with the cyclotron, he did, in fact, contribute a great deal to its development and to the general technique of the laboratory. Following these young pioneers, our laboratory has been blessed with a succession of fine men, and I wish there were time here to pay proper tribute to them all. May I at least acknowledge my appreciation of a great friend and valued scientific colleague, Donald Cooksey, who during the past three years has played an important part in the work of the laboratory and especially has been largely responsible for the improvement of the cyclotron. In thanking you for this greatly appreciated honor, I do so with the happy thought that I am the representative of these valued associates and intimate friends.

Perhaps I may be permitted to add a few remarks in the nature of a prognosis, for it seems clear that we are now on the threshold of a new scientific epoch, having much the same character as that which followed the discovery of x-rays and radioactivity. I need not recall the development of modern atomic physics and the benefits to the medical sciences that came from these discoveries. The recent discoveries in the domain of the atomic nucleus—notably neutron rays and artificial radioactivity—have similarly opened up new vistas of incalculable importance. Although I might more properly speak of the problems of the physical sciences that have come to view, with your permission I should like to call particular attention to the bearing of these recent advances in nuclear physics on problems of the biological and medical sciences; for there are grounds for the view that the fundamental problems of biology are at the moment of greater importance than those of physics.

From the moment of discovery it was apparent that neutron rays might have important applications in medical science, for although they are similar to x-rays in their penetrating power, the mechanism of their absorption in matter is quite different. Recent experiments indicate that neutron rays do indeed produce quite different biological effects from those produced by x-rays, shedding fundamental light on certain biological processes induced by ionization and giving strong hopes that for certain therapeutical purposes the neutron ray may be extremely valuable.

The discovery that it is possible to produce radioactive forms of the common elements is also of tremendous importance for biology. These artificial radioactive substances, which apart from their radioactivity are chemically and biologically indistinguishable from the ordinary elements, conveniently manifest their presence by the powerful radiations they emit. They are tagged atoms which are easily traced through a complicated biological system. During a visit in our laboratory last year, Professor A. V. Hill, the distinguished physiologist, emphasized his view of the importance of the artificial radioactive substances as tracer elements in biological research by predicting that future history will rank this technique of equal importance with that of the microscope. It will be said that the microscope revealed the cells while the artificial radioactive substances permitted the biologist in effect to see the atoms themselves. It seems clear that the biologist has at hand a powerful new technique and that we may look forward to significant advances in this field which otherwise would have been impossible.

It is a tremendous source of satisfaction that valuable contributions to biology and practical medicine are emerging from researches on the fundamental problems of atoms. Although the history of science records a convincing story of the great practical benefits that always accrue to humanity from fundamental research, nevertheless those of us engaged in pure science can not help but entertain occasional thoughts that possibly our efforts in solving some puzzling scientific problems may not be of greater significance than a fascinating game of chess. In this distinguished gathering it is not necessary to point out the essential unity of science or a justification for fundamental research, but may I confess that close association with these developments in nuclear physics having bearing on the medical sciences has made me appreciate more fully the fact that an advance of the horizon of knowledge in any direction uncovers territory of all the sciences.

In closing, Mr. President and members of the academy, may I reiterate my deep appreciation and thank you for myself and in behalf of my colleagues, who share with me this great honor.

ABSTRACTS OF PAPERS

The Volcano Tarawera in 1886: ARTHUR L. DAY. In any comparative study of hot-spring activity in the North Island of New Zealand and our own Yellowstone National Park one fact stands out in dominating relief. Primary volcanic activity in Yellowstone Park ended in quiet rhyolite flows in the Pliocene epoch, while at least two volcanoes in the New Zealand group are still intermittently active. Tarawera in 1886 was violently explosive, and out of the nine-mile rift which opened during this eruption there broke forth in 1902 the greatest geyser (Waimangu) of which we have a historic record. Three years later the geyser had, apparently, exhausted itself and no trace exists to-day of its point of emergence. This eruption of Tarawera and some of its consequences was described (with illustrations).

