

Pediatric Specialist Joins NIAMD Staff

Dr. Paul A. di Sant'Agnese, a specialist in the diseases of childhood, has been appointed to the staff of NIAMD, where he will direct and plan the clinical and laboratory research in cystic fibrosis, celiac diseases, and allied disorders. He assumed his new duties January 1.

Dr. di Sant'Agnese has been a prominent investigator in the field of childhood diseases. His work has received international recognition. His discovery that children with cystic fibrosis excrete excessive amounts of salt in their perspiration resulted in a "sweat test" now widely used in diagnosis of this disorder. He also did part of the early work on the immunization of infants against diphtheria, whooping cough and tetanus.



Dr. di Sant'Agnese

In May 1959 the National Cystic Fibrosis Foundation awarded him a plaque in recognition of his work in combating the disease, which is now recognized as the most common chronic disease of children.

(See PEDIATRICS, Page 2)



1960 Finds NIH Full of Wishes

THE arrival of the new year, the traditional time for taking stock of one's own and the world's situation and for making resolutions big or small, found some NIH people willing to tell the NIH RECORD what they hope for in 1960.

Nurses in the Cancer Nursing Service, CC, are unanimous in their wish for a cure for cancer. Jay Moleski, Head Nurse, adds, "... and more specifically, a cure for acute leukemia." Married just last month, Jay also wishes, "A long and happy married life."

Louise Burgess, Chief of the Service, wants more girls to choose careers in nursing and then join the CC staff, and Assistant Chief Ruth Metka tops them with, "Personally, I'd like to be in Alaska this year!"

Another travel wish was voiced by Sherry Haimes, Grants Assistant in the Endocrinology Study Section, DRG, who would like to make a visit to one of the NIH grants project sites in Paris.

Dr. Stuart M. Sessoms, Chief, Cancer Chemotherapy National

Service Center, NCI, wants to travel, too, but not very far. He says, "My wish is for some reasonable assurance that those of us in the 'Robin outpost' in Silver Spring will move back to NIH headquarters within the next two years."

Families were the main concern of several people, including Dr. L. Edgar Lee, Executive Secretary of the Pathology Training Committee, DGMS. He wishes, quite simply, for an offspring.

Since Ruth G. Gray, Office of the Associate Director, NIDR, is already a parent, she wishes for "a flexible time clock for working mothers, and the eleven-month school year for children."

Martin Geter, Plant Engineering Branch, DRS, wants world peace and understanding. Several others expressed personal preferences for the next Presidential election.

Jack Robinson, of the NIAMD Information Office, would like to find scientists who write like reporters, and reporters who think like scientists.

Dr. Seymour S. Kety, Chief, Laboratory of Clinical Science, NIMH, says, "My wish is that somebody, here or elsewhere, would discover a valid biological abnormality characteristic of at least some forms of schizophrenia. Such a finding would provide a bridge across the discouragingly empty hiatus between basic biochemistry and physiology and the problem of the hundreds of thousands of patients in our mental institutions suffering from diseases whose causes remain one of the great medical mysteries of today."

Dr. Hueper Wins Rosenthal Award For Cancer Work

Dr. Wilhelm C. Hueper, Head, Environmental Cancer Section, NCI, on December 27 received the Anne Frankel Rosenthal Memorial Award for Cancer Research for his pioneering studies in the environmental causes of cancer.

Administered by the American Association for the Advancement of Science, the award consists of \$1000 and is provided by the Richard and Hinda Rosenthal



Dr. W. C. Hueper

Foundation for outstanding accomplishment in the field of cancer research. It was presented to Dr. Hueper during the annual A.A.A.S. meetings in Chicago.

The award was given two years ago to Dr. Roy Hertz, Chief, Endocrinology Branch, NCI.

Dr. Hueper received his medical education as a pathologist in his native Germany and came to the U. S. in 1923. He joined NIH in 1948 when the Environmental Cancer Section of NCI was created.

