REPORTS

PURE AND APPLIED SCIENCE RESEARCH AT MELLON INSTITUTE, 1939–40

NINETY-ONE industrial fellowships—31 multiple and 60 individual fellowships—have been active in Mellon Institute during its fiscal year, March 1, 1939, to March 1, 1940. These programs of research have employed 167 fellows and 106 fellowship assistants. The institute has expended $1,181,639 in conducting these investigations and comprehensive studies in pure science in this period, during which much new fundamental research has been begun by industrial fellowships and pure science investigation has been considerably expanded. These research projects and their accomplishments are described in the twenty-seventh annual report of the director, Dr. Edward R. Weidlein, to the trustees of the institution.

In the Department of Research in Pure Chemistry investigations of cinchona alkaloids in relation to the chemotherapy of pneumonia have been continued on a wider scale. In the light of the experimental findings of the medical associates working with homologous and isomeric alkyl and hydroxyalkylapocupreine ethers, a systematic study of variously substituted two-and-three-carbon ethers is now in progress, and a series of quaternary salts of hydroxyethylapocupreine has been prepared and tested. While hydroxyethylapocupreine has been in constant medical use, no new clinical experiences have been published since the three-year summary presented last year. In a preliminary way it has been found that the synthetic cinchona derivatives have powerful bactericidal action against organisms of other groups than the pneumococcus. Sixty-one new preparations have been tested against the pneumococcus. The production of hydroxyethylapocupreine on a pilot-plant scale has been continued very successfully, and studies of methods and processing have permitted some simplification. Adequate availability of the drug has been assured for large-scale cooperative clinical investigations already organized.

Chemotherapeutic and immunological approaches to the study of pneumococcal and streptococcal infections have been continued with the aid of Mellon Institute in the Institute of Pathology of the Western Pennsylvania Hospital by a staff of eight. A number of derivatives of sulfanilamide have been examined for their therapeutic value, dosage, and toxicity, and it has been found that all these drugs are at least as effective as sulfanilamide and that certain of them cause in experimental animals the same type of urolithiasis reported in clinical practice. Additional research on the mode of action of the sulfonamide compounds has reinforced the anti-enzymatic theory previously postulated by this group which tends to explain the diversity of the therapeutic coverage of sulfanilamide. Other studies have pertained to the antigenic and serologic relationships of various dissociated bacterial forms in an effort to coordinate these fundamental interrelations with the diverse manifestations of disease in man and animals. The work on factors predisposing to infections of the type encountered in pneumonia and the common cold has been extended.

The nutrition fellowship of the Buhl Foundation has advanced the study of nutritive factors in relation to dental caries. Particular attention has been given to the beneficent effects of fluorine in the partial prevention of tooth decay. The data, derived from rats, indicate that, if there is a deficiency of fluorine at the time of formation of enamel, the caries-resistance of the teeth is lowered. In view of this evidence and the findings of other investigators, it has been urged by fellowship that consideration be given to the possibilities of the mass reduction of dental caries incidence by control of the fluorine content of community water supplies. The toxicity of fluorine must not be forgotten in any measures to alleviate dental caries.

Basic research, a prerequisite of progress in industrial hygiene, has been supported by Air Hygiene Foundation at Harvard School of Public Health, the Saranac Laboratory, University of Pennsylvania and Mellon Institute, where the organization has its headquarters. At Harvard two graduate fellows carry on engineering studies of value to companies associated with the foundation. In turn this arrangement helps train able men for the service of industry and government in the comparatively new field of industrial hygiene. Two broad investigations are sustained by Air Hygiene Foundation at the University of Pennsylvania. One of these researches deals with x-ray and seeks to place diagnostic procedure on a more practical basis for use in industrial plants, as in the physical examinations of large groups of workmen. In the other project at Pennsylvania the actual effect of silica on living cells and tissues is being observed. At Mellon Institute the foundation has a clearing-house for all its day-to-day activities, assisting in the correlation of data indispensable to the advancement of industrial hygiene. For instance, more and more regulation is being exercised by government in the field of occupational health. Obviously it is imperative that employers be kept informed of new laws pertaining to employee health. This work the foundation does for its member companies through its legal committee. The foundation has launched a survey of sick absenteeism among industrial workmen. This report on the high cost of sickness was submitted to

