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A New Type of Self-Sterility in Plants

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and Morris B. Hughes, ***Edisto Experiment Station***

Self-sterility that is caused by incompatibility between a plant's own male and female elements is a widespread phenomenon. Genetic interpretation of this phenomenon is generally based on the theory of oppositional factors. Two or more allelic factors are involved and these are termed S-alleles. According to this theory, a pollen grain is able to germinate on the stigma of the same flower from which it came, but if the S-allele carried by the pollen grain is identical with one of the two S-alleles present in the pistil, the pollen tube cannot grow down the style and fertilization is thus prevented. This is gametic determination of pollen behavior. The classical work on which this theory is based was done on a species of *Nicotiana.*

A new type of self-sterility was discovered in a species of *Crepis.* A logical interpretation of the experimental results obtained requires a very different hypothesis, including the following basic assumptions: (1) Sterility is caused by any one of a series of four S-alleles. The reaction is oppositional as in *Nicotiana.* But, because these factors differ in potency, one stronger allele may overcome the incompatibility that could otherwise have been caused by two weaker alleles. (2) No *Crepis* pollen will germinate on an incompatible stigma, regardless of whether the individual pollen grain carries a weak or a strong allele. Hence pollen behavior in *Crepis* is determined by the genotype of the plant from which the pollen came, not by the stigma on which it falls. This is sporophytic determination of pollen behavior. A genetic interpretation of the *Crepis* type of self-sterility is presented.

About Enzymatic Transphosphorylations

Otto Meyerhof and Harry Green,

University of Pennsylvania

The first type of transphosphorylation discovered was that brought about by the adenylic system, where phosphate groups of nucleotide polyphosphates, like adenosinetriphosphate (ATP), are transferred to other compounds without going through the stage of inorganic phosphate. The phosphate bond energy here can either remain the same (ATP → phosphocreatine), or be increased (ATP → phosphopyruvate), or be strongly decreased (ATP → primary phosphate ester).

After Axelrod (*J. biol. Chem.*, 1948, **172**, 1) had described a special type of transphosphorylation with nitrophenylphosphate mediated by acid phosphatase in the absence of adenine nucleotides, we found such transphosphorylation to be a general feature of biological phosphate esters with alkaline as well as with acid phosphatases. This transphosphorylation can be proved only by means of P^{32} because it becomes apparent in the increase of speed of synthesis of a phosphate ester in the presence of a phosphate donor; but it does not alter the final equilibrium. It was observed that this transphosphorylation occurs only from higher energy phosphate to lower energy phosphate and is the faster the greater the energy difference. Therefore, it is the greatest in the system, phosphopyruvate → glycerol. However, the nonbiological substance nitrophenylphosphate behaves exceptionally as a P donor; with acid phosphatase, transphosphorylation is much greater than would be expected from the energy content of its phosphate group.

Spontaneous Mutations of Bacteriophage and the Mechanism of Bacteriophage Reproduction

S. E. Luria, ***Indiana University***

(Introduced by T. M. Sonneborn)

Reproduction of a bacterial virus (bacteriophage) inside a bacterium is supposed to involve complex changes in virus structure. No active virus is recovered by breaking an infected bacterium open for several minutes after infection; active particles later appear and increase in number (Doermann). Mixed infection with related phages differing by two characters gives rise to recombinant phage types by a process similar to genetic recombination in sexuality (Hershey and Rotman). The proportion of recombinant individuals is the same in the final yield of phage from a bacterium and in the early, smaller yield from artificial breakage (Doermann); in both cases, the distribution of recombinants of each type from individual bacterial cells is random (Poisson distribution), indicating no clonal grouping of recombinants.

Experiments are presented showing the distribution of spontaneous "rapid lysis" mutants of phage T2 in about 3,600 bacteria. The distribution is clonal and very similar to the distribution calculated from the assumption of logarithmic (autocatalytic) reproduction of the genetic determinants involved, with a fixed probability of mutation per duplication. The mutation rate for the mutations tested (lumped) is about 1/5,000 per duplication.

The results are interpreted as proving that bacterio-

phage reproduction involves a phase of logarithmic reproduction of genetic material, followed by a terminal formation of active particles, with recombinations taking place at this terminal stage. The hypothesis of separate reproduction of genetic units, followed by their reassembly into active particles, proposed to explain phage reactivation (Luria) is shown to fit the requirements of the above interpretation.

Thermal Coagulation of Serum Albumin

Charles Huggins and Elwood V. Jensen,
University of Chicago

Depending on the pH of the medium, heat-denatured solutions of serum albumin form opaque synerizing coagula, clear nonsynerizing gels, or clots intermediate between these two types. The nature of the coagulum and the minimum albumin concentration required for gel formation have been interpreted in terms of intermolecular repulsive forces due to the net charge of the denatured albumin molecules.

In the presence of one equivalent of certain sulfhydryl reagents per mole of albumin, thermal coagulation of albumin solutions at pH 6.9 to 7.4 is markedly altered in that the least coagulable concentration is lowered, water binding is increased, and clear clots result. This effect is observed whether these substances destroy sulfhydryl groups by oxidation (iodine, hydrogen peroxide, iodosobenzoate), alkylation (iodoacetamide, chloropicrin) or metallation (Ag^+, Cd^{++}). Thus the properties of the opaque gel formed from untreated albumin in the pH range 6.9 to 7.4 depend in large degree on the presence of a free sulfhydryl group. To exert its marked effect on coagulation, the one free sulfhydryl group of serum albumin must have a unique place in the protein molecule.