Dr. Hueper's major interest is in the histopathology, cytology, causation, and prevention of cancer. Much of his scientific research has been in the area of experimental cancer, with special emphasis on environmental and occupational factors known or suspected of causing cancer. His research has also included the etiology and histology of arteriosclerosis, toxicology and pharmaceuticals, parathyroid hormone effects, and blood diseases.

Annual CU Meeting Set

The NIH Federal Credit Union will hold its annual meeting on Wednesday, January 13, at 12:30 p.m. in the CC auditorium.

The meeting agenda will include the annual reports of officers and committees, election of directors and credit committee members, and declaration of the dividend.

Institutes Sponsor Monthly Information Meetings

The NIH Information Officers' staff meeting, held weekly, is being sponsored the first meeting of each month by Institute and Division information offices.

The first such meeting, held in November, was conducted by the NCI Office of Information and Publications. The discussion topic was "Responsibility for Public Understanding of Research and Related Programs of NIH." Panel members were Dr. Robert H. Felix, Director, NIMH; Dr. Howard B. Andervont, Chief, Laboratory of Biology, NCI; and Mrs. Ruth Dudley, Information Officer, NINDB.

The NHI Heart Information Center sponsored the December

meeting. In order to acquaint Information Officers more fully with some important resources for special information, the following speakers described the work of their organizations: Dr. Stella L. Deignan, Director, Bio-Sciences Information Exchange; William J. Holliman, Jr., Statistics and Analysis Branch, DRG; and Col. Frank B. Rogers, Director, National Library of Medicine.

On January 7 the NIAID Information Office has arranged to have Ernest G. Moore, Director, Agricultural Research Service Information Division, USDA, discuss the information program of his organization.

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Dr. Shelokov Receives Guatemalan Award

Dr. Alexis Shelokov, Director of the Middle America Research Unit, Laboratory of Tropical Virology, NIAID, recently received the Rodolfo Robles Award in recognition of advice and personal assistance given to the Republic of Guatemala during an outbreak of poliomyelitis.

The award for excellence in the field of medicine was presented to Dr. Shelokov by Dr. Eduardo Rodriguez Rouanet, Director of Pediatrics of Guatemala, who traveled to Panama to make the presentation for the Guatemalan Minister of Health.

Dr. Shelokov, a Commissioned Officer in the Public Health Service now on duty in Panama, has forwarded the medal to the U. S. State Department. When he retires from the Commissioned Corps, the State Department will return it to him.



Dr. Alexis Shelokov (left) receives the Rodolfo Robles Award from Dr. Eduardo Rodriguez Rouanet, Director of Pediatrics of the Republic of Guatemala.

Dr. J. A. Scigliano Appointed to CCNSC

Dr. John A. Scigliano, Chief of the Clinical Center Pharmaceutical Development Service since February 1953, has been assigned to a new position as research pharmacist and chemist in the Chemistry Section, Cancer Chemotherapy National Service Center.

Dr. Scigliano will be responsible for the procurement of drugs in the CCNSC program, and particularly for the research and development of finished dosage forms for the clinical drug evaluation program. He is a Senior Pharmacist, PHS. The transfer was effective January 4.

An active participant in many employee functions, Dr. Scigliano served last year as president of the NIH Recreation and Welfare Association.

PEDIATRICS

(Continued from Page 1)

Since 1951 Dr. di Sant'Agnese has been in charge of clinical and research programs in cystic fibrosis at Babies and Presbyterian Hospitals in New York City, and Assistant Professor of Pediatrics at Columbia University College of Physicians and Surgeons. From 1944 to 1953 he was chief of the pediatric division of Vanderbilt Clinic in New York.

After interning at the Willard Parker Hospital in New York, Dr. di Sant'Agnese served as assistant resident and later as chief resident of the New York Post Graduate Hospital. He received his M.D. degree at the University of Rome Medical School, and Sc.D. degree at Columbia University.

Dr. di Sant'Agnese will also serve as Clinical Professor of Pediatrics at Georgetown University Medical School, and as Director of William F. Green Cystic Fibrosis Clinic, Children's Hospital, D. C.

