Meetings and Societies

Chemical Basis of Development

The McCollum Pratt Symposium on the Chemical Basis of Development was held 24–27 March 1958 at Johns Hopkins University. The program was opened by B. H. Willier, who traced the development of embryology in the United States, from the work of Louis Agassiz through that of the Johns Hopkins and Chicago schools.

Clement L. Markert said that the major problem of embryology is the study of development as a dynamic process and cited experiments indicating that the chemical environments condition the further development of the cell. He pointed out that embryonic cells produce qualitatively different products in mixed culture and in pure culture and that this suggests an interaction among cells that results in new enzymes. He proposed the possibility that the genes are not the same in cells from embryo to adult form and suggested that the manifestation of gene activity is perhaps only possible at certain levels of differentiation. He cited experiments on the esterases of mouse tissue, of which there are approximately 20, separable by electrophoretic mobility. Varying patterns developed during successive stages of differentiation of mouse liver. Furthermore, liver cells in tissue culture lose most of their esterases, even though they continue to grow. The hypothesis was proposed that the chromosomes of the fertilized egg are not identical with the chromosomes of the adult and may acquire new proteins, thus altering their activity. These proteins might possibly be the inducers.

R. D. Allen described a study of the cortical granules and their role in the development of the fertilization membrane of the *Arbacia* egg. Since the latent period of the cortical reaction is temperature-dependent, the reaction is probably chemical. Experiments with eggs in capillary tubes indicate that the fertilization membrane is the result of local reactions. Heat or pressure can prevent the extension of the fertilization membrane. Thus, an egg elongated in a narrow capillary could be fertilized at both ends. Allen measured the rate of conduction of the cortical reaction in the egg and found that the Q_{10} is dependent upon the stretching of the membrane. These experiments give further support to Loeb's hypothesis of surface cytolysis as the mechanism of the development of the fertilization membrane. Indeed, the surface cytolysis proposed by Loeb may actually be a lytic process around the cortical granules.

F. E. Lehmann of the University of Bern discussed the pole plasm, which is Nadi reactive. It accumulates around the vegetive and animal poles and can be centrifuged to either pole without altering development. However, experiments with displacement by centrifugation of the pole plasm to regions other than the vegetive poles produced eggs which did not divide. Experiments with the displacements of the spindle demonstrate also that intracellular organization of the blastomere is as important as the intercellular organization of the blastema in embryogenesis.

A. E. Mirsky's experiments on nuclear differentiation and function were based on three postulates: (i) that there are the same chromosomes in the nucleus of the salivary gland of *Drosophila* as in the sperm and egg; (ii) that there is constancy of deoxyribonucleic acid (DNA) content of the nucleus; and (iii) that the histones of all cells are similar. He showed that there is a high-energy generating system in the nucleus which produces adenosine triphosphate (ATP) separately from the cytoplasmic system. Deoxyribonucleic acid is apparently a cofactor in ATP synthesis. The meaning of the expression *cofactor* was discussed, and the conclusion was drawn that DNA is "necessary" for the formation of ATP, but there is no direct evidence for a catalytic role of DNA in this formation of ATP in the nucleus. The amount of nucleotide in the nucleus is related to the amount of ATP in the nucleus. Evidence was also presented for the influence of the adjacent cytoplasm on nuclear activity and for a biochemical response to cytoplasmic changes. For example, the nuclei of the pancreas of a fasting animal are much less active than the nuclei of the pancreas of a fed animal. Two reports were cited as indicating that the nucleus operates in a sodium environment. Although there is some potassium in the nucleus, the sodium content is apparently much higher than the potassium content. If potassium is kept constant in the medium, sodium ion stimulates nuclear protein synthesis as measured by the uptake of labeled glycine. The sodium concentration that has the highest effect is approximately 0.065*M*. Abelson's experiments with the frog oocyte, in which it was shown that the nucleus concentrates Na^{24}, were also cited. Evidence for the differentiation of the nucleus was cited, such as the presence of hemoglobin within the nucleus of red cells, the fact that there is no myoglobin in the nuclei of muscles, and the variation in the ratio of nuclear to cytoplasmic arginase in different organs, such as liver and kidney. Furthermore, the nucleus is impermeable by certain antibodies which do permeate the cytoplasm. Stone's demonstration of the dedifferentiation of iris to lens must indeed involve a nuclear change. As special effects of the nucleus on the cytoplasm, the following were cited: first, that deoxyribonucleic acid synthesis, as demonstrated by Hogeboom and Schneider, is a function mainly, if not exclusively, of the nucleus; second, that the nucleus dominates ribonucleic acid synthesis, which controls protein synthesis in the cytoplasm. Finally, that nuclear deoxyribonucleic acid controls synthesis of ribonucleic acid in the nucleolus, which is much more active than the cytoplasm, as measured by the uptake of radioactive phosphate into ribonucleic acid of the nucleolus and the cytoplasm. A very interesting experiment which was cited by Mirsky involved the inhibition of synthesis of ribonucleic acid after treatment of the nucleus with deoxyribonuclease. This loss of ribonucleic acid synthesis could be restored by the addition of a number of different preparations of deoxyribonucleic acid.