The University of Rochester–Bishop Museum Geological Expedition to Lau (Eastern Fiji): J. EDWARD HOFFMEISTER and HARRY S. LADD (introduced by T. Wayland Vaughan). In January of 1934, the writers left Rochester for several months of geological work in the Lau Islands (eastern Fiji). Twenty-six islands were studied and nine geologic maps were prepared of the most im-

portant of these. Large collections of rock specimens, fossils and water samples were made which have since been studied by various specialists. Twelve separate studies are now ready for publication. Available data support the following conclusions: Igneous rocks of three periods of volcanism occur in the islands. Rocks of the first period are chiefly andesites and occur widely throughout Lau. Those of the second period are chiefly olivine basalts and have a somewhat more restricted distribution. Odinites, representing the third period of volcanism, occur in a few places. Agglomerate is the commonest rock type, but tuffs, flows and dikes are present in many places. It appears that there have been two main periods of limestone deposition. The older and more wide-spread of these was deposited during the interval between the first two periods of volcanism and can be correlated with the upper part of the "Lower Miocene" of the East Indian section (Stage "f" of the Van der Vlerk-Umbgrove classification). The younger of the two limestones was laid down following the second period of volcanism, and contains a greatly different fauna from that of the older. Some of the Lau Islands have been described as elevated atolls. Our studies indicate, however, that the basin shapes of these atoll-like islands are due to atmospheric solution and marine erosion acting on elevated submarine banks. The petrographic study of the limestones has given a considerable amount of information about their origin and extent of alteration.

Methods of inducing chromosome doubling in plants by treatment with colchicine: A. F. BLAKESLEE and A. G. AVERY. A number of chemicals have been tested with Datura and other plants in an effort to induce hereditary mutations. Narcotics had previously been found effective in inducing doubling of chromosomes in roots, but chloral hydrate and nicotine were found ineffective in inducing chromosome doubling in stems which alone bear seeds and thus might lead to production of 4n races. The alkaloid colchicine we have found will induce an abundant production of branches with doubled chromosome number. When seeds are heavily treated, all the seedlings may be affected. The stem becomes swollen while the growth of root and plumule is checked; buds are abnormally arranged leading to sectors with roughened leaves characteristic of mixed 4n and 2n tissue like spontaneous 4n sectorial mutations. Normal 2n tissue tends to outgrow the mutated 4n tissue, but the latter may include the whole shoot. Between one half and one third of plants from treated seeds have produced 4n flowers. Apparently sectors of 8n tissue have been secured by treating 4n plants as well as by heavy treatments of 2n individuals. Tetraploid tissue involving the flower may readily be determined by examination of pollen. In Datura and Portulaca the determination by pollen size has been checked by chromosome counts. Doubling in adult tissue has been induced by immersion of twigs in solutions and in agar, by treatment of buds with mixtures of colchicine and lanolin and by spraying with solutions. By use of colchicine changes have been induced which are interpreted as due to doubling of chromosomes in the following genera: Datura (several species), Portulaca (2 species), Cosmos (2 species), Phlox, Stellaria, Nicotiana, Digitalis, Mirabilis, Tropaeolum, Cheiranthus, Raphanus, Cucurbita, Trifolium, Medicago and Allium. If control of chromosome doubling by chemical means proves of general application, as seems to be the case, the plant breeder will be able to work with greater precision in his efforts to control the evolution of economic forms both of plants propagated vegetatively and of those reproduced by seed. For example, it should be possible, starting with a sterile hybrid, to synthesize a pure-breeding double diploid which would have hybrid vigor and the desirable characteristics brought about by tetraploidy. This we have apparently succeeded in doing with a species hybrid in Nicotiana. Doubling chromosome number would give enlarged flowers and fruits to the horticulturist and through triploids would be the basis of a wide range of $2n+1$ types. Tetraploidy and presence of unbalanced extra chromosomes are known to have been factors in the origin of a large proportion of our most desirable varieties of fruits and flowers. In addition to increase in size of organs of the plant, tetraploidy has changed a self-sterile to a self-fertile form, a dioecious to a hermaphroditic race, an annual to a perennial, and has increased winter hardiness. The ability to induce chromosome doubling, therefore, is of importance to practical as well as to theoretical genetics.

The determination of color in the vasa efferentia of Drosophila melanogaster: CURT STERN and ERNST HADORN (introduced by C. B. Davenport). Males of *Drosophila melanogaster* which possess pigmented eyes (wild, carnation) contain yellow colored testes and vasa efferentia. In males with unpigmented eyes (white) the testes and vasa are colorless. Gonads and ducts originate independently and only later in development become attached to each other. By means of transplantation of testes from genetically "colored" into "uncolored" larvae and *vice versa*, a dependence of the pigmentation of the host ducts on the implanted gonad was demonstrated. No influence on the coloration of the vasa is observed when the implant does not become attached to a duct except in a few cases, in which vasa of uncolored constitution possess small colored spots. However, when the implant connects with a vas, either by itself or after having formed a compound gonad with a host testis, the ducts may show a pigment condition which does not correspond to their genetic constitution. Ducts of "colored" genotype may remain completely or partially colorless when attached to unpigmented testes, and ducts of "colorless" genotype may form pigment over all or part of their surface. In the latter case often both vasa are pigmented though only one is attached to a colored gonad. Whether the pigmentation of the ducts is induced by contact with genetically "colored" testis tissue or whether it is due to overgrowth of pigmented cells from the testis is undecided.

