action as an analgesic is very much like that of morphine—with this important difference, that it is not habit-forming and does not produce the disagreeable and dangerous by-effects of the opiates.

Renal insufficiency produced by partial nephrectomy. Some factors influencing renal function: ALFRED CHAUTIN and STEPHAN LUDEWIG. The effect of feeding diets containing varying percentages (10, 20, 40 and 80) of whole meat to intact, unilaterally nephrectomized and partially nephrectomized rats has been studied. The kidney damage was progressively greater with increased protein ingestion as demonstrated by the urea (Addis) ratio and by the increased volumes of dilute urine excreted during a concentration test. In partially nephrectomized animals the blood urea and urine urea concentrations at any given urea ratio were greater, the higher the protein intake. It was found that the blood urea concentration and the urine specific gravity were good qualitative indicators for kidney function. The $\frac{\text{urea ratio}}{\text{kidney weight}}$ ratio was constant for the intact and unilaterally nephrectomized rats on all dietary groups. The value for the $\frac{\text{urea ratio}}{\text{surface area}}$ ratios increased with added increments of whole meat in the diet. These values were proportional to the degree of renal hypertrophy.

How cars go out of control: analysis of the driver's reflexes: YANDELL HENDERSON. To be published later.

Biographical memoir of William Stewart Halsted: W. G. MACCALLUM. (Read by title.)

An oscillograph with a memory: A. W. HULL. It is possible to record electrical events which happen prior to the time of opening the camera shutter, by utilizing the phosphorescence of the screen of a cathode ray oscillograph. The oscillograph is allowed to write continuously, the record fading out as fast as it is written except for the slight phosphorescent lag. With ordinary willemite screens this lag is about 1/25th of a second. If the event, which may be entirely unexpected, is made to trip the shutter of a camera set to photograph the screen, the resulting photograph will contain the record of what hap-

pened after the event, during the time the camera shutter was open, plus that which happened during the 1/25th of a second prior to the event. In this way it is possible to obtain records of disturbances, such as are back in a rectifier, which give not only the full history of the event but also the circumstances which led up to it. This instrument is being used to study the behavior of rectifiers and Thyratrons.

The production and use of high rotational speeds: J. W. BEAMS, University of Virginia (introduced by S. A. Mitchell). The use of air-driven turbines supported on air bearings to produce high rotational speeds is outlined. A few simplifications and improvements in the method¹ of spinning rotors in a vacuum as well as in gases at various pressures are described. The maximum rotational speed is limited only by the strength of the rotor. The rotor spinning at high speed in a vacuum or in gases at comparatively low pressure is shown to be suited to problems in centrifuging. Since the attainable peripheral speed of the rotor is well above the average speed of the molecules for most gases at ordinary temperatures, it may be used as a velocity selector for molecules. A method is proposed for the separation of isotopes which takes advantage of the combined separation due to centrifuging and this velocity selection. The adaptation of high-speed rotors to several other uses, such as the very rapid rotation of mirrors or the measurement of the velocity of ions and fast particles, are briefly discussed.

The optical constants and photoelectric emission of potassium: HERBERT E. IVES and H. B. BRIGGS. A theory of photoelectric emission from thin films of photo-active material on a specular metallic base, proposed some years ago,¹ predicts the photo-emission to be conditioned by the optical absorption of the photo-active material. In order to calculate this absorption a knowledge of the refractive indices and extinction coefficients of the materials involved is necessary. These data have not been available for the alkali metals, which are the most important photoelectric emitters, in the region of the spectrum which is crucial to the above theory, namely, the ultra-violet. An apparatus for polarimetric analysis has been constructed with quartz elements, and used, by the photographic method of Voigt,² to determine the optical constants of a layer of potassium deposited on the back of a specially selected 60° fused quartz prism. Complete data for the visible and ultra-violet spectrum have been obtained. Applying these data

in the theory, a very striking agreement with experimentally determined potassium photo-emission through the spectrum is obtained. The sharply marked maximum of emission in the ultra-violet is predicted at the right wave-length, and the enormous enhancement of emission when the incident light is polarized with the electric vector parallel to the plane of incidence is an immediate consequence of the unusual optical properties of the alkali metal.

The international adoption of the Giorgi System of M. K. S. units by the International Electrotechnical Commission, June, 1935: A. E. KENNELLY.

Heights and weights of 275 public school girls in ten consecutive years: EDWIN B. WILSON.

Studies on new narcotics: LYNDON F. SMALL. In the course of a systematic search for new drugs capable of replacing morphine, many interesting variations of the morphine structure have been made, and several consistent relationships between constitution and physiological action discovered. The similarity in general physiological effect between certain of the structural and configurational isomers of morphine and codeine leads to the hypothesis that position of groups in space is more important than nuclear location of functional groups in this series. The hypothesis has been supported by results obtained with dihydropseudocodeinone and dihydroisomorphinone, isomers of Dicodid and Dilaudid, synthesized by the application of special hydrogenation technique. A functional group in the 6-position of the morphine nucleus appears to affect physiological activity to a much greater degree than the same group in the 8-position. When, however, the group at the 8-position is of such nature that it lies out of the plane of the nucleus, it may through a favorable configuration exert a physiological action greater than that of the group having an unfavorable configuration in the 6-position. By treatment of dihydrothebaine with methylmagnesium iodide, a new type of codeine derivative, containing a methyl group in the hydro-aromatic ring III has been prepared. The Grignard reagent adds at the ether linkage and the enol ether double bond of dihydrothebaine, and the enol ether group immediately undergoes hydrolysis. A phenolic ketone results, and by the action of bromine and sodium hydroxide on this ketone the 4,5-ether ring can be closed again. Reduction of the ketone group gives a codeine homolog designated as 7-methylcodeine.

(To be continued)

OBITUARY

WALTER HOUGH

THE United States National Museum lost one of the oldest and most highly esteemed members of its scientific staff when Dr. Walter Hough died suddenly of heart failure, in his seventy-seventh year, on September 20, 1935. Entering the service of the Museum

as a copyist in January, 1886, he won advancement, through constantly increasing familiarity with museum problems and through his ready knowledge of many widely diversified subjects, to a succession of positions that culminated in his appointment as head curator, department of anthropology, on March 1, 1923. His successful administration of this latter office was recognized by three separate extensions beyond the established age for retirement of federal em-

¹ Beams and Pickels, *Rev. Sci. Inst.*, 6: 299, 1935.

² *Phys. Rev.*, 38: 1209, 1931.

³ *Physik. Zeitschr.*, 2: 303, 1901.