Dr. R. M. Wilder Dies; First NIAMD Director

Dr. Russell Morse Wilder, the first director of NIAMD from January 1951 to June 1953, and emeritus member of the staff of the Mayo Clinic, died in Rochester, Minn., on December 15 of a cerebral hemorrhage. He was 74.

A specialist in the diseases of metabolism and nutrition, Dr. Wilder made major contributions to the literature and scientific knowledge of human dietary requirements. He made several surveys on the nutrition status of human populations, wrote nine editions of "A Primer for Diabetic Patients," and contributed to the very important pioneer work in the enrichment of bread and flour.

The National Vitamin Foundation created the Russell M. Wilder Fellowship in 1954 in honor of his more than 40 years of service to medicine and public health.

Dr. Wilder's research earned him widespread recognition and honor. In August 1959 he was made an honorary member of the American Dietetic Association. He received the Joseph Goldberger Award in Clinical Nutrition in 1954 from the American Medical Association. He was a fellow of the American College of Physicians, the American Medical Association, past president of the American Diabetes Association, and held memberships in major scientific organizations.

He is survived by his wife, Mrs. Lucy Wilder, and two sons, Russell, Jr., and Thomas.



Dr. R. M. Wilder

Chemotherapy Meeting Sponsored by CCNSC

The Cancer Chemotherapy National Service Center, NCI, sponsored a conference in Washington, D. C., in November attended by more than 630 clinicians and other scientists who are participating in the cancer chemotherapy research program.

Numerous speakers and members of discussion panels presented reports on the results of chemotherapy research in the laboratory and the clinic. The subjects included the status of laboratory and clinical studies of various classes of anticancer agents, such as the alkylating agents, steroids, and antibiotics; and the chemotherapy of acute and chronic leukemia, Hodgkin's disease, breast cancer, and a number of other malignancies.

Speakers Agree

In the main, the speakers agreed that there is a pressing need for better correlation between the results of drug testing in animals and clinical trials, but that additional statistical evaluation of screening procedures can probably overcome this difficulty. The suggestion was made that additional statistical information for this purpose might be obtained through the use of a broader spectrum of experimental tumors and through the modification of the design of clinical studies to provide suitable data for interpretation.

Other Steps Cited

Dr. Sidney Farber, other speakers, and members of the audience pointed out the accomplishments of this program in addition to those in developing drugs to be used in man. Some of these are:

- Training large numbers of young clinicians to carry out statistically designed clinical studies.
- Developing close working relationships among clinicians, statisticians, and scientists from many other disciplines.
- Acquiring basic data concerning the natural course of cancer, and obtaining definitive data on end results of current methods of treatment.

by his wife, Helen Barley, who resides in Silver Spring, and by his mother, Mrs. Melda Barley of Martinsburg, W. Va., as well as two brothers and two sisters.

Donald E. Medley, 39, a guard in the Plant Safety Branch, OAM, died suddenly, December 11, following a brief illness. A resident of Hyattsville, he had been employed in the Guard Section at NIH for over four years. Mr. Medley is survived by his wife, Anna L. Medley, of the home address, and by two sisters, Isabel M. and Bettie Jean, of Miami, Fla.

OBITUARIES

Arthur Washington, 64, died November 27 at the Newton D. Baker VA Hospital in Martinsburg, W. Va. He was a business services laborer in the Office Services Branch, OAM.

A resident of the District of Columbia, Mr. Washington had been with NIH since 1941. He is survived by his wife, Nancy Lee, who is employed at NIH in the Housekeeping Section, CC.

Charles R. Barley, 46, died in the Washington Hospital Center, December 13, after a brief illness. A reports and records analyst in the Office of the Chief, Statistics and Reports Branch, DRG, he had been employed at NIH since 1947.

Mr. Barley was a native of Bakers Summit, Pa. He is survived

Science Section

This two-page section is devoted chiefly to summaries of research findings that have been reported by scientists of the National Institutes of Health. This section is prepared by the Office of Research Information, NIH, and the Information Offices of the Institutes and Divisions.



Dr. Elsworth R. Buskirk, NIAMD, inspects a Weddell seal in Antarctica.