J. Gall described the unusual structure of the lampbrush chromosome. Electron micrographs showed that there is a core strand in these chromosomes which is deoxyribonucleic acid, and that coiled around it is the mass of ribonucleic acid. At each node in the long lampbrush chromosome, lateral loops appear. These loops, too, are made of a central core of deoxyribonucleic acid, around which is apparently stretched ribonucleic acid. The action of deoxyribonuclease results in the formation of clumps of ribonucleic acid where the lateral loops had been. Experiments with stretching the lampbrush chromosome gave evidence for the loop nature of the lateral structures of the chromosomes.

Vincent cited some experiments concerning the nucleolar chemistry of the starfish. Apparently there are at least two forms of ribonucleic acid, based on the rate of uptake of P_{32}. There appear also to be two proteins in the nucleolus,

one of which has a histidine end group. Each of these proteins is associated with one of the ribonucleic acid fractions. The P_{32} is first taken up into ribonucleic acid of the nucleolus and then appears in the nucleotides.

M. V. Edds discussed the origin and structure of the intercellular matrix. Although the ground substance of cells is generally homogeneous, the mucopolysaccharide, even from adjacent areas, appears to be different. For example, the cornea contains mainly keratosulfate as the ground substance, with a small amount of chondroitinsulfate. On the other hand, the sclera contains mainly chondroitinsulfate and a small amount of keratosulfate. The function of mucopolysaccharide may be manifested through mucoproteins. The ground substance of cartilage appears to be chondroitinsulfate A and a noncollagenous protein. There is no obvious or immediate relation between the large molecules of the ground substance and the growth and development of the organism. Data on the crystallization of hydroxyapatites from metastable solutions of calcium or phosphate were given. Only normal collagen preparations will stimulate crystallization of the hydroxyapatites. Abnormal spacings of collagen result in no crystallization. The hypothesis is presented that mucopolysaccharides present in the tissues may prevent calcification of all collagens except that collagen which has the proper spacing. As an experimental model, unreconstituted collagen was demonstrated not to form apatites, whereas the normally reconstituted collagen will form apatites from metastable calcium and phosphate solutions.

Hewson Swift discussed the origin and function of cytoplasmic particulates, most of which, with the exception of the mitochondria, appear to be membranes. He described the various portions of the endoplasmic reticulum, including the cell membrane—for example, the infoldings of the kidney cell on electron microscopy. The other membranes are the nuclear membrane, the Golgi apparatus, the rough reticulum with its ribonucleic acid content, and the smooth reticulum. The ergastoplasm was described as sheets of membrane, highly basophilic, containing large amounts of ribonucleic acid, possibly involved in secretory function. In addition to these membranes there is a great deal of basophilic material apparently not associated with membrane. The studies of ribonucleic acid turnover with C_{14} adenine in *Drosophila* reveal several things: first, that ribonucleic acid is an integral part of the chromosomal material—a finding which is consistent with Gall's studies on the lampbrush chromosomes. Further, the ribonucleic acid turnover, as evidenced by the uptake of C_{14} adenine, showed that the chromosomal ribonucleic acid is most active, the nuclear next active, and the cytoplasmic least active. There does not seem to be a particulate component containing ribonucleic acid which is common both to nucleus and to cytoplasm. There are filaments projecting through both sides of the nuclear membrane, and these filaments appear to be ribonucleic-acid–containing.

T. Yamada discussed embryonic induction. Guinea-pig bone-marrow extracts, partially fractionated by centrifugation and ethanol precipitation, induced mesodermal and ectodermal development. Heat treatment of bone-marrow extracts produces a peculiar effect. Mesodermal activity is slowly destroyed with prolonged heating, but neural changes such as anencephaly, deuteroencephaly, and spinal cord effects appear after heat treatment and disappear with longer heat treatment. This differentiation between effects of the same bone-marrow extract suggests a multiple set of compounds capable of inducing particular tissue types. It was pointed out in the discussion that when a tissue type is induced by the bone-marrow extracts, it is an organized tissue type; this indicates that there must be intercellular reaction among the cells of a particular type to produce an organ-like structure, and that the inducer possibly might induce merely the "tendency" toward development of a certain type of tissue and not the organization of the tissue. This would be conditioned by the growth of the cells within that area.