foundation members at their fourth fall meeting late in 1939. On that occasion cost figures were presented to show that "good health is good business"—a translation of industrial health into terms of dollars-and-cents. A forum was held at the meeting which helped clarify the concept that industrial health pays double dividends: first, in dollars and cents; secondly, in improving industrial relations and public good-will, the very basis of business. During 1940 the foundation program will include continuation of the researches mentioned. It will also embrace: (1) Further study of sick absenteeism, looking toward reducing the staggering "hidden" losses which employers and employees suffer from this cause; (2) an industry-wide engineering survey of existing exhaust systems, many of which are now inadequate, for the purpose of assisting member companies to cope with problems in this field; and (3) expansion of the foundation's industrial hygiene surveys which are made for member companies. A special bulletin on the subject of organic solvents as they relate to the problem of industrial health will soon be published. Each month the foundation issues a digest of the current literature on industrial hygiene.

The pearl fellowship continued to seek by chemical and physical methods additional data on pearls and mother-of-pearl. X-ray powder photograms of natural pearl aragonite and natural crystalline aragonite have shown that the two forms of orthorhombic calcium carbonate are fundamentally identical in structure. For quick, accurate determination, in which many pearls can be examined at one time, the x-ray fluorescent method is exceedingly useful. The cause of the fluorescence of cultured and fresh-water pearls has been found to lie in the chemical composition.

As a result of investigations carried out by the chain fellowship, the donor has been able to announce the development of several types of arc welding electrodes formerly not included among its products. Recognizing the potentialities of powder metallurgy and the need in this field for a high quality iron powder, methods have been perfected by another fellowship for the preparation of electrolytic iron powder. Since 1934 sub-commercial activities have been carried on progressively at the donor's plant, and as a result many industrial applications for this pure iron powder have been established and early commercialization of the procedure on a large scale is expected. During the second year of the acid recovery fellowship the survey being made of the waste pickle liquor problem has been extended to include studies of twelve methods of disposal without by-product recovery and forty-two processes for the treatment of the liquor with recovery of by-products. Marked improvements in three older processes and laboratory investigations of two newly proposed processes have been reported during the year.

The multiple fellowship on organic synthesis is in its twenty-sixth year of research on problems pertaining to the preparation and use of synthetic organic chemicals. During the year 1939–1940 the fellowship has followed its policy of developing new products on an experimental scale and studying their possible applications in industry. New uses for products already available have also been investigated in an effort to broaden their markets. Work was continued on problems pertaining to hydraulic fluids, gas purification and dehydration, alkyl silicate coatings, improved wood-stain solvents, evaluation of and improvements in wetting and dispersing agents, water-soluble lubricants, volatile inhibitors, and new amine products. The chemical hygiene fellowship has obtained during its first two years experimental data on some of the physiological properties of over 100 synthetic organic compounds, most of which had not previously been studied pharmacologically. It is the aim of the fellowship to detect any hazards in handling these compounds, so that adequate protection of workmen can be planned in advance of exposure. Its further object is to determine the safety of suggested applications of the compounds, from studies of their physiological properties. The greatest need for facts is in the field of vapor effects.

In 1939 the fellowship on meat merchandising described a new and rapid method for the tendering of edible flesh. Following the completion of consumer acceptance tests in Pittsburgh, during which a series of eight stores distributed the novel Tenderay beef to their customers for periods ranging from three to eight months, a commercial plant was installed in Cleveland, having a weekly capacity of 60,000 pounds of beef and supplying 78 stores. From a store average of about 600 pounds per week there has been an increase, in ten months, to approximately 1,000 pounds per week, a gain of over 60 per cent. In order to care for all the stores operating in the Cleveland district, the plant has been enlarged to provide approximately 110,000 pounds per week. A second company plant was completed in Cincinnati during February, and plants in Chicago, Columbus and Detroit are ready to begin operations. An independent packer on the eastern seaboard started production of a Tenderay plant in February, another firm has a plant under construction in the Middle West, and plans are being drawn for four additional plants. It is estimated that by June 1 plants in operation will be tendering three million pounds per week. The multiple fellowship on food varieties perfected recipes for and brought to the stage of commercial production three new desserts in the donor's line of junior foods. Another new variety in the strained foods line was developed and put into production. Research on the calcium availability of

strained foods has proceeded far enough to indicate marked differences in the utility of the calcium contained in them. The fellowship has cooperated in the development of new uses in the food field for edible cereal cellulose.