Rat embryo development in circulating fluids: J. S. NICHOLAS (introduced by Ross G. Harrison). The embryonic tissues of the rat possess the capacity of growing and differentiating under various experimental conditions. This has been tested by transplantations either

within the uterus or to sites other than the uterus in which the fate of the developing tissues can be followed, and also by a series of explanations involving an entirely different environment in which the embryo develops. The results of the transplantations showed that the tissues either separately or in combination were capable of a greater degree of differentiation than that obtained by the conventional tissue culture methods. The explanations showed that some factor limiting growth and differentiation was present in the conventional type of tissue culture since conditions were inadequate to maintain normal growth rate and to regulate developmental form. In order to secure material for analysis, a type of tissue culture employing a circulating system was devised and the following results obtained. Growth and development occur more regularly and more like the normal processes in circulating cultures than in the conventional type; embryos develop in fluids either from their own species or those from widely separated groups; they are not injured by gradual changes in temperature between 70° and 110° F.; they can adapt to variations in hydrogen ion concentration and also to changes in pressure over a comparatively wide range. The present method has permitted continuous observations during the critical ninety-six hours of development during which the definitive embryo is formed.

Interpretation of certain infantile growth curves: C. B. DAVENPORT. To test the application of the autocatalytic monomolecular reaction theory of Robertson to the growth of the arms of infants, the proximal and distal segments of various babies' arms were measured from birth to 12 months. During this period the humerus continues a rather uniform growth, whereas the radius nearly ceases to grow, toward the end of the first year. The brachial index (radius $\times 100 \div$ humerus) changes from, on the average, 90 at birth to 78 in the adult. The reduction in growth of the radius is ascribed to an inhibitory factor furnished by a human gene which keeps the fore-arm from the excessive length attained in anthropoid apes, especially the gibbon and which is in them adapted to arboreal life. The growth of each individual part in man is controlled by laws of its own, the end result of which is a greater fitness to environment of the organism as a whole.

Stimulus intensity as a determiner of the characteristics of behavior in the fetal guinea pig: LEONARD CARMICHAEL (introduced by Walter R. Miles). This paper reports an experimental study of the effect of the intensity of stimulation upon the character of behavior released in a typical fetal mammal at characteristic stages in motile prenatal life. The first set of experiments was conducted upon a series of fetuses by the use of stimuli of known temperature above or below the physiological zero of the organism. The second set of experiments was conducted by the use of pressure stimuli produced by calibrated von Frey esthesiometers. The technique of both experiments is briefly described and quantitative results are given which support the conclusion that the intensity of the stimulus itself is an important factor in determining the character of fetal behavior released by stimulation. In general, at all fetal stages studied and in all typical rflexogenous zones, the more intense stimuli released larger and more generalized patterns of response than did the less intense stimuli. The bearing of these results upon such questions as the problem of the origin of reflexes is pointed out.

The action of synthetic male hormones upon the differentiation of sex in the chick embryo: B. H. WILLIER (introduced by Frank R. Lillie). Solutions (propylene, glycol, sesame oil) of the synthetic male hormones, androsterone, dehydroandrosterone and testosterone propionate, in dosages from 0.02 mg–2.0 mgs, were introduced into eggs incubated from 48 to 72 hours. Development was continued until the sixteenth to eighteenth days. By using embryos with a sex-linked plumage character the original sex was readily ascertained. In the genetic females these substances modify the form and structure of the gonads and gonoducts. The right ovary hypertrophies into a cylindrical testis-like body consisting of medullary tissue and testicular cords in various stages of formation. The left ovary likewise assumes a testis-like form. With low dosages of the hormone its medulla hypertrophies; with higher dosages (0.75 to 2.0 mgs) the cortex degenerates more or less and testicular cords appear in the medulla. The testicular cords appear only at the hilus and beneath the degenerating cortex. Those in the latter position are sterile. The two oviducts respond quite differently: the left becomes rudimentary, the right abnormally long. The Wolffian ducts and certain mesonephric tubules which begin to hypertrophy with low dosages, become enormous when 1 mg or more is given. In the genetic males the gonads and gonoducts react differently to the various hormones used. With testosterone propionate the testes are reduced in size but remain essentially normal in form and structure. Oviducts never persist. Androsterone and dehydroandrosterone, however, produce a strong feminizing action similar to that of oestrone and oestriol (Willier *et al.* '37), *i.e.*, the left testis becomes a flattened ovary-like body consisting of both ovarian and testicular tissues (ovotestis), while the right retains its testicular character. Both oviducts persist and may hypertrophy. The Wolffian ducts and certain mesonephric tubules hypertrophy as they do in the genetic females. The results clearly show that androsterone and dehydroandrosterone have both masculinizing and feminizing effects on the differentiation of the sex glands and ducts, while testosterone propionate has a masculinizing effect only.