Self-Duplication of Genes and Specific Interaction Between Identical Macromolecules

Herbert Jehle, ***University of Nebraska***
(Introduced by H. J. Muller)

In the process of synapsis of homologous chromosomes in meiosis we encounter highly specific interactions between molecules with a specificity depending on a pair of large molecules' being identical or almost identical. Such specific interaction offers also a means of explaining self-duplication of genes in cell reproduction. The building up of a duplicate by the original gene is understandable as a bit-by-bit collection of molecules (e.g., closed peptide chains) readily available from the surrounding medium—molecules which happen to be identical with the constituent molecules of the original gene, and which are attracted near to them. Hereafter, chemical bond formation will provide for the synthesis of a complete daughter gene from the selectively attracted constituents (Muller, H. J., *Proc. roy. Soc.*, 1947, **134B**, 1; *Cold Spr. Harb. Sympos. quant. Biol.*, 1941, 306ff; *Amer. Nat.*, 1922, **56**, 32). In looking for an explanation of specific attraction (*op. cit.*) between identical large molecules we have to keep in mind that synapsis and, even more so, self-duplication are very general processes of unbelievable *versatility*, processes working for all kinds of genes so as to make even mutations accurately inheritable. The *accuracy* makes exact self-duplication usually unfailing throughout the sequence of many chromosome generations. We investigated the quantum-mechanical behavior of a pair of rigid molecules which interact with each other by means of the vibrating electric dipole moments which accompany the molecules' thermally excited vibrations. Each one of the molecules shows, because of anharmonic resonance between commensurable modes, a statistical preference for certain phase relations between these modes (using the language of the correspondence principle). A pair of those molecules interacts strongly if it is an identical pair, because of these phase preferences.

The Follicular Phase of the Menstrual Cycle in the Rhesus Monkey

George W. Bartelmez, ***University of Chicago***

The lining of the uterus (endometrium) is a target organ for ovarian hormones and when complete data are available, provides favorable material for observations on variability in endocrine responses. At the end of the follicular phase there are certain responses which appear to be adaptations for the survival and transport of spermatozoa in a presence of a ripe egg. Two such features are present to some degree in all of our 20 cases: (1) The epithelial cells are producing a thin secretion which contains glycogen and a mucin. (2) The edematous swelling of the endometrium reduces the cavity of the uterus to a narrow cleft. This is significant because of the activity of the uterine musculature at this time. The time relations within the cycle are highly variable; thus the liberation of the egg is indicated between the 7th and the 26th days of the cycle. Seven of the preovulatory and four of the immediately postovulatory endometria resemble earlier stages of the follicular phase; the others cannot be distinguished from some of the succeeding progravid phases. The differences between the groups are (1) in the shape and the amount of accumulated secretion in the glands, (2) in the form of the gland cells, and (3) in the relative number of enlarged stroma cells. The differences cannot be correlated with the time of ovulation in the cycle. Two factors seem to be involved: variations in the proportions of the available hormones and in the susceptibility of the several tissue elements.

The Factorial Description of Temperament

L. L. Thurstone, ***University of Chicago***

The description of mental endowment has progressed considerably from that of a single index of general intelligence to a profile of indices, one for each of the known

primary mental abilities. The domain of personality has not been studied so intensively by multiple factor methods but several studies indicate that here also an adequate description is possible with a limited number of parameters or factors. Since dependable objective tests of personality have not yet been developed it is customary to depend on responses to a large number of questions about personality. The more stable characteristics of personality, including conative and emotional traits, are called *temperament* to distinguish them from the more changeable personality traits.

In a factorial study with 340 questions about personality it was found that seven factors account for the major part of the variance. These factors are linearly independent but they are correlated in the experimental population. These factors of temperament have been tentatively named as follows: 1) general activity, 2) impulsiveness, 3) emotional stability, 4) sociability, 5) athletic interest and strength of physical effort, 6) ascendance in the sense of dominance and leadership, and 7) reflectiveness in the sense of introspectiveness and introversion. A short schedule of 20 questions for each of these factors has been assembled for a general description of temperament. This schedule does not attempt to appraise the deeper sources of conflict and motivation.

On Gravitational Effects and Brain Development

S. W. Britton, *University of Virginia*

(Introduced by S. A. Mitchell)

Genetic and environmental factors together may be said to define the character of living things. Determinacy of form and function cannot be specifically assigned, although certain features of life appear to have been fostered by environmental agencies. Whereas solar and other radiant effects have long been recognized, the influence of gravitational attraction on organisms has been given little consideration. Not alone gross but even finer structures, including specialized orientation mechanisms, have been patterned by or in response to gravity.

Some mammals die rather quickly when exposed in the head-up position; other forms subaltern to man show marked bodily changes, and in many cases normal consciousness may not long be maintained. Carotid arterial pressure and flow are significantly reduced, and femoral venous return to the heart is greatly decreased. Even the smaller apes show these failures in compensation. Correlated are hyperglycemic and later hypoglycemic changes, and alterations in the brain wave patterns. Frequent muscular movement may aid in extending survival over several hours.

Subhuman primates normally exhibit various degrees of uprightness, but maintain such posture usually no more than one-quarter of the 24-hour day. Man alone stands erect with little or no functional disturbance; yet conversion from arboreal life took place within less than 1 percent of biological history. Contemporaneous with development of orthograde progression, the human brain showed its greatest growth and differentiation. The force of gravity exerted linearly through the body significantly influenced conformation and growth. Delicately balanced arterial reactions, better oxygenation, and enhanced venous removal of metabolic products became possible in the head end. Special sensory and cerebral mechanisms have probably benefited particularly, through improved circulatory conditions.

The Visualization of Viruses within Infected Tissues

Ralph W. G. Wyckoff, *National Institutes of Health*

A wide variety of particles of macromolecular dimensions can now be seen under the electron microscope. Virus diseases are caused by such particles and a number of these can be visualized both in purified suspension and within the tissues they infect. This ability to see viruses carries with it the possibility of studying in very direct fashion how they are produced within the living matter that is their host.

The resolution of existing electron microscopes is sufficiently high so that there is no problem in seeing particles the size of the smallest viruses. Present difficulties in determining how virus particles are produced are of another character and arise mainly from difficulties in recognizing these particles among the great mass of macromolecular detail that is visible within both healthy and diseased cells. Series of electron micrographs are shown of cells diseased with several plant and bacterial, animal and insect viruses within which the probable infectious particles can be recognized. These photographs illustrate the nature of the problems encountered and the kind of information that can be gained through this approach to the fundamental question of the relation between a virus and its host.