The multiple fellowship on mineral products continued work on by-product silica from plate-glass manufacture. The practicability of the use of Garspar, one of the products of fellowship research, to replace coarse sand and cullet in a glass batch was proved. On the fellowship on optical glass research on the durability of experimental glasses has been made the basis for the development of improved optical glass. The study of chemical reactions that can take place between a glass surface and different reagents has eventuated in the selection of methods by which the outer polished surface of a lens may be changed without affecting the mass of the glass.

On the multiple fellowship on sulfur a number of new projects have been studied in the laboratory in preparation for commercial introduction. Two novel materials, evolved through the reaction of sulfur with organic compounds, are now receiving pilot plant-scale development. The physical nature of sulfur cements has been constantly under study and recently methods of evaluating sulfur cements have been reviewed in assistance to the American Society for Testing Materials. For the multiple fellowship on protected metals the cupriferous cement Hubbellite has shown good performance for floor surfaces. The outstanding property of this cement results from the oligodynamic action of the copper compound in it. Hubbellite provides simply by washing a self-sanitizing floor that does not depend upon the use of disinfectants. The same fellowship has devised a fireproofing system, involving the use of a new plaster composition (expanded vermiculite aggregate and gypsum), by means of which fire-resistive periods have been attained that are far in excess of those heretofore possible wtih comparable weights and thicknesses of accepted materials.

In research by the multiple fellowship on anthracite greenhouse and field tests have shown the value of Pennsylvania anthracite ashes for soil-amendment purposes. Work has also continued on the uses of anthracite ashes and colliery refuse for industrial purposes, especially in the fields of building materials and thermal insulation. During the past year the fellowship published a full testing procedure for water heaters fired with solid fuels, and completed an engineering study of the design of anthracite bins for both automatic and hand-fired appliances. The multiple fellowship on petroleum refining has been pursuing work on examining petroleum oils by micro-methods. A thoroughgoing fundamental study of the constitution of certain lubricating oils and a previously initiated investigation on determining the physical properties of mineral and vegetable waxes have been continued, as also have been studies of refining methods for gasoline and of procedures for protecting petroleum products against harmful oxidation. The prototype engine testing work, aimed at a better knowledge of combustion engine deposits, has been conducted actively. It has been possible to establish clearly some of the fundamentals of the phenomenon known as oil-ring clogging and to point out its meaning in connection with engine-oil consumption. The fellowship on watch technology has progressed toward the development of the ideal watch oil. A large number of compounds have been synthesized, and properties vital to the quality of a watch and instrument lubricant have been determined. The ninth and tenth years of the safety fuse fellowship have been devoted to basic research on the waterproofings used on fuses with the object of improving the present products and of obtaining accurate knowledge of the domestic supply of petroleum asphalts. The properties of asphalts made from crudes produced in major American oil fields have been determined; several of these asphalts yield satisfactory waterproofing coatings.

The program of investigation on new uses for cotton and its by-products, established by the Cotton Research Foundation in 1937, has been followed creatively. The subjects of research include not only problems of immediate practical importance, but also long-range fundamental studies which will contribute basic information on the chemistry and physics of the various products derived from the cotton plant. Eight scientists are engaged in this work at the institute, and four universiy research grants are in operation. During the year the fellowship has benefited from the sponsorship of the National Cotton Council, for which the Cotton Research Foundation is now serving as the technical agency. Researches on the physical and mechanical properties of the cotton fiber are being prosecuted constantly. The knowledge that has been obtained in this basic study is being applied successfully to practical problems, particularly in the use of cotton in tire cords and similar industrial products. The possibility of employing lower grades of lint, linters, and hull fiber in the manufacture of finer grades of paper is being accorded research. Contributions have stimulated considerable interest in the wider utilization of hulls, an abundant cotton by-product. Cottonseed proteins, particularly the globulin, have received much attention by the fellowship.