NIH Scientists Visit Alaska, Antarctica on Survey Trips

Research survey missions took National Institutes of Health scientists to opposite ends of the earth in recent weeks. National Institute of Arthritis and Metabolic Diseases scientists, Drs. G. Donald Whedon, Assistant Director, and Heinz Specht, Chief of the Laboratory of Physical Biology, visited Anchorage and Fairbanks, Alaska, and Dr. Elsworth R. Buskirk, physiologist in the Metabolic Diseases Branch spent ten days on the Antarctic continent, all gaining a firsthand knowledge of research programs being carried on in extreme cold weather areas.

Visit Installations

Dr. Buskirk, with Dr. Dorland J. Davis, Associate Director in Charge of Research, National Institute of Allergy and Infectious Diseases, were the NIH members of a ten-man group invited to the Antarctic by the National Science Foundation.

The group visited research installations where they reviewed the activities of the Antarctic Research Program of the Foundation and provided advice to the responsible investigators. Team members familiarized themselves with Ant-

arctic research as currently sponsored by the National Science Foundation and with the U. S. Navy's supply problems peculiar to the area.

The trip also was planned to enable the group to bring back knowledge of the problems faced in such research for the benefit of other professional investigators of cold physiology and immunology in the United States.

View Research Facilities

Drs. Whedon and Specht visited the Bureau of State Services' Arctic Health Research Center at Anchorage to view environmental physiology research facilities there. Since problems of environmental medicine are felt to be of increasing importance as world population progressively moves into colder climates, efforts are being made to learn what future developments in the field of physiological research on the effects of cold are most likely and should be pursued.

Drs. Whedon and Specht also visited the Aero-Medical Laboratory at Ladd Air Force Base near Fairbanks, and the Geophysical Institute at the University of Alaska, College, Alaska, potential NIH collaborators.

Octulose, First Eight-Carbon Sugar In Nature, Discovered by NIAMD

The first eight-carbon sugar to be found in nature has been discovered by scientists at the National Institute of Arthritis and Metabolic Diseases. The rare sugar was isolated by Drs. A. J. Charlson and Nelson K. Richtmyer, of NIAMD's Laboratory of Chemistry, and has been found in both the avocado and the sedum plant.

Two of the most common sugars occurring in nature are glucose and fructose, which contain six carbon atoms in each molecule. Only two seven-carbon keto sugars, or heptuloses, are known to exist, and until now they were thought to be the highest carbon sugars in nature. Co-discoverer of one of these heptuloses was Dr. C. S. Hudson, chief of NIAMD's Laboratory of Chemistry from 1929 to 1951.

Avocados Analyzed

Isolation of the eight-carbon sugar (octulose) by the NIAMD scientists resulted from a study of California avocados. These fruits were being analyzed for polysaccharide content by Dr. Charlson, a visiting scientist from South Africa, when he noticed an unusual cherry spot appearing briefly on the paper chromatograms used in the analysis. It was this observation that first indicated the presence of the rare sugar. Pulp from one hundred avocados was then collected and thoroughly fractionated, and yielded approximately one gram of the octulose.

The NIAMD investigators then turned to the sedum plant and were able to isolate an octulose from this source also. They chose

the sedum because, like the avocado, it was known to contain a seven-carbon sugar and thus might also contain sugars of even higher carbon content. Almost 400 pounds of the plant were fractionated. They yielded 16 one-hundredths of a gram of the eight-carbon sugar. Analysis of the two octuloses showed that they were identical, and the new-found sugar was given the chemical name *D-glycero-D-manno-octulose*.

Dr. Horecker Contributes

At the moment, one can only speculate about the biological significance of a sugar with such high carbon content. After the seven-carbon sugars were discovered in 1917, they remained laboratory curiosities for many years. They were suddenly brought into prominence several years ago by the work of Dr. Bernard Horecker, also of NIAMD, who found an enzyme in rat liver that could synthesize one of the heptuloses, and showed a heptulose to be a vital link in the important oxidative or alternate pathway of glucose metabolism. Since then, heptulose has been isolated from beef liver and from almost all plants, where it participates in the early stages of photosynthesis. What role octulose may play in plant and animal metabolism remains to be determined.