Failure of progesterone to prevent resorption of embryos in rabbits castrated in very early pregnancy: WILLARD M. ALLEN and GEORGE P. HECKEL (introduced by Carl G. Hartman). Crude progesterone-containing extracts of the corpus luteum are capable of maintaining pregnancy to term in rabbits castrated eighteen hours after mating (Allen and Corner, 1930). Data from experiments by them show that in each case (10 animals) in which the daily dose was 0.4 rb.u. or more, normal embryos were present on the eleventh day. When the quantity was less, embryos were not always present. In direct contrast to these results with crude extracts, we have found purified, oestrin-free, progesterone-containing

corpus luteum extracts and progesterone itself practically incapable of maintaining pregnancy. Twelve animals, each castrated the day after mating, were given from 0.4 to 1.5 rb.u. of hormone daily and an exploratory laparotomy done on the eleventh day. In eight animals no embryos were present. In one animal there were several resorbing implantations. In the other three there were normal embryos, but only one of these was successfully carried to term, the other two resorbing their foetuses prior to the twenty-first day. The only hormone, in addition to progesterone, known to be present in the crude extracts and not in the highly purified extracts or in progesterone is oestrin. Consequently we have given both oestrin (progynon-B) and progesterone to a small group consisting of six animals and have obtained normal embryos on the eleventh day from five of them.

Azacyanines: L. G. S. BROOKER and R. H. SPRAGUE (introduced by G. H. Whipple). In most cases the appearance of color in organic compounds is dependent on the presence in the molecule of long chains of atoms which are linked together by alternate double and single bonds, so-called conjugated chains. In the polymethine dyes the chains are of the type $=CH-CH=CH-CH=CH-$, etc., and previous workers have found that replacement of a $-CH=$ group in certain polymethines by N usually either makes but little difference to the color or else deepens it. The thiacarbocyanine dyes contain the trimethine chain $=CH-CH=CH-$, and we have found that if the central $-CH=$ group of a red dye of this class is replaced by N the color is deepened to bluish-red, in accordance with the above rule. But on the other hand, if a terminal $-CH=$ group is replaced by N the color is lightened to yellow. A theory is offered which explains this apparent anomaly and which furthermore is in agreement with the observed colors of dyes containing the chains $=N-CH=N-$ and $=N-N=CH-$. The dye containing the chain $=N-N=N-$ has also been made, but its color is anomalous unless a further assumption is made, when it, too, falls into line.

General transformations and optics: EDWARD KASNER. A double infinity of curves in space for which orthogonal surfaces can be constructed is called a *normal congruence.* If such congruence is reflected or refracted in any isotropic medium it remains a normal congruence, and therefore the concept is important in geometric optics. The author finds all transformations of lineal elements which convert the normal type into itself. The infinite group obtained is isomorphic with the contact group of surface elements. The only transformations of the new group which convert curves into curves are those of the conformal group. It is shown that if the involution type of pair of partial differential equations is invariant we obtain the contact group. An equivalent problem is connected with integrable Monge equations. Finally the general theory of transformations converting line elements into surface elements is developed. This leads to very extensive new classes of transformations. Elements of higher order are studied.

Measurement of solar radiation from high altitude sounding balloons: B. O'BRIEN, L. T. STEADMAN and H. S. STEWART, JR. (introduced by Charles G. Abbot).

The photographic emulsion as a tool in nuclear research: T. R. WILKINS (introduced by A. H. Compton). Fine-grained photographic emulsions have been used for a number of years to record the tracks of alpha rays. Some, but not all, of these emulsions have been found to respond to protons as well. If the grains are too small the emulsion may still be sensitive to alpha rays but have become insensitive to protons. For intermediate sized grains, the emulsion responds both to protons and alpha rays. For slightly larger grains a differential response is secured—the grain-spacing in the grains of a track varying not only for the different particles but varying along the track of any given particle. A properly chosen photographic emulsion thus provides a remarkable tool for identifying nuclear atomic particles and also of estimating the energies of the particles both from total track length and from the grain-spacing. Standardization curves for certain emulsions will be given for alpha rays, deuterons and protons and some examples of the application of the techniques in studying disintegrations produced by cosmic rays and also by radioactive radiations.