Quantitative Measurements of Cerebral Blood Flow and Cerebral Oxygen Consumption in Man

Carl F. Schmidt and Seymour S. Kety,

University of Pennsylvania

It was suggested on theoretical grounds (Kety, S. S. and Schmidt, C. F. *Amer. J. Physiol.*, 1945, 143, 53) that cerebral blood flow could be measured quantitatively in man by means of the Fick Principle, i.e., by dividing the amount of a gas (such as N_2O) taken up by the brain per unit time by the amount of the same gas yielded by each unit of blood in passing through the brain at the same time. The numerator could be obtained from the N_2O content of cerebral venous blood when it had reached equality with that of arterial blood, indicating that the brain had reached saturation with N_2O at the prevailing

arterial tension. The denominator would be the integral of the cerebral arteriovenous N_2O difference during the period preceding saturation, which was usually about 10 minutes with the gas mixture used (N_2O 15%, O_2 21%, N_2 64%). The validity of this proposal was proved by calibration against direct measurements of cerebral blood flow in monkeys (*op. cit.* and Kety, S. S. *Methods in medical research.* Chicago: Year Book Publishers, 1948. Vol. 1). Given a value for cerebral blood flow, cerebral oxygen consumption could be computed from this and the prevailing cerebral arteriovenous oxygen difference. By this method studies of these functions have been made under a variety of physiological and pathological conditions. The results indicate that the human cerebral circulation is quite labile, behaving much like that of animals, e.g., exhibiting lack of strong influence by vasoconstrictor nerves. A striking parallelism between cerebral functional activity and cerebral oxygen consumption has been found in anesthesia by pentothal and ether, insulin coma, diabetic acidosis, cerebral arteriosclerosis, and brain tumor. These findings confirm in the human brain the general concept (Barcroft, J. *The respiratory function of the blood.* Cambridge, Mass.: Cambridge University Press, 1914) that the oxygen requirement of an organ runs parallel to its functional activity.

Embryonic Transplantation by the Vascular Route[1]

Paul Weiss and Gert Andres, *University of Chicago*

In order (a) to study the fate of embryonic tissue cells introduced into the embryonic blood stream, and (b) to test their effects on organ development and growth, the following method was devised. A suspension of ground embryonic tissue in Tyrode solution (about 0.05 cu mm, containing about 1000 cells) is injected slowly by micropipette into a small extraembryonic vein of chick embryos of three days' incubation or older. The injected cells pass through the heart into the arterial system of the embryo, causing acute circulatory disturbance, embolisms and hemorrhages (mostly in brain and liver). Of 340 injected embryos, 222 (74 percent) survived and developed further, 23 of them beyond hatching.

In a first test of the technique, cells from a potentially pigmented breed (Barred Plymouth Rock) were injected into unpigmented hosts (pure breed White Leghorn). Donor tissues were ground 24-hour embryos or 4-day limb or wing buds. Seven of the white hosts developed dark patches of skin and feathers containing donor-type pigment. This proves that injected cells can survive in the blood stream, escape into the tissues, reach their normal sites, and multiply and differentiate there in typical fashion. Teratomas were observed in some cases.

When tissue suspensions containing presumptive pigment cells were injected directly into white embryos, the latter likewise developed colored patches in distant areas, indicating the formation of embryonic metastases by the vascular route.

Aside from permitting controlled cell dissemination for research on growth, differentiation, and tissue affinities, the technique lends itself readily for better controlled administration of hormones, antibodies, and chemicals.

[1] This work was aided by the Dr. Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago and the American Cancer Society, Committee on Growth.

Hemolysin Production in Intact and Splenectomized Rabbits

William H. Taliaferro and Lucy G. Taliaferro,

University of Chicago

The rise and decline of hemolysin have been followed at frequent intervals by photometric methods in rabbits following single standardized intravenous doses of sheep red cells (ranging from 2 to 250×10^7 cells). The rise and fall of antibody titers in each animal may generally be fitted to successive discontinuous semilogarithmic curves described by

$$A_t = A_0 e^{kt}$$

where A_0 and A_t are antibody titers at time zero and t, respectively; and k is the constant of increment. Comparison of intact and splenectomized rabbits indicates that the spleen ordinarily forms most of the antibody during the first phase of immunization. Splenic antibody generally accumulates in the serum rapidly with a constant value for k for several days. Thereafter, it may accumulate at a lesser rate for several more days. At the end of this period, it disappears at a rate which indicates that the half-life ranges from about 4 to 13 days, with the most convincing values in the lower range. Nonsplenic antibody sources continue to form antibody at a rate lower than the spleen and maintain serum antibody at a lower level over many months. With the largest single dose of antigen, the peak antibody titer in splenectomized animals may persist essentially unchanged for several weeks. Thus, after a single dose of antigen, the spleen apparently forms a relatively large quantity of antibody within a short period, whereas the rest of the antibody-forming sites maintain a low antibody level over a long period.

Reality Culture and Value Culture

A. L. Kroeber, *Columbia University*

Apart from social structure, language, and perhaps other constituents, two ingredients of culture first contrasted by Alfred Weber are science and technology (which he calls "civilization") as against philosophy, religion, and art (which he calls "culture"). Science and technology are human cultural activity directed toward preexistent nature, toward discovering and utilizing it. Philosophy, religion, art are only indirectly or partially slanted at nature: they are creative in themselves, and constitute rather the realm of meanings and values. I propose therefore to distinguish the two ingredients as reality culture and value culture. (The use by Weber and others of "civilization" and "culture"

is confusing because it is now customary to use "culture" to denote the sociocultural or extraorganic totality of which the two contrasting groups of activities are only part.)

The distinction is useful in that it helps define that respect (reality relation) in which culture is not only most readily transmissible and retentive but accumulative as a whole; and because it also defines those activities (with value relations) through which particular cultures are most nearly unique, that is, differentiated stylistically. However, the polarity is incomplete. Science is productively active in spurts much like the arts, manifests similar clustering of great minds, and even shows a measure of stylization according to period or area similar to that in the arts. In short, every culture is sufficiently integrated to prevent its parts or constituents from functioning as wholly independent variables.