M. Sussman reported on cellular interaction in slime mold development. There are two types of cells in each strain of slime mold. In a study of aggregation of slime molds it was found that the number of aggregation centers is proportional to the density of cells and that at optimal density the number of centers is proportional to the number of cells. He showed that there was a certain cell type directly related to the centers of aggregation, and he called this the "I" cell. This cell is anatomically different from the others in that it is several times larger. Centers can be caused to form (induced) by the insertion of an "I" cell into a colony of cells, and to achieve this effect the presence of the "I" cell is required for only about five minutes. The "I" cells are always present in a constant ratio to the total number of cells. This ratio is characteristic for the strain of mold. Evidence was produced that the "I" cells secrete or emit a diffusable substance. Mutant cells which do not aggregate can be caused to do so by the presence of A-type cells; this suggests an interaction of the A-type cells with "I" cells. A study, by Barbara Wright, of the substance (crazin) secreted by the "I" cells showed that urine of pregnant women and estrogenic substances had similar effects to crazin but that crazin itself had no estrogenic effect. Enzyme studies of the various growth stages of the slime mold show patterns characteristic of the general morphology and metabolism of the cell. For example, the amoeba form is an anaerobic form. The content of oxidative enzymes in these tissues is very low. The transition from amoeba to plasmodium is aerobic, and the enzymes of aerobic metabolism increase sharply at this point, particularly the Krebs cycle enzymes.

R. DeHaan discussed morphogenetic movements. Studies with acetylcholine as it affected the chick embryo led to the finding that the folding of the neural crest was inhibited by chelating agents. The effect was reversed by the addition of high concentrations of calcium to the medium. This led to the hypothesis that folding of layers is caused by a change in the surface of the cell, resulting in the appearance of calcium binding sites between adjacent cells. The calcium is then formed into a bridge which pulls the adjacent cells together, causing foldings.

Jean Pasteels described work on the comparative cytochemistry of cells, presenting experimental evidence for the specificity of cytochemical reactions of centrifuged eggs. He showed that, on centrifugation in various positions, similar types of stratification occurred in the three species examined. The various types of staining material went to the same pole in each species examined and formed bands of the same kind.

S. C. Shen discussed changes in enzymatic patterns during development. He used a copper thiol compound of choline as a substrate for the histochemically demonstrable choline esterase. In the formation of retina the first demonstrable choline esterase activity was on the surface of ganglion cells. After the bipolar neuron bodies appear, a choline esterase active layer develops between the synapses of the ganglion cells and the bipolar cells. Later this synapse layer splits into two, and finally four, layers of synapses, each set of synapses staining strongly for the choline esterase reaction. Further studies with the neuromuscular junction indicate a high choline esterase concentration right at the junction. Studies with amphibian muscle revealed that each muscle fiber received a nerve fiber only at the end of the cell, and that here alone is there choline esterase. However, the nerveless animal develops choline esterase in the tips of the muscle fibers at the same time as the control. If there is no innervation, due to the removal of the neural crest of that region, the choline esterase activity at the ends of the muscle disappears. As further demon-

stration that it is muscle cells which develop the choline esterase and that the initial stimulus need not come from nerve cell, muscle cells grown in tissue culture develop choline esterase. Both these sets of experiments suggested, in general, that choline esterase forms on the postsynaptic membrane without need for the presynaptic member for induction of the choline esterase activity.

Melvin Cohn reported on the induction and control of protein synthesis in development. In a study of permease it was found that a small molecule such as galactose can induce a change in the enzymatic composition of the cell that can be transmitted. It was further shown that, even if a few molecules of galactose remained in the progeny of the cell, the inducible enzyme will be present throughout the progeny. Therefore, induction is similar to mutation, for the progeny of the induced organism can maintain the enzyme as long as even a trace of inducer is present. If the inducer is completely removed, the cell reverts to the original type and the progeny can no longer be induced to form enzyme.

Werner K. Maas discussed the feedback inhibition of enzyme synthesis byproduct as a controlled mechanism in enzyme synthesis. Using the enzyme ornithinetranscarbamylase, he found that formation of the enzyme is inhibited in *Escherichia coli* by arginine. This inhibition of ornithinetranscarbamylase synthesis can be demonstrated within a few minutes after the arginine content of the medium is increased.

Studies of the developmental aspects of nitrogen metabolism in amphibians were reported by Brown and Cohen, who showed that tadpoles excrete mainly ammonium ion as the nitrogenous waste, whereas frogs excrete mainly urea. The activity of the urea cycle enzymes in the liver is parallel to the ratio of urea to ammonia.