Double ionization of atoms: F. K. RICHTMYER and R. E. SHRADER. The origin of x-ray satellites—faint spectral lines appearing on the short wave-length side of the more prominent lines—long remained a puzzle until Coster and Kronig (*Physica,* 2: 13, 1935) suggested that the doubly ionized state requisite for the production of these lines could be produced by a kind of internal photoelectric absorption of energy—the so-called Auger effect. Tests in this laboratory and elsewhere have tended to confirm this suggestion as a working hypothesis to explain the relatively high intensity of these lines in certain atomic number ranges. According to the Coster-Kronig theory, the satellites of the x-ray line $L\alpha$ ($L_{III} \rightarrow M_{IV,\ V}$) should be strong in the atomic number range $40 < Z < 52$ (about); should be very weak or absent in the range $52 < Z < 72$; and should reappear above Hf72 (about) and increase in intensity for higher atomic numbers. These predictions are in qualitative agreement with data from spectrum plates. We have made measurements of the line $L\alpha$ and its accompanying satellites for nine elements in the range Ta73 to Th90, by means of a two-crystal ionization spectrometer of high resolving power and precision. Making the somewhat arbitrary assumption that $L\alpha$ is symmetrical about its point of maximum intensity, as a means of locating the background of the satellite structure, we have determined the intensities of the satellites relative to $L\alpha$ (ratio of areas) with the following results:

*Ta73	2.1%	Pt78	5.3%
W74	3.3	Au79	6.7
Re75	4.4	Pb82	6.2
Ir77	5.2	Th90	6.2
		*U92	5.4

* Preliminary data.

These data provide added quantitative support to the Coster-Kronig theory. The senior author wishes to ex-

press his thanks to the Carnegie Corporation of New York for a grant in aid of this research.

An improved cyclotron: ERNEST O. LAWRENCE and DONALD COOKSEY. This paper describes in some detail an improved and larger cyclotron, which has been in operation now for two months. Ions are accelerated to circles 30 inches in diameter within electrodes (dees) having an internal width of 3 inches. These wider dees have resulted in a much larger current output, and the larger diameter has made possible higher energies. At 4.7 million volts steady deuteron currents of 100 microamperes are obtained. At 6.8 million volts the deuteron current is about 40 microamperes, while at 7.8 million volts, the present operating voltage, the currents are between 3 and 10 microamperes. The variation of the output current with the applied high frequency voltage indicates that with increase of high frequency power input the obtainable currents above 7 million volts will be approximately equal to those obtainable at lower voltages. The yield of neutron rays from this cyclotron is as great as would be obtained from a mixture of beryllium and several hundred kilograms of radium. Moreover, artificial radioactive substances are producible in amounts equivalent in temporary radioactivity to several grams of radium. This cyclotron has many practical operating conveniences, not the least important of which is the use of rubber gaskets instead of wax, solving the problem of a leak-proof vacuum system.

Proton-induced radioactivities: L. A. DUBRIDGE and S. W. BARNES (introduced by E. O. Lawrence). A cyclotron patterned after the design of Lawrence and Livingston has been used for the investigation of nuclear reactions produced by protons of energy up to about 4 m.e.v. Previous proton work, confined to energies below about 1 m.e.v., has revealed two types of proton reactions in light elements: (1) radiative capture and (2) capture with alpha-particle emission. Further examples of these reactions for heavier elements (*e.g.*, Zn) have been found in the energy range 1–4 m.e.v. In addition a new type of reaction in which the proton expels a neutron has been found to set in at energies above about 2.5 m.e.v. This reaction leads in nearly every case to a positron emitting radioactive isotope which decays to the original bombarded isotope. The mass relations are thus quite simple and show that for any element this reaction becomes energetically possible for protons of energy equal to 1.8 m.e.v. plus the maximum energy of the positrons (usually .5 to 3 m.e.v.). The following are the isotopes and periods for which this reaction has been established: $O^{18} \rightarrow F^{18}$ (107 min); $Cr \rightarrow Mn$ (40 m); $Co^{59} \rightarrow Ni^{59}$ (?) (2.5 hr); $Ni \rightarrow Cu$ (2.7 hr, 10 hr); $As^{75} \rightarrow Se^{75}$ (109 m); $Se \rightarrow Br$ (16 m, 40 m, 5 hr, 34 hr) ?. Activities in several other elements have also been found and the reactions are now being identified. A larger accelerating chamber is soon to be installed which will allow the studies to be extended up to proton energies of 6 to 7 m.e.v.