Summation in the Auditory Sensory Process

Hallowell Davis, ***Central Institute for the Deaf***

Last year we suggested that when the frequency of sound waves is high a summation of the stimulating effect of several sound waves is probably required to initiate a nerve impulse. In electrophysiological experiments on the ear of the guinea pig we have recently obtained evidence for such summation.

Our sound stimuli are very brief trains of waves at 2000, 4000, or 8000 cycles per second. The amplitude of the waves rises to a maximum during the third wave and then declines with almost equal rapidity. Such a "tone-pip" at moderate intensity sets up not more than one nerve impulse in any one nerve fiber and excites only a restricted group of nerve fibers. At 2000 c the nerve impulses are synchronized in well-defined volleys, each volley associated with a particular sound wave. At 8000 c, however, we find no such association. Also, at 8000 c near threshold, the first nerve impulses are set up by the fifth wave, two waves *after* the maximum amplitude of the tone-pip. This clearly indicates that there is summation of the stimulating effect of several sound waves. At 4000 c there are still clear volleys of nerve impulses associated with particular sound waves, but summation can also be demonstrated.

The ear acts like a digital machine at low frequencies and signals the time of arrival of each sound wave as far as its refractory period permits, but at high frequencies it acts like an analogue computer that integrates over several waves. The ear seems to respond to a high frequency tone-pip as a whole, and not to the individual sound waves.

Chemistry of the Adrenal Cortex

Edward C. Kendall, ***Mayo Foundation***

The hormones of the adrenal cortex were separated in crystalline form and identified about fifteen years ago through the efforts in this country of Wintersteiner and Pfiffner, and Kendall and his associates, and of Reichstein and his associates in Switzerland. The war stimulated efforts to prepare these compounds from suitable starting material which would allow their manufacture on a large scale. A method for the preparation of 11-dehydrocorticosterone (compound A) was devised in my laboratory in 1944, and in 1946 L. H. Sarett, in the research laboratory of Merck and Co., Inc., prepared compound E by a method which was not practical for large scale production. Subsequently a method was devised for the conversion of a precursor of compound A into compound E. Through a joint effort on the part of Merck and Co., Inc. and the biochemical laboratory of the Mayo Foundation a practical procedure has been evolved for the conversion of desoxycholic acid into compound E.

In 1948, in cooperation with P. S. Hench, C. H. Slocumb, and H. F. Polley, compound E was given to patients who had rheumatoid arthritis and rheumatic fever. The results were obvious and encouraging in all patients, without exception. Compound E was then designated cortisone.

The study of cortisone in clinical medicine has now been extended to use of this hormone in a large number of other so-called nonmicrobic diseases. These have also responded favorably. These results have disclosed new concepts concerning the defense mechanism of the body.

Cortisone is the most complicated pharmaceutical product which has been prepared by synthetic methods. It is scarce and very expensive. Many attempts have been made to find other compounds more simple in chemical structure and easier to manufacture which would act vicariously for cortisone. These have been tested on patients who have rheumatoid arthritis. Not one of these compounds has produced the typical and invariable effects of cortisone.

These observations suggest that the tissues of the body are not able to convert closely related compounds into significant amounts of cortisone, and that cortisone, or 17-hydroxycorticosterone (compound F) are elaborated only in the adrenal cortex.

The Effects of Cortisone and ACTH on Rheumatic Diseases

Philip S. Hench, ***Mayo Clinic***

Because patients with rheumatoid arthritis were observed to develop remissions during pregnancy or jaundice, it was concluded that this usually progressive, crippling disease was potentially reversible through the action of an "antirheumatic substance X" which might be a bisexual steroid hormone. Later it was noted that pregnancy or jaundice sometimes gave temporary relief in certain other conditions also: hay fever, migraine, psoriasis, and sensitivity to eggs. Hence it was postulated that substance X was not disease-specific, not specific merely in rheumatoid arthritis, but was group-specific. After using various procedures and substances related to jaundice or

pregnancy, generally with negative results, it was decided to study the effect of the adrenal cortical hormone, 17-hydroxy-11-dehydrocorticosterone (Kendall's compound E), later renamed cortisone.

To patients with various rheumatic and articular diseases cortisone has been given, also the pituitary adrenocorticotropic hormone (ACTH) which stimulates responsive adrenals to produce cortisone or a cortisone-like substance such as compound F. These two hormones produced marked improvement in cases of rheumatoid arthritis, with reduction or disappearance of symptoms, objective manifestations, and biochemical abnormalities. But, with certain interesting exceptions, the improvement has been temporary; relapses have occurred quickly when use of these hormones was discontinued. Cortisone and ACTH have also suppressed the acute manifestations of rheumatic fever. Preliminary results suggest that these harmones also affect temporarily a variety of nonrheumatic conditions.

These hormones are powerful agents which affect many tissues besides the muscles and joints. Certain undesirable effects may result from prolonged or excessive administration; so far these have been reversible. But until more is known about the clinical effects and metabolism of these hormones they should be used for investigative purposes. Their value presently is to provide a means to study the mechanisms underlying onset and remission of certain diseases.

American Research on Cortisone

Chester S. Keefer, ***Evans Memorial Hospital, Boston***

The Committee on the Investigation of Cortisone of the National Academy of Sciences allocated approximately 1000 grams of Cortisone to 30 investigators in 26 institutions from August to January, 1950. The objectives of the committee were to distribute an important chemical of great biological significance to qualified research workers so that information concerning its mode of action, its clinical effects, and its side effects could be obtained. This report will summarize the results that have been reported to the committee.

The Mechanism of Secretion of the Adrenal Cortical Hormones

C. N. H. Long, ***Yale University School of Medicine***

The remarkable effects of cortisone and the adrenocorticotropic hormone (ACTH) in alleviating rheumatoid arthritis, rheumatic fever, and certain allergic states have focused public attention on two hormones whose physiological properties have been the subject of a great deal of investigation during the last fifteen years. Actually, cortisone was isolated from the adrenal gland by Kendall and his colleagues in 1936 and ACTH was obtained in highly purified form from sheep pituitaries by Li, Simpson, and Evans in 1942, and from hog pituitaries by Sayers, White, and Long in 1943. Since no other physiological property of ACTH is known besides its capacity to stimulate the secretion of cortisone or allied compounds by the adrenal cortex, it was soon recognized that the effects of the injection of ACTH would be identical with those produced by the administration of cortisone.