R. E. Eakin showed that the Needham data on the chick embryo excretion of nitrogen, which are still used as a demonstration of the rule that ontogeny parallels phylogeny, are incorrect. In the chick embryo there are not three cycles of nitrogen excretion, including intially an ammonia cycle, a urea cycle, and finally a uric acid excretion, similar to that in the adult animal. It appears that the urea formed is derived almost exclusively from the arginine of the yolk, and that there is no urea synthesis cycle at any time in the development of the chick. The arginase concentration diminishes during the growth of the chick as the arginine is used up (converted to urea). Decrease in the amount of ammonia in the allantois is shown to be a dilution effect and not the result of excretion of ammonia by the embryo at any time. It is demonstrated that the formation of uric acid begins and increases to the adult level during the development of the embryo.

James Ebert discussed the formation of antibodies during development and pointed out that there is no convincing evidence of antibody formation by the embryo and, furthermore, that, following birth, there is a characteristic period of delay, variable among species, during which there is no antibody formation. The effect of organ grafts on homologous organs of the host was demonstrated by the grafting of adult spleen into nine-day chick embryo allantoic membrane. This causes a marked growth in the embryo. This is organ specific, occurring only in the thymus and liver and spleen. It is animal and species specific and is age specific in the chick, for the developing chick becomes resistant to this effect at approximately 18 days. There is a peak in the susceptibility to the graft shortly after hatching. This effect can be found in a microsomal and supernatant fraction but not in the nuclear or mitochondrial fraction of the homogenized graft. If the graft is in contact with the host long enough, the host is decomposed. This is called the graft against host reaction. Since all of the tissues which showed this reaction are reticuloendothelial tissues, it appears that whenever living cells capable of an immune reaction are put in contact with an individual incapable of forming antibodies, the graft reacts against the host with an immune reaction which destroys the host. This suggests an explanation of the well-known phenomenon in which the injection of bone marrow is followed by a slow reaction of the foreign material against the host. These delayed deleterious effects have only recently been studied and were described as sequelae of experiments in the prevention of radiation sickness by injection of bone marrow. The same type of serious reaction occurs in individuals with deficiency in antibody formation who are treated with bone marrow.

R. E. Billingham took issue with the statement that the embryo was incapable of an immune reaction, because, he said, there is a peculiar reaction developed in the embryo which is not manifested by antibodies but which changes the reactivity of the embryo to antigen. This he called the "tolerance response phenomenon." This phenomenon is seen in the red-cell chimeras, in which two different types of red cells can be found because of intermingling of the blood stream of nonidentical twins *in utero*. Once these chimeras are developed, they can receive, without reaction, transfusion of blood from one another. Experimentally, baby mice inoculated with spleen cells from a foreign strain are able to take skin grafts from this strain without rejecting the graft. They have, therefore, become tolerant to the foreign strain even though uninoculated litter mates reject the grafts. The foreign cells are apparently kept in the spleen, lymph nodes, white cells, and bone marrow, and not in the liver. This tolerance is not tissue specific, but it is absolutely genetically specific. Dizygotic cattle twins become chimeras through mixing circulation and will accept grafts from each other but not from brothers, sisters, or mother. Tolerance is not inversely proportional to time of injection. There appears to be an optimum time for response. This temporal variation is different for different strains in relation to the same host. On the other hand, the further apart the donor and recipient are in genetic constitution, the earlier must be the application of the sensitizing material. This phenomenon is an explanation of the reason why animals do not react to their own tissues. They apparently develop a tolerance response because the tissues are present at all times during the course of the development. If a tissue is segregated so that its protein can only with difficulty come in contact with its reticuloendothelial system, there is a possibility that the animal can be immunized against its own tissue. For example, guinea pigs can be immunized against their own sperm. This is probably because the sperm appear late in the course of the development of the animal and some of the sperm proteins are not present during the early development of the lymphoid system. Furthermore, it is possible to develop antibodies to the lens of the eye. The lens develops with no lymphoid drainage and with, apparently, "physiologic quarantine." Patients with Hashimoto's disease (an inflammatory disease of the thyroid gland) have been found to show antibodies to thyroglobulin. It seems that thyroglobulin escapes into the lymphatic system and there stimulates the formation of antibodies. These antibodies then attack the thyroid gland. Normally the thyroglobulin does not escape into the circulation. The brain has no lymphatic drainage, and brain tissue from an animal injected into the same animal can produce an immunologic response. Furthermore, the brain will accept a homograft. Therefore, it is not capable of immunologic response. If lymphoid tissue is injected into a one-day-old mouse, a runt is produced which is almost devoid of lymphoid tissues and is tolerant to homografts. Tolerance represents a specific failure of the immunologic response mechanism and, it may be, development of the ability to destroy antigenic material. Injection into mice, on the day of birth, of 5 to 10 times 10^6 lymphoid cells causes 100 percent of the mice to show a transient tolerance re-

sponse and 80 percent to keep homologous grafts for at least 100 days.