Superinfection in virus-induced tumors: JEROME T. SYVERTON and GEORGE PACKER BERRY (introduced by Thomas M. Rivers). Papillomata induced in domestic and cottontail rabbits by Shope's papilloma virus have been easily superinfected with a number of other filterable viruses, both alone and in combination. Furthermore, the carcinomata, which in certain instances follow the papillomata in both types of rabbits, have similarly been infected with viruses. In addition to Shope's papilloma virus, the viruses employed in these studies have included herpes virus, B virus, virus III, vaccine virus and *Virus myxomatosum*. Evidence of superinfection has been derived from histopathological appearance, recovery of the virus by suitable animal passage and identification by immunological procedures. Since extraneous viruses, extraneous in that they have no etiological significance for the tumor under investigation, can be implanted with ease in virus- and in non-virus-induced tumors, it follows that the mere presence of a virus in a tumor is no proof that the virus is producing that tumor. These findings emphasize the necessity for conservatism in evaluating the rôle of a virus recovered from a tumor, for example, the rôle of papilloma virus in the carcinomata which follow papillomata.

The vascular pattern of the tumor transplant with a possible explanation of one method of metastasis: A. GORDON IDE and STAFFORD L. WARREN (introduced by G. H. Whipple). A transparent window of cellulose acetate film base is placed on the inner and outer surfaces directly upon the subcutaneous tissue in the ear of the rabbit. A fragment of Brown-Pearce rabbit epithelioma is transplanted under the outer window. The development of the characteristic pattern of capillaries growing up, around and into the growing tumor may be observed under rather high magnifications (900 times) with proper technique. The development of a large, open, sinesoidal vessel at the growing tumor edge has been observed twice. In addition, a motion picture record (in color) has been made of a fairly large blood vessel partially stripped of endothelium so that direct washing in and out of serum, red blood cells and apparently tumor material can occur with ease. Several pieces of tumor material appear to drift into the blood stream in this film. Because of the extremely rich, vascular network of large, thin-walled vessels and the frequency of rupture of the latter by very minor trauma, it is highly probable that tumor fragments both living and dead drift into the blood stream in far greater numbers than has been supposed.

The effect of freezing on the growth of mammalian transplantable tumors: G. BURROUGHS MIDER and JOHN J. MORTON (introduced by Harvey Cushing). It has been shown by previous investigators that primitive forms of life can withstand freezing temperatures. Interesting observations have been recorded on the freezing of bacteria and viruses. A combination of freezing and desiccation has made it possible to store bacteria and their products for long periods of time, thus saving the necessity of repeated transfers. Malignant tumors of rats and mice have been tested by others for their ability to withstand freezing temperatures. The results obtained have been conflicting. In the experiments reported here,

rat carcinomas and mouse sarcomas have been subjected to freezing temperatures, ranging from -40° C. to -60° C. Studies have been conducted with respect to the rate of freezing; the duration of time in the frozen state; the physical state of the frozen material; and the effect of repeated freezing and thawing. Mouse sarcoma cells were not damaged to any appreciable extent by rapid freezing within five minutes or prolonged freezing for 24 hours. Progressively growing grafts could be obtained from this frozen material in approximately the same proportions as from the normal tumor. Rat carcinoma cells when rapidly frozen once at - 60° C. showed evidence of damage by a latent period before growth occurred in animals grafted with these cells. There was also a diminished percentage of success, as only about half as many tumors were obtained after this treatment. Freezing and thawing for four times did not alter this result. But cells dispersed in a saline medium were still more sensitive, giving only a small number of tumors. When frozen and desiccated in the lyophile apparatus the cells were rendered incapable of further producing tumors on transplantation. These experiments have been designed to establish a definite lethal point for freezing effects on tumor cells. When this has been determined, problems bearing on immunity to transplantation; on the extraction of growth stimulating and inhibiting substances; and on the possible demonstration of a filterable agent will be carried out. From the standpoint of immediate utility, it may be possible to carry laboratory animal tumors in a frozen state, thus obviating the necessity for repeatedly transplanting them to living animals.