Furthermore, it has become evident that unless there is a prior secretion of ACTH by the anterior lobe of the pituitary, no augmentation of adrenal cortical secretion can occur. The question, therefore, as to the circumstances that are associated with an increased secretion of ACTH and the mechanism by which they cause the secretory cells of the anterior pituitary to release this hormone has become a problem of no little importance. Apart from the interest surrounding the elucidation of an important bodily function, an understanding of the mechanisms governing the secretion of the adrenal cortical hormone might well allow the development of more available agents by which the pituitary itself could be stimulated to produce sufficient ACTH, and hence of cortisone, to bring about the alleviation of certain disease states. Such an effect would obviate the necessity of administering either hormone, since all present evidence indicates that there is no insufficiency of pituitary-adrenal cortical function in individuals afflicted with arthritis or allied disorders. Rather it would appear that relief of these conditions is achieved only when amounts of ACTH or cortisone in excess of normal bodily needs is continually administered. However, since continued overdosage with either of these two potent hormones is known to be associated with the development of a number of undesirable events, the question of the feasibility of their long continued administration to man remains to be determined.

A variety of methods have been devised to determine an increased rate of secretion of the cortical hormone. Of these, only two lend themselves to the measurement of rapid changes in the secretory rate of this gland. The first of these, applicable only in experimental animals, depends on the observation that stimulation of the adrenal cortical secretion by ACTH is accompanied by a decline in the cholesterol and vitamin C content of the gland. Although it is believed that the decline in cholesterol is due to its transformation into the cortical steroids, no adequate explanation has been advanced for the association of this vitamin with the secretory mechanism. Nevertheless, either or both these chemical changes can be used as indirect indicators of increased secretion. Indeed, the depletion of ascorbic acid in the gland by ACTH is used as an assay method for the standardization of ACTH preparations for clinical use.

The second method depends on the capacity of cortisone and its allied compounds to bring about a reduction in the number of the eosinophilic cells of the blood. This method can, of course, be used in man, where a rapid reduction in the number of these cells can be taken as evidence of increased adrenal cortical secretion.

Using either of these methods, or others of lesser sensitivity, it has been shown that a wide variety of circumstances acting within or without the body bring about increased ACTH secretion and hence that of the adrenal

cortex. So different are these circumstances, including as they do changes in environmental temperature, pain, trauma, infections, and even strong emotional states, that the question arises as to what may be their common denominator in producing activation of the anterior lobe of the pituitary.

Two explanations have been advanced. The first was suggested by the work of Ingle, Higgins, and Kendall and has been expanded recently by Sayers. The latter concludes that all these various circumstances increase the tissue utilization of cortical hormone, thus lowering its level in the blood. In consequence, the anterior pituitary responds by secreting additional ACTH in an attempt to restore the original blood level of the cortical hormone and thus ensure an adequate supply for the needs of the emergency.

The second suggested mechanism rests on the observation that the majority of the circumstances associated with an increased cortical secretion are also those that provoke an increased degree of activity of the autonomic nervous system with a concomitant increased secretion of epinephrine. In support of this view it has been shown that the injection of epinephrine in physiological amounts is capable of stimulating ACTH secretion.

The experimental evidence supporting both these hypotheses will be presented. It leads to the present conclusion that both types of activation of ACTH secretion are available to meet an increased demand for cortical hormone. The ability of epinephrine to activate the anterior pituitary must now be added to the previously known functions of this hormone. As was pointed out by the late W. B. Cannon, the physiological responses induced by epinephrine are of a kind that enable the organism to adapt itself to emergencies. The participation of the anterior pituitary and adrenal cortex in this response is particularly necessary by reason of the increased requirement for their hormones that such emergency states appear to demand.

The Chemical Combination of Insulin with Muscle and Its Hormonal Regulation

William C. Stadie

Maloney Clinic, University of Pennsylvania

The complete understanding of the problems associated with diabetes is largely dependent upon a greater knowledge than is now available of the chemical or physical mechanisms by which insulin affects the metabolism of mammalian tissue.

Effects of insulin upon metabolic reactions in intact cells, either *in vitro* or *in vivo*, have been unequivocally demonstrated by many workers. This is in sharp contrast to the difficulty in demonstrating unequivocal effects upon cell-free enzyme systems. Irrespective of the precise mode of action of insulin, it is conceivable that once having entered the cell, insulin might attach itself to some morphological element. This initial direct combination of insulin with the intact cell might indeed be the initial obligatory reaction required for the further metabolic activity of the hormone. We (Stadie, W. C. *et al. Amer. J. med. Sci.*, Sept. 1949) have succeeded in demonstrating that such chemical reaction occurs.

The demonstration was accomplished in the following way: A hemidiaphragm from a normal rat is equilibrated for one minute or less in a medium containing a small concentration of insulin. During this brief exposure to insulin, firm combination has occurred with some constituent of the muscle cell, and the combined insulin alters the metabolic pattern of the muscle. This is shown by the fact that invariably the insulinized hemidiaphragm, when equilibrated in a glucose-containing medium (with no added insulin), utilizes more glucose and synthesizes more glycogen than an appropriate non-insulinized control.

This phenomenon has been studied in the normal rat under a variety of conditions, and in rats with endocrine abnormalities, or those injected with various hormonal preparations. The results indicate that the chemical combination of insulin with muscle is under hormonal control. It is concluded that this phenomenon plays an important role in the regulatory mechanism of carbohydrate metabolism in the normal and diabetic animal.