Morgan Harris discussed the selected uptake and release of substances by cells. He showed that the passage of proteins into cells can be demonstrated with fluorescent antibodies. Phagocytosis or pinocytosis are possible mechanisms for the movement of protein into cells; the uptake is of the size of globules. In tissue culture the amount of protein formed in cells cannot be accounted for by the decrease in amount of amino acids. After several days, more than half the cell protein can be shown to come from the protein of the medium. Protein fractions from spleen, liver, and brain are active in promoting the growth of tissue cultures. The spleen is somewhat more active than the others. The protein fraction is effective without the nucleic acid. It is suggested that the nucleic acid of nucleoproteins may act as a stabilizing factor, for freezing and thawing destroy the protein activity but not the nucleoprotein activity. Lactic acid production by tissue culture showed that the addition of heterologous serum caused an increase in glycolytic rate. Glycolytic rate was defined as the rate of production of lactic acid. On the other hand, embryo extract produces a lower glycolytic rate. Greater formation of lactic acid can be shown in muscle cell cultures than is reported for tumor tissues by Warburg and by Burk and others. In the discussion of this paper it was brought out that protein is not used by cultures of HeLa cells, that the lactic acid formation by tissue culture is a function of the substrate rather than a function of the metabolism of the cell, and that it is impossible to compare lactic acid formation by one type of cell with that by another unless the same substrates have been used.

N. T. Spratt studied control mechanisms in development and demonstrated several factors controlling chemically the growth of cells. In tissue cultures, the smaller the population of cells, the poorer the resistance of the cell population to changes in the environment. This was shown to be the result of the requirement for carbon dioxide. The more cells there were present, the more carbon dioxide was formed, producing a more favorable environment for all the cells. The effect of various sugars showed that there was a differential in the need for carbohydrates in various areas of the embryo. The chick embryo thrives best on a medium containing glucose or mannose. Maltose, fructose, and galactose will each support more or less growth, in decreasing order. Each of these is less effective than glucose. Pyruvate and lactate are very poor supporters of development, particularly of neural tissue. As the concentration of carbon available is lowered, the brain is first affected. The most active cells appeared to be most affected by alterations in the substrate. Alterations in ions show that with diminution of potassium in the medium there is fairly normal growth of most tissues but essentially no development of the heart. Oxygen removal causes serious changes in the most active centers of the embryo. A condition of anaerobiosis and the presence of malonate and cyanide permit development of the heart but of no other organ. Fluoride prevents development of the heart, but the brain is not affected. The effect of fluoride can be reversed by pyruvate. Iodoacetate inhibits development of the brain and the central portion of the embryo, and this effect is reversed by pyruvate. It seems as if the changes of embryogenesis are much too subtle to be simple effects of carbon dioxide, carbon source, oxygen supply, and so on. Surviving liver and heart slices and homogenates inhibit the development of embryonic tissues when there is intimate contact between the embryo and the tissue. Heating the tissue or taking it out of contact with the embryo keeps it from having this effect. The following functions, in ascending order, parallel the increase in carbon source: maintenance, movement, differentiation, and growth. In general, as a nutritive source, carbohydrate is less effective than amino acid, which is less effective than protein in the form of albumin, which is less effective than yolk protein.

Rita Levi-Montalcini, in the study of the chemical stimulation of nerve growth, showed that extracts of sarcoma stimulated the growth of sensory and sympathetic nerve tissue but not motor nerve tissue. This could be demonstrated in increase in cell activity, in mitosis, and in the speed of differentiation of cells. It could be shown that this soluble material stimulates the growth of nerve cells in tissue culture. Snake venom and extracts of salivary gland of the mouse were seen to have the same effect. S. Cohen studied the nature of this stimulating agent and found that it was active in tissue cultures at a concentration, for tumor extract, of 15 mg/ml; for snake venom, of 6.5 μg/ml; and for submaxillary gland extract, of 1.5 μg/ml. Neurotoxic snake venom showed no greater activity than other kinds of snake venom. A purification of the factor showed that it was a protein, stable in 0.1*M* alkali. Its molecular weight by sedimentation was approximately 20,000. It was not found to have the activity of any of the known enzymes of snake venom. Although its activity is inhibited by antisera to snake venom, the activity of the protein obtained from salivary gland is not inhibited by antibody to snake venom. In a study of the formation of nerve fibers by tissue-cultured cells under the influence of the nerve-growth factor, it was found that indoacetate could inhibit this growth but that cyanide, fluoride, and dinitrophenol could not. Glucose or mannose are needed for growth of the fibers. Phenylalanine is also needed. This was shown indirectly because there is apparently enough amino acid in the tissues to prevent a nutrition experiment from being performed. But parafluorophenylalanine will inhibit the growth of fibers.