Thirteen fellowships started their researches during the fiscal year 1939–40: Concrete, Constructional Resins, Gartex, Gas By-products, Gas Purification, Graphite, Metalworking, Oil Cleaner, Sterilamp, Suture, Tar Distillation, Tar Synthetics, and Tar Treatment. Another new fellowship (Petrolatum) began operation in March. Six fellowships concluded

their investigations: Calgonizing, Chromium, Cotton Yarns, Draft, Slag, and Tar Acids.

During the calendar year 1939, 7 bulletins, 26 research papers and 54 other articles came from the institute. Thirty-two United States patents and 35 foreign patents on fellowship inventions proceeded to issue. The total publications for the 29 years ended December 31, 1939, have been 18 books, 140 bulletins, and 1,734 journal contributions; 755 United States patents and 811 foreign patents were granted during the same period. Bulletin No. 4 in the institute's bibliographic series, which was published in the fall of 1939, lists the books, bulletins, journal contributions, and United States and foreign patents of the institutional membership, 1911–1938, inclusive.

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SPECIAL ARTICLES

FACTORS AFFECTING THE INSULIN CONTENT OF PANCREAS

IN 1939 Best, Haist and Ridout[1] reported that fasting or feeding fat produced a fall in the insulin content of pancreas of rats and that the subsequent provision of a balanced ration led to the restoration of the insulin level to normal values.

Similar experiments have been carried out in hypophysectomized rats. The insulin content of the pancreases of rats 26–66 days following the removal of the pituitary glands was slightly less than that of intact animals fed *ad libitum,* but did not significantly differ from that of control animals receiving the same caloric intake. The average values obtained were 20.4 units of insulin per group of 10 rats for the hypophysectomized animals and 20.1 units of insulin per group of 10 rats for the "paired-fed" controls.

Feeding fat for one week to hypophysectomized rats led to a fall in the insulin content of pancreas in those which survived. This decrease was slightly greater than that of the control group. Feeding a balanced diet for 7 days to hypophysectomized rats previously fed fat for one week led to the restoration of the insulin content of pancreas to normal values.

These experiments demonstrate that the lowering of the insulin content of pancreas as a result of feeding fat and the restoration to normal as a result of feeding a balanced diet can be obtained in hypophysectomized rats. It is suggested that the production and liberation of insulin, according to the need for it, can be regulated by the pancreas in the absence of the pituitary gland.

We have recently found that partial pancreatectomy in dogs produces no change in the insulin content of the pancreas unless enough pancreatic tissue has been removed to cause diabetes. In this case the insulin content shows a marked decrease.

The daily administration of insulin to fasted rats decreases the insulin content of the pancreas to levels appreciably lower than those secured by fasting or fat feeding alone. These findings, considered in conjunction with histological results, suggest that the β cells of the islets of Langerhans are "rested" by fat feeding, fasting and insulin administration.

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[1] C. H. Best, R. E. Haist and J. H. Ridout, *Jour. Physiol.,* 97: 107, 1939.

TOXICITY OF EXTRACTS OF THE POSTPARTUM RABBIT UTERUS[1]

IT is unusual that crude saline extracts of a tissue are toxic on administration to animals of the same species. Extracts of the postpartum rabbit uterus, however, taken one to fifteen hours after delivery, were found to be extremely toxic to normal rabbits.

In some unpublished data obtained in this laboratory, it was observed that the uterus of the pregnant rabbit becomes markedly edematous two to three days before delivery, and that this edema slowly recedes during the next six to eight postpartum. Four different, crude, saline extracts were made from such edematous uteri, taken within fifteen hours after delivery. These were prepared so that 1 cc of solution represented one-half gram of tissue. They were then injected into a total of 15 animals. Death resulted within 2 minutes in 12 animals on intravenous injection of 8 cc or less. Of the remaining two animals, one survived a 10 cc injection but succumbed on the following day after administration of an additional 1 cc. The second animal survived a 10 cc injection but also died on the next day after being given an additional 4 cc.

These extracts were also toxic when administered intraperitoneally, although a large dose was required and a longer time elapsed before death occurred. Three animals injected by this route were given three daily doses of 10 cc and each succumbed after receiving a total of 30 cc.

Extracts prepared in the same way from uteri of non-pregnant animals were not toxic. Four such extracts were injected intravenously in daily doses of 10 cc until two animals each received a total of 50 cc, a

[1] Aided by a research grant from the University of California.