Sickle Cell Anemia Hemoglobin

Linus Pauling, Harvey A. Itano, Ibert C. Wells, Walter A. Schroeder, Lois M. Kay, S. J. Singer, and R. B. Corey, *California Institute of Technology*

Amino acid analyses of hydrolyzates of normal human adult hemoglobin and sickle cell anemia hemoglobin have shown that there is no difference in the number of residues of the acidic and basic amino acids in these molecules. There may be small differences in the number of residues of leucine, serine, valine, and threonine. Preparations of hemin chloride and the dimethyl ester of the heme porphyrin from the two hemoglobins have been found to be identical. The globin preparations resulting from acid acetone treatment of the two hemoglobins give the same electrophoretic patterns. The difference of 0.23 pH units in the isoelectric point of the hemoglobins cannot be attributed to difference in the number of acidic or basic amino acid residues, but is presumably the result of a change in ionization constants of acidic and basic groups resulting from a difference in folding of the polypeptide chain.

The amount of sickle cell anemia hemoglobin in the erythrocytes of 25 individuals having the sickle cell trait has been determined, and values within the range 25 percent to 44 percent have been observed.

Photosynthetic Efficiency of the Tomato Plant as Influenced by Light Intensity and Temperature

F. W. Went, *California Institute of Technology*

In the new Earhart Plant Research Laboratory of the California Institute of Technology plants can be grown under conditions of completely controlled light, tempera-

ture, humidity, and rate of air movement. Tomato plants, grown under artificial light of 2,000 foot-candle intensity, developed normally and were quite as heavy as plants grown in full sunlight for the same length of time and the same photoperiod. Their fruiting however, amounted to only about 25 percent of the fruit production in daylight.

It was found that for plants all grown in exactly the same light intensity, temperatures of 20°–23° C, coupled with nyctotemperatures of 10°–20° C, gave the greatest dry matter production. On the assumption that the dry matter exclusive of ash of a tomato plant has a caloric value of 3,700 calories per gram, and that one foot-candle equals 16 ergs/cm²/sec, it was found that under optimal temperature treatments over a growing period of 2½ months, 17 percent of the light energy which reached the tomato plants was transformed into chemical energy.

Dry matter production turned out to be a good measure of photosynthetic efficiency. Values can be obtained over much shorter growing intervals, provided the plant material is uniform. This can be achieved to a sufficient degree with young tomato plants, and they showed photosynthetic efficiencies of 16 percent to 18 percent at 1,000 ft-c and of 10 percent to 12 percent at 2,000 ft-c. These values are all obtained under arbitrary spectral composition of the light, and might be higher for optimal distribution of wavelengths. Even without corrections for respiration and reflected and transmitted light, efficiencies can be calculated which ten times surpass the efficiency of field-grown plants. This provides a basis for expecting higher crop yields per acre if conditions are created to make full use of the potential photosynthetic efficiency of plants.

The Trisection of Horn Angles

Edward Kasner, ***Columbia University***

A horn angle is formed by two curves A and B, touching at the vertex V. Such an angle is bisected by a curve C if the image of A in C is B. Trisection is defined by successive symmetry (all constructions are invariant under conformal transformation).

If the curves A and B are circles, the bisector and the two trisectors are also circles; and the constructions can be effected with the traditional ruler and compass.

The general measure of a horn angle is an invariant of third order, but for circles second order terms are sufficient.

The Intermediate Nucleus and the Hydrogen Bomb

William D. Harkins, ***University of Chicago***

Two relations discovered by Harkins and Wilson and by Harkins in 1915 and 1926 are related to the efficiency of an atomic bomb. According to the former, one pound of hydrogen by a loss of mass in conversion into helium gives as much energy as the combustion of ten thousand tons of coal. This heats the sun and the stars.

The 1926 paper considered that all nuclear reactions give an intermediate-compound nucleus. All atomic bombs owe their explosive characteristics to the exceedingly short life of this intermediate nucleus. In the uranium bomb, U^{236*} is formed by the action of a slow neutron on U^{235}. In a hydrogen bomb containing tritium the percentage loss of mass would be relatively high, since the exceedingly stable nucleus He^4 is produced. The reaction would be

$$H^3 + H^3 \longrightarrow He^{6*}$$
$$He^{6*} \longrightarrow He^4 + 2n + 11.4 \text{ Mev.}$$

However, tritium is too costly. Ordinary hydrogen would give the greatest energy if it could be converted completely into helium of mass 4, but presumably this requires a series of reactions, and is too slow. Deuterium, which is hydrogen of mass 2, will be employed according to the following reaction:

$$H^2 + H^2 \longrightarrow He^{4*}$$
$$He^{4*} \text{ or } \begin{cases} \longrightarrow He^{3*} + H^1 + 4 \text{ Mev} \\ \longrightarrow He^{3*} + n^1 + 4 \text{ Mev.} \end{cases}$$

although the energy is only about one-third of that given by tritium. Lithium deuteride or tritide would reduce the volume employed.

Structural Chemistry of the 5f Elements

W. H. Zachariasen, ***University of Chicago***

The crystal structures of some two hundred compounds of the elements from actinium (atomic No. 89) to americium (atomic No. 95) have been investigated. The results of these systematic studies have led to a satisfactory understanding of the structural chemistry of these elements and of the relationship to similar groups of elements in the periodic system.

In the solid state the following bona fide valencies are exhibited by the elements under consideration:

Ac	Th	Pa	U	Np	Pu	Am
3			3	3	3	3
	4	4	4	4	4	4
		5	5			
			6	6	6	

The crystal structure results show that for a given valence state the atomic or ionic radius slowly decreases with increasing atomic number. Thus the tetravalent ionic radius decreases from 0.98 A at thorium to 0.88 A at americium.

This contraction in atomic dimensions is due to electrons entering the 5f shell. A similar contraction in size was found by V. M. Goldschmidt for the 4f elements.

That a 5f series of elements might begin near the end of the periodic system was long suspected. Indeed, the suggestion was first made by Niels Bohr thirty years ago.

The trivalent state is the important one for the 4f elements, although some 4f elements may exhibit divalent or tetravalent states as well. In contrast the triva-

lent, tetravalent, and hexavalent states are of comparable importance for the 5f elements.