Leslie Foulds described the developmental aspects of carcinogenesis. Observation of the development of breast tumors in mice revealed the fact that tumors would grow with each pregnancy and would regress at parturition. In mice bearing several tumors this cycle could be repeated many times. Finally, one of the tumors would fail to regress following pregnancy and would continue to grow at the same rate as previously. This tumor, however, would be malignant and could be histologically demonstrated to be so. The tumor which becomes malignant is not necessarily the first one that appeared. The histologic type of the tumors which appeared and regressed was markedly different from the histologic type of the tumor which appeared and continued to grow beyond parturition. At times, two or more of these new tumors would grow within the "plaques" of tumors which regressed with parturition. The small islands of potentially malignant cells lying within the subcutaneous tissues were discussed in relation to their similarity to the islands of malignancy which developed within the "plaques" in the mammary tumors.

Elio Borghese discussed the growth of organs in tissue culture. He showed the effect of induction of organ structure across distances which prevented contact of cell processes. An interesting effect of insulin—shortening of the shafts of bones, and epiphyses—was demonstrated.

Derst Hadorn, in studies of fruit flies, investigated the role of genes in the developmental processes. The suggestion was made that the further the process of ontogenesis has advanced, the more genes are necessary for growth. Certain genes are apparently essential for particular phases of development. An experiment was reported in which the relation between uric acid metabolism and the eye pigment isoxanthopterin was established. It was found that xanthine oxidase is missing from the *Drosophila* mutant "rosy." Xanthine oxidase is necessary for the oxidation of both xanthine and hypoxanthine as well as for the oxidation of the precursor of isoxanthopterin. Therefore, it was noted that the step-wise insertion of characteristics of gene action is not necessarily related to the apparent action of the gene, for the precursor of isoxanthopterin is not found in the animal till long after xanthine oxidase appears. Other lethal mutants

have been demonstrated which cannot synthesize protein from hydrolyzed protein. These protein mutant effects can be demonstrated by analysis of the hemolymph.

Carroll Williams discussed the hormonal regulation of metamorphosis. Experiments with the pupation of the moth suggest that specific cells appear to be programmed for various stages through which the organism develops and that certain hormonal stimuli accelerate or induce the growth of the organism along these programmed paths. As an example, cuticle formation by the epidermal layer was cited, as well as experimental evidence developed on the basis of the movement of areas of color, hairiness, and intersegmental membranes. The prothoracic gland apparently controls the conversion of pupa to adult. The hormone isolated from the prothoracic gland of the silkworm by Karlson and Butenandt has been named by them "ecdyson." This appears to be the growth hormone for all arthropods, which comprise more than 90 percent of the animal kingdom. Ecdyson, alone, stimulates both growth and differentiation of all tissue except muscle. Growth and differentiation of muscle requires a neurohormone apparently secreted by neurosecretory cells in the brain. Both the medial and lateral neurosecretory cells of the brain are needed to produce brain hormones. Pilocarpine can block the neurosecretory effect. This has been shown to be due to the imidazole ring structure. The brain hormone is a trophic hormone for the prothoracic gland. The diapause begins when the brain "shuts off." "Low temperature" starts the brain again. Therefore, the brain appears to be itself subject to neuronal stimuli. The slowing down of differentiation is due to another hormone called the "juvenile hormone," found in the corpora allata. The hormone of the corpora allata has been concentrated and seems to be a steroid. Beef adrenal cortical extract has the capacity to do the same thing as the juvenile hormone, but none of the known steroids has been identified as the juvenile hormone.

A report by André Glinos on the mechanism of liver growth and regeneration demonstrates that in normal serum there is an inhibitor to the mitotic activity of the liver. This inhibitor has been related to the albumin concentration of the serum. Even a small increase in the albumin content of the extracellular fluid of the liver inhibits the formation of albumin by liver cells and actual growth of liver tissue as determined by mitotic counts. On the other hand, diminution of albumin content of the extracellular fluid stimulates growth, mitosis, and albumin formation by the liver cells. This feedback mechanism is concerned solely with albumin synthesis and growth. Since albumin synthesis occurs only in the liver, there is no relation of this effect to the growth of any other tissues.

A detailed report of the proceedings of this symposium, edited by McElroy and Glass, will be published by the Johns Hopkins Press.

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Weak Interactions

The American Physical Society and the Oak Ridge National Laboratory are sponsoring a Conference on Weak Interactions to be held in Gatlinburg, Tenn., 27–29 October. Although as planned the specialty of the conference will be β-decay, it will also be concerned with π- and μ-decay, as well as strange particle decay. There will be invited speakers at each session to review the subject for the session. Each session will also have contributed papers.