The NIAMD scientists presented their finding in part at the September meeting of the American Chemical Society and also published a preliminary communication in the *Journal of the American Chemical Society*.



Dr. Dorland J. Davis, NIAID, beside hut used by Capt. R. F. Scott in 1902.

New Drug Increases Survival Time of Mice With Leukemia

Laboratory tests of a new alkylating agent, cyclophosphamide, have shown that it is markedly effective in prolonging survival in mice with advanced L1210 leukemia. Dr. Montague Lane, National Cancer Institute's General Medicine Branch, has reported that cyclophosphamide produced up to 200 percent increase in median survival beyond that of untreated, control animals.

Cyclophosphamide [N,N-bis-(beta-chloroethyl)-N', O-propylene phosphoric acid ester diamide] is a member of the class of compounds known as "nitrogen mustards." It was developed in the laboratories of Asta-Werke, A. G., West Germany, in 1957, and its synthesis was reported in the scientific literature by Arnold and Borseaux in 1958. The effectiveness of the compound against animal tumors was reported in 1958 in a series of papers by Arnold, Borseaux, and Brock.

Initial clinical investigations were conducted at the University of Marburg, Duisberg, and Kiel; and preliminary reports on the usefulness of the drug as an anticancer agent were published in the German literature in 1958 by Gross and Lambers, and others. The compound is known as B-518 in Europe, and is sold there by Asta-Werke under the name of Endoxan.

In this country, it is marketed as Cytozan by Mead Johnson and

Company, Evansville, Ind. Within the past few weeks, Mead Johnson has distributed technical information about cyclophosphamide to physicians throughout the country. The compound is being studied under the program of the Cancer Chemotherapy National Service Center and in the intramural research program of the National Cancer Institute.

In the present study, the drug was most effective when given once a week beginning 5 or 7 days after the tumor was implanted in the test animal. Several mice were alive 35 days after tumor implantation; untreated mice had a median survival of 9 to 10 days.

The drug was equally effective when administered by oral, subcutaneous, or intraperitoneal route. The optimum dose for oral treatment was higher than for either parenteral route. Toxicity was in general similar to that produced by nitrogen mustard.

Cyclophosphamide was much more effective than the antifolate agent, methotrexate, or the alkylating agent, nitrogen mustard, in prolonging the survival of leukemic mice when the optimum dosage schedule for each agent was used. A strain of leukemia resistant to 6-mercaptopurine was as susceptible to cyclophosphamide as the original strain. The study is reported in the *Journal of the National Cancer Institute*.

Dental Caries in Rats Seen Infectious and Transmissible

Studies which show dental caries in laboratory animals to be an infectious and transmissible disease involving a penicillin-sensitive flora were reported by Dr. Paul H. Keyes, of the National Institute of Dental Research, at the Greater New York Dental Society.

The caries resistance-susceptibility phenomenon in convention-

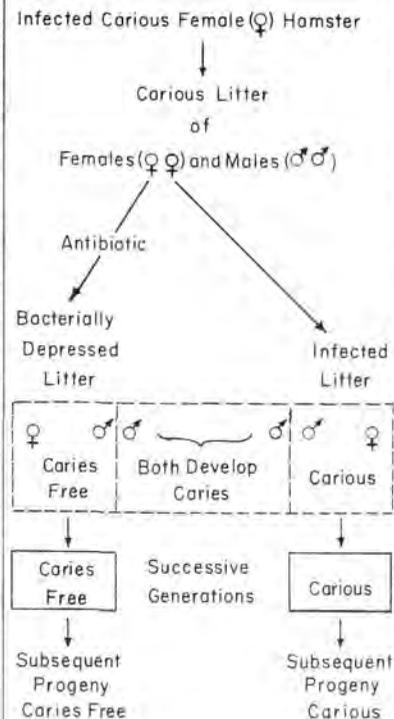
al laboratory animals has until recently been attributed primarily to genetic factors and to systemic developmental effects presumably induced by diet and nutrition.