The various 5f elements are closely related as regards their structural chemistry. Analogous compounds have as a general rule analogous structures. A 5f element is only slightly larger than the corresponding 4f element. As a consequence one observes a close crystal chemical relationship between 4f and 5f elements in the trivalent and the tetravalent states.

The Compressibility of Metals

Linus Pauling, *California Institute of Technology*

It has been found that an expression for the dependence of the volume of a metal or similar substance with atoms held together by covalent bonds on the pressure can be derived by assuming that each atom interacts with its neighbors in the way corresponding to a Morse potential function. Bridgman's high pressure data for many substances can be accounted for satisfactorily in this way.

The Limiting Negative Pressure of Water Between 0° and 50° C

Lyman J. Briggs, *National Bureau of Standards*

A further study has been made of the limiting negative pressure of water, at temperatures ranging from 0° to 50° C, by the method described at the 1949 Washington meeting of the Academy. (*Science*, 1949, **109**, 440.)

The limiting negative pressure of water is found to be profoundly influenced by temperature. The negative pressure reaches its maximum value of 277 bars between 8° and 10° C. It drops to 263 bars at 25° C and 215 bars at 50° C. But it is in the region between 5° and 0° that the effect of temperature is most striking. Below 5° the limiting negative pressure drops sharply and progressively, until near 0° it is less than 10 percent of its maximum value.

The experimental results cannot be explained by changes in density. The total change in the density of water in heating from 0° to 5° C is only 0.00013. At 25° an equal change in density is produced by changing the temperature 0.5°. In the first temperature interval a 10-fold change in the limiting negative pressure takes place; in the second, the change is only 0.4 percent.

The observed results may be accounted for as follows: When water is cooled to 4° C, aggregates of molecules begin to form; they grow in size as the temperature is progressively lowered; they are irregular in shape and do not pack as closely as single molecules, as shown by the observed decrease in density; consequently, voids must exist between the aggregates; as the molecular aggregates increase in size, so do the voids; the water column ruptures when a given void cannot withstand the applied negative pressure.

Eddy Current Damping of a Superconductor

W. V. Houston and Nils Muench, *The Rice Institute*

To investigate the electromagnetic ponderomotive force on a superconductor, a tin sphere was suspended from a torsion fiber in a horizontal magnetic field. Above the transition temperature the damping constant was proportional to the conductivity. Below the transition temperature it dropped to less than one part in 10^5 of its value at 4.2° K.

According to the usual theory of eddy current damping, the damping constant should be proportional to the conductivity for conductivities in the usual range. A sufficiently high conductivity, however, will lead to a vanishing damping force, but will be accompanied by a large restoring force. No change in period of the necessary magnitude was observed.

According to the London theory, the supercurrents exert no force in the body of the superconductor and should produce no damping or change in period under these experimental conditions. However, small ordinary currents may also be expected which should lead to some damping and change in period. The accuracy of the measurements was insufficient to detect such effects and the results are in conformity with the London prediction.

Electrical Ponderomotive Forces within Material Bodies

J. Slepian, *Westinghouse Electric Corporation*

In classical electromagnetism the electrical force acting on a charged probe or small body is operationally defined as that force which must be added to the assumedly completely observable mechanical forces to restore otherwise failing classical particle mechanics. For a large body, rigid or nonrigid, lying in empty space, we may also define a total electromagnetic ponderomotive force as that force which added to the presumably observable total mechanical force restores otherwise failing mechanics. For such a body, the total electromagnetic force thus operationally defined may be undetermined by applying Maxwell's stress tensor in the empty space surrounding the body.

Very generally it is believed that specifically electromagnetic ponderomotive forces, volume and surface, exist within material bodies. Presumably these electromagnetic forces are to be defined by balancing properly with the mechanical stress tensor within the body.

One may attempt to define this mechanical stress tensor through the mechanical force required to keep the strain unchanged on making a cut along an element of surface within the body. However, in an electromagnetic field the force so obtained is not derivable from a tensor.

We may define as a possible electromagnetic stress tensor any tensor whose components are functions of the field vectors, E, D, H, and B, and the charge and current densities σ and i, and which in empty space, i.e.,

where $E = D$, $H = B$, $\sigma = 0$, and $i = 0$ reduces to Maxwell's electromagnetic stress tensor. Then we define the associated mechanical stress tensor through the vector difference between the calculated electrical surface force for the sides of the cut, and the mechanical force observed there, this difference being derivable from a tensor.

These two largely arbitrary tensors meet all the requirements of mechanics and electromagnetism and no experiment can distinguish between the validities of the various sets of such possible tensors. There is then no physically significant uniquely definable volume and surface electromagnetic ponderomotive force within a material body.

Rancho Santa Fe Conference concerning the Evolution of the Earth

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Institute of Geophysics, Los Angeles

Under the joint auspices of the National Academy of Sciences, the University of California, and the California Institute of Technology, a round table discussion concerning the evolution of the earth was held at Rancho Santa Fe, California, on January 23, 24, and 25, 1950. The conference was attended by 24 scientists representing the subjects of astronomy, chemistry, geochemistry, geology, fluid dynamics, physics, geophysics, and oceanography. The discussion was informal, no prepared papers being presented. The stimulating ideas of Dr. Urey presented at the November, 1949, meeting of the National Academy were a central theme, and discussion covered many aspects of the problem of the earth's evolution. The following topics were among those discussed:

1. Theories of the origin of the earth from materials of moderate temperatures, to form an earth nonmolten at the outset.

2. Consideration of the spacing of the planets in the solar system (''Bode's Law'') in terms of a statistical ''mixing length'' in the fluid mechanics of turbulence. The implications of the apparent differences and similarities in the earth and its neighboring planets and in their atmospheres; the composition of cosmic materials and of the earth.

3. The nature of the chemical environment during the earth's origin which is required by or is consistent with present postulates concerning the internal composition of the earth, and with present knowledge of its atmosphere and oceans.

4. The available sources of geological energy and their adequacy to perform the work of continent- and mountain-building. The fractionation of the original crustal material of composition of stony meteorites into dunite and basalt may provide an adequate mechanism for the continued growth of continents. Recent summaries of the age relations of the major pre-Cambrian orogenics in North America appear to furnish significant indications of the history of the growth of this continent.