Summaries of contributed papers

should be sent to J. L. Fowler, Oak Ridge National Laboratory; the deadline date is *24 September*. These summaries may be, but do not necessarily have to be, somewhat longer than the 200-word abstract customarily used by the Physical Society, and may also include a few figures somewhat in the style of Letters to the Editor. They should not, however, exceed 600 words in length. Standard 200-word abstracts should also be submitted, for these will be published in the *Bulletin* of the American Physical Society.

Medicine and Biology

The eleventh annual Conference of Electrical Techniques in Medicine and Biology will be held in the Nicollet Hotel, Minneapolis, Minn., 19–21 November, under the sponsorship of the American Institute of Electrical Engineers, the Institute of Radio Engineers, and the Instrument Society of America. The meeting will be chiefly devoted to the use of computers in medicine and biology.

One special session will be on the possibility of applying computers to the theoretical and clinical problems of electrocardiography. Another session will deal with computers in electroencephalography. A third special session will be on the inverse problem of developing computer application on the basis of biological coding, biological transducer designs, and biological logic. The meeting is open to all scientists, engineers, and physicians. Abstracts, 250 words, should be sent before *1 October* to Mr. Robert Erskine, Minneapolis–Honeywell, 2753 4th Ave. S., Minneapolis, Minn.

Mental Health Seminars

"Implications for Psychiatry of Recent Researches on Animal Behavior" will be the general topic of the second International Seminars on Mental Health to be presented in October by the Post-graduate Center for Psychotherapy. Konrad Z. Lorenz, director of the Max Planck Institute of Westphalia, Germany, will address a series of conferences on his recent findings in the field of ethology which will help throw new light on man's behavior.

Lorenz's schedule follows: 10 October, evening panel discussion, "Social Aggression and its Inhibition in Animals: Implications for Psychoanalytic Theory," New York Academy of Medicine; 12–15 October, Josiah Macy, Jr. Foundation conference, Princeton, N.J.; 16 October, research seminar, Yale University School of Medicine, New Haven, Conn.; 20 October, 1958–59 Downey seminars on "Modern Concepts in Psychiatry," Veterans Administration Hospital, Downey,

Ill., Northwestern University Medical School VA Training Program; 21–24 October, Menninger Foundation, Topeka, Kan. (including Menninger Forum, 22 October); 26 October, all-day conference (by invitation only), "Unlearned Communicative Processes Between Animals: Implications for Bio-social Adaptation Theory," Postgraduate Center for Psychotherapy, New York; 30 October, evening panel discussion, "Physiological and Psychological Aspects of Unlearned Motor Patterns: Afferent Control, Spontaneity and Relations to Learning," American Museum of Natural History (cosponsor), New York.

The Postgraduate Center for Psychotherapy has established the International Seminars on Mental Health to present at the Postgraduate Center and throughout the United States distinguished scientists from abroad to introduce new ideas and approaches that may be integrated into American psychiatric theory and practice. The seminars, which are sponsored by the World Federation for Mental Health, are underwritten by a grant from the Samuel Rubin Foundation.

Air Pollution

At a meeting in Washington in August a group of specialists in air pollution control met with Public Health Service officials to discuss plans for the first national conference on air pollution to be held 18–20 November at the Sheraton Park Hotel, Washington, D.C. The plans call for plenary sessions—with addresses by scientists, industrialists, and government officials—and group meetings in which recommendations will be formulated for future action. Subjects to be considered will include effects of air pollution on health, control methods, economic factors, and so forth.

The planning group that met in Washington included the chairmen and cochairmen of six discussion panels: Arie J. Haagen-Smit, Division of Biology, California Institute of Technology, and H. C. McKee, Southwest Research Institute, San Antonio, Tex.; S. L. Hanauer, Department of Air Pollution Control, City of New York, and Leslie Chambers, Los Angeles County Air Pollution Control District; John T. Middleton, Citrus Experiment Station, University of California, and Arthur Crago, American Cyanamid, Brewster, Fla.; Malcolm H. Merrill, California Department of Public Health, and James P. Dixon, Commissioner of the City of Philadelphia; Leslie Silverman, Harvard University School of Public Health, and W. C. L. Hemeon, Hemeon Associates, Pittsburgh, Pa.; Louis C. McCabe, Resources Research, Inc., Washington, D.C., and Harold W. Kennedy, County Counsel of Los Angeles.

Forthcoming Events

October

12–17. American Acad. of Ophthalmology and Otolaryngology, Chicago, Ill. (W. L. Benedict, 100 First Ave. Bldg., Rochester, Minn.)