Amino acids (natural and synthetic) as influencing hemoglobin production in anemia: GEORGE H. WHIPPLE. We wish to submit evidence that histidine, leucine and phenylalanine (both natural and synthetic forms) may under certain conditions exert a definite influence upon the regeneration of red cells and hemoglobin in standardized dogs made anemic by blood withdrawal. It has been believed by chemists and physiologists that the natural forms of the amino acids are much more active in protein metabolism than the optical isomers or the synthetic dl forms. The evidence relating to hemoglobin production (internal protein synthesis) indicates that in an emergency (anemia) the dog can use all forms of certain amino acids to increase the hemoglobin production.

Injected plasma protein utilized by phlorizinized dogs: W. B. HAWKINS (introduced by G. H. Whipple). Dogs were made diabetic by means of phlorizin and then were given dog plasma protein by mouth or intravenously. The injected protein promptly disappears from the blood stream, but there is no excess nitrogen or sugar eliminated in the urine. There is no loss of protein in the urine. When the plasma protein was fed, it was digested, and subsequently there was an excess of nitrogen and sugar, indicating amino-acids had been formed with conversion of some of them to sugar. It is evident that the metabolism of the protein, when fed, is different than when it is injected. It is suggested that there is a partial katabolism of the injected protein with the formation of large aggregates. The various body cells then reassemble these large aggregates and form their own peculiar type of protein.

New results on the absorption of insulin from the alimentary tract: JOHN R. MURLIN, LAWRENCE E. YOUNG and WILLIAM A. PHILLIPS (introduced by E. G. Conklin). This is a study of the mechanism underlying absorption of an undigested native protein, with very obvious practical applications. The advantage of insulin over other proteins of similar molecular weight or solubility is that its effect on blood sugar level furnishes a good measure of the absorption rate. Proof of the possible absorption of insulin, when protected from destruction by pepsin of the stomach and trypsin of pancreatic juice, is now entirely conclusive. But wide individual differences remain and dosage requirements to produce therapeutic results are high. Recent studies in our laboratory demonstrate that two classes of substances put into the intestine with insulin promote its absorption: (1) Those which clean the mucosal surface of mucin; and (2) those which lower surface tension. Weak acid or alkali belong to the former class; bile salts, saponin and hexylresorcinol to the latter. The last-named substance in weak solution of the pure substance, together with weak soda solution and 100 units of insulin, in *some* dogs will accelerate absorption of the protein sufficiently to produce a sharp fall in blood sugar in more than 80 per cent. of the trials; in other animals not more than 50 per cent. The most favorable reaction of the mixture swallowed is at pH 9.9 to 10.5 (electrometric). The most favorable surface tension is in the neighborhood of 31 to 33 dynes per cm (stalagmometer). Heptyl- and octyl-resorcinol are no better than hexyl. There is a strong probability that the alkyl derivatives of resorcinol exert some hydrotropic effect on the solubility of proteins, thereby affecting the isoelectric point. Just how useful or practical these results will prove to be in the treatment of human diabetes remains to be seen.

Enterocrinin, an intestinal secretory hormone: E. S. NASSET (introduced by Eugene F. DuBois). Surgical transplantation of segments of small intestine to the mammary glands provided test animals with which it was possible to demonstrate the existence of a blood-borne excitant for the intestinal glands (Nasset, Pierce and Murlin, *Amer. Jour. Physiol.*, 111: 145, 1935). In a search for the humoral agent it was soon discovered that simple extraction of the small and large intestines of several species, including man, yielded a very active intestinal secretagogue for which the term *enterocrinin* is proposed. With the development of a rapid method of assay it was possible to keep pace with the chemical fractionation of the extracts so that at present enterocrinin is obtained in the form of a white, water-soluble powder active in doses of 0.2 to 0.4 mg per kilo of body weight. The early results with crude extracts were complicated by diminished blood pressure and excitation of the pancreas. The present method of preparation eliminates the substances responsible for these side effects. Since enterocrinin acts in the presence of atropine, does not depress the blood pressure nor excite the pancreas, it can not be acetylcholine, histamine or secretin. The evidence at hand warrants the conclusion that it is a new hormone, the

function of which is to stimulate the production of all components of the intestinal secretion, including the digestive enzymes.