5. Evidence for the continued growth of oceans was presented.

6. A method for estimating the compressibility and density of materials under pressures as high as those occurring in the central parts of the earth was reported.

The Thermoluminescence of Rocks

Farrington Daniels and Donald F. Saunders,

University of Wisconsin

Many rocks when heated emit light due to the release of electrons which have been driven into traps by radiation from traces of radioactivity over geological periods of time. Most fluorites, limestones, and potassium feldspars exhibit this phenomenon.

Of 1500 samples of common rocks examined, over three-quarters showed visible thermoluminescence.

Automatically recorded curves were obtained giving the intensity of light as a function of time while the rock samples were heated at a rate of about 50° C per minute. The intensity peaks in the curves are characteristic of the minerals present in the rock, the radioactivity content, the impurities in the minerals, and the geological history of the rock.

Thermoluminescence has been produced in minerals and pure crystals by exposure to radioactive cobalt produced in the Nuclear Reactor at Argonne National Laboratory. The gamma-induced thermoluminescence curves have been compared with the natural thermoluminescence curves in attempting to interpret the geological history of the samples.

The pattern of thermoluminescence as photographed can be correlated with the patterns of radioactivity as obtained by exposure to nuclear track photographic plates and, hence, shows the distribution of radioactive minerals in granites.

The shape of the gamma-induced thermoluminescence curves from limestones can be used as a tool for ascertaining if samples from different localities are from the same rock stratum.

The study of mineral crystals which have been adjacent to radioactive minerals in nature makes possible the determination of radiation damage produced by very long exposure to radioactivity.

Paleotemperatures of the Upper Cretaceous

Harold C. Urey, Samuel Epstein, Heinz A. Lowenstam and Charles R. McKinney, *University of Chicago*

The relative abundance of the oxygen isotopes in calcium carbonate differs from that of the water from which it is deposited and varies with the temperature of deposition. These physical facts make possible the use of the relative abundances for the measurement of temperature. Such a thermometer is difficult to use, but

it may have great durability and hence make possible the measurement of temperatures in past geological ages. In order that this thermometer shall be effective, it is necessary that living organisms lay down their shells in equilibrium with the sea, that the effects shall be preserved with time, that the oceans shall have a constant isotopic composition, and that a mass spectrometer of sufficient precision and reliability be constructed.

We have found that all these various difficulties can be overcome, though there is considerable error due to geographical variation of the isotopic composition of sea water in the present oceans and presumably this may have existed in the past. Using such a thermometer we have found that the temperatures of the Upper Cretaceous seas of the southeastern United States, England, and Denmark were remarkably constant at about 16° C. The organism used for most of this work has been *Belemnitella americana,* which has a particularly compact structure. The uniformity of this temperature may be due to the better circulation of water in the Upper Cretaceous seas, though the possibility of error due to variation in isotopic composition cannot be excluded.

Technical Papers

The Availability of Various Manganese Oxides to Plants

L. H. P. Jones and G. W. Leeper

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Manganese deficiency of cereals is normally confined to soils of pH higher than 6.5, and to relatively few types in this range. The majority of neutral and alkaline soils can provide plants with ample manganese and most of these "healthy" soils contain large amounts of manganese (100 ppm or more) present as oxides which are insoluble in water but easily reducible (*5*). Such oxides may comprise many structural types of different degrees of oxidation, although they are conventionally referred to as manganese dioxide.

TABLE 1

X-ray structure	Preparation	Value of n in MnO_n	Response of Algerian oats	
			Rendelsham soil§	Yambuk soil‖
Manganous manganite	W* (*3*)	1.99	Cure	Cure
Pyrolusite 1	W (*1*)	1.97	Cure	Partial Cure
Pyrolusite 2	D† (*1*)	2.00	Nil	Nil
Manganite	W (*4*)	1.52	Cure	Cure
Hausmannite 1 ..	W (*4*)	1.35	Nil	Nil
Hausmannite 2 ..	D‡	1.35	Nil	Nil
Cryptomelane and γ-MnO_2 ...	Ore	...	Nil	Nil

* W : Prepared in the wet way.
† D : Prepared in the dry way.
‡ Heat treatment of hausmannite prepared in the wet way.
§ The Rendelsham soil is a grey calcareous peat of pH 7.9 from South Australia.
‖ The Yambuk soil is a grey calcareous peat of pH 8.0 from Victoria.

We have compared several oxides, both natural and synthetic, for their ability to supply manganese to oats when mixed with soils on which oats had previously failed through manganese deficiency. The added manganese in all cases amounted to 90 ppm of the soils as a uniform mixture. The plants were grown in the open in glazed pots. As the figures show (Table 1), the effects ranged from zero to complete cure.

Only oxides prepared in the wet way were successful. Electron microscopy showed that all oxides prepared in the wet way had large specific surface. This in its turn implies a large area of contact of root with oxide, which seems to be needed for success. But failure of hausmannite shows that structural type is also important.

The oxides were also compared in the laboratory for their rate of releasing manganese to a weakly reducing solution. A solution of quinol in normal ammonium acetate as used earlier for soils (*5*: see also *2*, p. 20) failed different result (Table 2), giving a good correlation with pot tests.

TABLE 2

X-ray structure	Response of oats (see Table 1)	Ammonium acetate-quinol	Water-quinol
		%*	%*
Manganous manganite ..	+	94	57
Pyrolusite 1	+	100	33
Pyrolusite 2	−	87	14
Manganite	+	100	35
Hausmannite 1	−	91	8
Hausmannite 2	−	6	7
Cryptomelane and γ-MnO_2	−	78	14

* Manganese extracted, expressed as percentage of total amount from 10 mg oxide with 0.05% quinol solutions at pH 7. One hour contact.

The last experiment suggests that the combined effect of a reducing agent and a concentrated electrolyte is too drastic. Quinol alone, or in the presence of a dilute electrolyte, removes only those manganous ions that are