In a series of studies on the nature of dental caries in hamsters and rats (O-M), Dr. Keyes, Laboratory of Histology and Pathology, has demonstrated that a penicillin-sensitive bacterial flora may be of equal or greater pathologic significance in the induction of this disease.

It now appears that the source of the caries producing microbial flora in young animals is from the alimentary tract of the mother, and that animals lacking this flora may acquire it by cross-infection contact with caries active animals.

However, the cariogenic flora, while it can be transmitted between members of the same strains, is not ubiquitous in the general laboratory environment, and may in fact require considerable time to become established at pathogenic levels.

Work now in progress suggests that there may be limitations either to the extent the flora of one species can be transmitted to another, or to the degree it will be pathogenic if transmitted. This observation may explain, in part, why previous attempts to induce caries in laboratory animals by the inoculation of non-indigenous strains of bacteria have failed.



Asian Flu in Alaska Gives Opportunity for Valuable Observations

Outbreaks of Asian influenza on St. Paul Island and St. Lawrence Island in the Bering Sea were investigated by scientists of the Arctic Health Research Center, Alaska Department of Health, and National Institute of Allergy and Infectious Diseases' Rocky Mountain Laboratory, Hamilton, Montana. Each outbreak arose from a single introduction of virus, affording an unusual opportunity for identifying the precise time limits of virus activity in each community.

The populations of each of these two islands experienced outbreaks of respiratory disease during the fall of 1957. In each instance it was possible to identify the source of infection.

The outbreaks were explosive in character and lasted for a period of only three weeks, at which time all susceptible individuals had become infected. Eighty-two percent of residents on St. Paul Is-

land and 87 percent of residents on St. Lawrence Island developed symptoms characteristic of influenza.

These are unusual communities in that there is very close contact between households during the individuals' various activities, which probably accounts for the rapid and wide distribution of Asian influenza virus.

Antibody surveys of serums collected in the areas indicated that there had been no previous experience with swine influenza virus, but there was evidence that there had been widespread infection due to both influenza A and A-prime virus in the past. Apparently morbidity from the Asian influenza outbreak was not affected by antibodies present from previous influenza infections.

This study again emphasizes the information that can be obtained from studies of infectious diseases in remote communities where it is possible to investigate outbreaks essentially unassociated with other illnesses. This study by Dr. Robert N. Philip and associates of the NIAID Rocky Mountain Laboratory was published in *Public Health Reports*.

Relate Social Class To Parental Values

In their investigations of the relation between social class and parental values and the exercise of parental authority, Dr. Melvin L. Kohn of the Laboratory of Socio-Environmental Studies and Dr. John A. Clausen, Chief of that Laboratory, National Institute of Mental Health, found significant differences between the ways in which working-class and middle-class parents attempt to shape the character of their children.

Working-class parents tended to emphasize the importance of obedience, conformity, and what were taken to be "middle-class values" a generation ago. Middle-class parents tended to stress the development of responsibility, and the importance of happiness and creativity. The parents all had a child aged 10-11 and in the fifth grade at school.

The investigators also found that the conditions under which middle- and working-class parents punish their pre-adolescent children physically, or refrain from doing so, appear to be quite different. Work-

ing-class parents are more likely to respond in terms of the immediate consequences of the child's actions, middle-class parents in terms of their interpretation of the child's intent in acting as he does.

This reflects differences in parents' values: Working-class parents value for their children qualities that assure respectability; desirable behavior consists essentially of not violating proscriptions. Middle-class parents value the child's development of internalized standards of conduct; desirable behavior consists essentially of acting according to the dictates of one's own principles. The first necessarily focuses on the act itself, the second on the actor's intent.

In a related study, it was found that the father-son relationship is much closer and warmer in the middle-class family than it is in the working-class family. All of the above differential factors are being studied in terms of the relationship between social status and rates of mental illness. The investigators have reported their findings in *The American Journal of Sociology* and *The American Sociological Review*.