Reversible heat activation of the enzyme carboxylase within a living cell: DAVID R. GODDARD (introduced by William Albert Setchell). A manometric method has been devised for studying the activity of the enzyme carboxylase in living cells. The method depends upon the fact that the anaerobic production of carbon dioxide is poisoned by sodium fluoride, but that the liberation of carbon dioxide by the enzymatic decarboxylation of pyruvic acid is not inhibited. This method has been applied in following the reversible activation of carboxylase in living spores. The ascospores of the fungus, Neurospora, are dormant. Exposure of the spores to temperatures of 50° C. or higher for a few minutes induces germination several hours after returning to room temperature. Measurements of carboxylase activity at 25° C. have shown that the dormant spores have zero activity, but that the heat treated (activated) spores have a marked carboxylase activity. Under anaerobic conditions the carboxylase activity falls to zero after two or three hours at 25° C. The full carboxylase activity may be regenerated by a second heat treatment. The activation of carboxylase is therefore reversible and may be controlled at will.

Movements of potassium during muscular contractions: W. O. FENN (introduced by W. J. V. Osterhout). Further evidence is presented to show that potassium is lost from muscles during contraction, whether voluntary or resulting from electrical stimulation. The data are most complete for cats and rats, but a loss can also be demonstrated in frogs if the period of stimulation is sufficiently long (one and a half hours) and the individual contractions are not so frequent as to cause excessive fatigue. A continuous tetanus fatigues the myoneural junction and inhibits the contraction and the loss of potassium. The loss of potassium is not determined by the degree of asphyxia of the muscle, for it was greater in the soleus muscle with a low lactic acid content (100 mgm per cent.) than in the gastrocnemius muscle with a high lactic acid content (608 mgm per cent.). Moreover, cutting off of the blood supply to a stimulated muscle diminishes the loss of K more or less in proportion to the diminution in the amount of tension developed. The loss of K is not proportional to the number of nerve impulses delivered to the muscle, for it is less for a continuous tetanus than for an intermittent one. An increase of K in the blood is regularly observed during stimulation, but not over 10 per cent. of the total potassium lost can be accounted for in the blood.

On the kinetics of recovery during the refractory period in nerve: H. A. BLAIR (introduced by K. T. Compton). It appears likely that by means of stimuli of short equal durations and variable strengths one is enabled to describe the refractory period of nerve in terms of, and only in terms of, the ratios, $S = K/h$, K being the rate of accumulation of the excitatory state per unit stimulus and h being the threshold value of the excitatory state. At the end of the absolute phase, this state, S, beginning at O returns to its end point, S_o, at a rate proportional to the distance remaining. The end point, however, depends upon the rate of some oxidative process which is raised by the response and which recovers exponentially to its resting value. When its recovery is fast there is no supernormal phase of excitability, but when it is slow there is a supernormal phase as well as an evident after-potential which is associated in some way with the excess oxidation. The time constant of the recovery of the state, S, is independent of pH, and of fiber size to some extent, but is increased about three-fold with 10° C. rise in temperature. The time constant of the oxidative process varies similarly with temperature but is increased very greatly on going from acidic to alkaline media. If both of these processes are chemical, a method is provided of studying the reactions concerned with much greater accuracy than is ordinarily possible. In any case, the mode of variation of the time constants of these processes with different reagents and conditions should throw considerable light on the nature of the excitatory mechanism and of the refractory state.

The cortical representation of respiratory movements: WILBUR K. SMITH (introduced by George L. Streeter). The deduction is ordinarily drawn, from both subjective and objective data, that in man the cerebral cortex is able to influence respiratory movements. Evidence to indicate that this is not an attribute of the human cortex alone is obtained from electrical stimulation of the cerebral cortex in mammals. In the cat and dog, under light ether anesthesia, an inhibitory effect upon breathing characterized by a temporary cessation or slowing is most easily elicited from an area in the gyrus compositus anterior. A less marked but definite inhibitory effect is obtained from most of the cortex of the sylvian and ectosylvian gyri, and in the cat from the gyrus proreus as well. Increase in the depth of anesthesia results in abolition of the response, the area in the anterior composite gyrus being the last to succumb. A similar inhibitory effect is obtained in the monkey from the cortical region just caudal to the lower end of the inferior precentral sulcus. From other areas of the cortex a marked acceleration of breathing can be obtained. Recordings from the diaphragm show that the effect is bilateral. A reversal of response sometimes occurs, especially under very light anesthesia. The inhibitory and acceleratory areas are present on both sides of the brain. Undercutting the area abolishes the response, but it may then be obtained by stimulation of the cut ends of the nerve fibers. The response is not abolished by section of the corpus callosum, by removal of one hemisphere, by bilateral section of the phrenic nerves and the vago-sympathetic trunks or by section of the spinal cord below the origin of the phrenics. Changes in arterial pressure usually occur simultaneously with the respiratory alterations. Neither effect is abolished by denervation of the carotid sinuses.

(*To be concluded*)