13–15. Association of American Medical Colleges, 69th annual, Philadelphia, Pa. (W. Darley, AAMC, 2530 Ridge Ave., Evanston, Ill.)

13–15. National Electronics Conf., Chicago, Ill. (L. W. Von Tersch, Michigan State Univ., East Lansing.)

13–16. Society of Exploration Geophysicists, 28th annual intern., San Antonio, Tex. (C. C. Campbell, Box 1536, Tulsa 1, Okla.)

13–17. American Soc. of Civil Engineers, annual conv., New York, N.Y. (W. H. Wisely, ASCE, 33 West 39 St., New York 18.)

14–15. National Acad. of Economics and Political Science, fall annual, Washington, D.C. (D. P. Ray, George Washington Univ., Washington 6.)

15–17. American Ceramics Soc., Glass Div., Bedford, Pa. (C. S. Pearce, 4055 N. High St., Columbus 14, Ohio.)

19–22. Land and Water, Soil Conservation Soc. of America, 13th annual, Asheville, N.C. (H. W. Pritchard, 838 Fifth Ave., Des Moines 14, Iowa.)

19–24. American Soc. of Anesthesiologists, Pittsburgh, Pa. (J. E. Remlinger, 802 Ashland Ave., Wilmette, Ill.)

19–26. Allergology, 3rd intern. cong., Paris, France. (S. M. Feinberg, Medical School, Ward Memorial Building, 303 East Chicago Ave., Chicago, Ill.)

19–26. Medical Hydrology, 21st intern. cong., Madrid, Spain. (Dr. Francon, 55, rue des Mathurins, Paris 8e, France.)

20–21. Rubber and Plastics Instrumentation, natl. symp., Akron, Ohio. (D. R. Davis, General Tire and Rubber Co., Central Research Lab., Akron 9.)

20–22. American Oil Chemists' Soc., fall, Chicago, Ill. (Mrs. L. R. Hawkins, 35 E. Wacker Drive, Chicago 1.)

20–23. American Acad. of Pediatrics. Chicago, Ill. (E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill.)

20–23. American Psychiatric Assoc., Kansas City, Mo. (1700 18 St., NW, Washington 6.)

21. American Soc. of Safety Engineers, annual, Chicago, Ill. (J. B. Johnson, 425 N. Michigan Ave., Chicago 11.)

22–24. American Assoc. of Petroleum Geologists, southwestern, Mineral Wells, Tex. (R. H. Dott, Box 979, Tulsa 1, Okla.)

22–24. Aviation Medicine, 4th annual symp., Santa Monica, Calif. (T. H. Sternberg, UCLA Medical Center, Los Angeles 24, Calif.)

22–26. American Soc. for the Study of Arteriosclerosis, annual, San Francisco, Calif. (O. J. Pollak, P.O. Box 228, Dover, Del.)

23–25. National Soc. of Professional Engineers, San Francisco, Calif. (K. E. Trombley, NSPE, 2029 K St., NE, Washington 6.)

23–25. Rocket Technology and Astronautics, intern., Essen, Germany. (Deutsche Gesellschaft fuer Raketentechnik und Raunfahrt, e.v., Neunsteinerstrasse 19, Stuttgart, Zuffenhausen.)

24–25. International Conference on the Insulin Treatment in Psychiatry, New York, N.Y. (M. Rinkel, 479 Commonwealth Ave., Boston 15, Mass.)

24–25. Taxonomic Consequences of Man's Activities, symp., Mexico, D.F. (H. C. Cutler, Missouri Botanical Garden, St. Louis.)

24–28. American Heart Assoc., San Francisco, Calif. (J. D. Brundage, 44 E. 23 St., New York 10.)

27–28. Child Research in Psychopharmacology, conf., Washington, D.C. (S. Fisher, Psychopharmacology Service Center, Natl. Inst. of Mental Health, Bethesda 14, Md.)

27–28. Plant Physiology, 9th annual research cong., Saskatoon, Saskatchewan, Canada. (D. T. Coupland, Plant Ecology College of Agriculture, Univ. of Saskatchewan, Saskatoon.)

27–29. Radio, Institute of Radio Engineers, fall meeting, Rochester, N.Y. (V. M. Graham, EIA, 11 W. 42 St., N.Y.)

27–29. Weak Interactions, APS conf. (by invitation), Gatlinburg, Tenn. (J. L. Fowler, ORNL, P.O. Box X, Oak Ridge, Tenn.)

27–31. American Inst. of Electrical Engineers, fall general, Pittsburgh, Pa. (N. S. Hibshman, AIEE, 33 W. 39 St., New York 18.)

27–31. American Public Health Assoc., St. Louis, Mo. (B. F. Mattison, 1790 Broadway, New York 19.)

(See issue of 15 August for comprehensive list)