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PROGRESS REPORT ON RESEARCH AND TRAINING CENTERS IN IMMUNOLOGY IN THE DEVELOPING COUNTRIES

(Item 7 of the Agenda)

PROGRESS REPORT ON
RESEARCH AND TRAINING CENTERS IN IMMUNOLOGY
IN THE DEVELOPING COUNTRIES

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In our highly developed technological society, the capacity for independent creative scientific work is not only essential to the economic growth and welfare of individual countries but is also rapidly becoming a sine qua non of true political independence. A country that does not have the ability to carry on its own scientific research must rely on outside help for the solution of basic problems related to the welfare of its people and is thus subject to outside influences and controls that may prove no less restrictive than the economic or political controls of years past. Inasmuch as no nation, no matter how powerful or wealthy, has or can have a monopoly on creative scientific research, and since the results of basic research in most fields are published and become freely available, every country that has the potential for research can--and should--make use of it for its own purposes. Similarly, new discoveries, from whatever source, enter the pool of human

knowledge, and the contributions of a small or developing country may equally well be of value even for the most advanced and powerful nations. In this sense, countries doing even a small amount of independent scientific research become partners in the family of nations, while those unable to do such work must continue to rely on outside aid. There is little doubt that as years go by the need for all nations to join together in the creative scientific endeavor will become more acute.

The World Health Organization naturally cannot deal with the needs of the developing countries in all areas of creative research. However, in the fields of immunology and immunochemistry the enormously rapid advances over the past 25 years have had particularly significant implications at the international level. Accordingly, on the basis of studies by five scientific groups carried out in 1962 (1), an Immunology Unit was established at WHO in 1963 under Drs. Howard C. Goodman and Zdenek Trnka. One of the major tasks of this unit has been to set up research and training centers in immunology in the developing countries. After preliminary visits, centers were set up in Ibadan, Nigeria; São Paulo, Brazil; Mexico City, Mexico; and Singapore. It is planned that these centers will serve as nuclei for the work being done in these fields in their respective regions of the world. A fifth center at Lausanne is intended to function as a coordinating base for the other four (2, 3).

The centers have the following aims: (1) to expedite and assist persons engaged in scientific research in immunology and immunochemistry in the corresponding geographical areas; (2) to bring about increased contact between scientists in these areas of the world with workers in Europe, North America, and Australia; (3) to encourage new research on problems of special importance to these areas and to aid in the planning of such programs; (4) to set up training courses

in immunology and immunochemistry for promising scientists and to produce a core of highly creative immunologists; and (5) to provide each region with the facilities that are necessary for carrying on first-rate scientific research in immunology and immunochemistry.

The immediate advantages of the centers are the following: (1) The program is carried on in the regions in which the individuals are needed, thus helping to reduce losses from migration. (2) The needs of the center for materials, equipment, library facilities and the like are taken care of on a continuing basis, so that research can be carried on without delays and complications. All too frequently, gifted fellows returning with great enthusiasm from one or more years in major scientific centers become totally frustrated when they try to set up an adequate laboratory in which to continue their work. (3) The centers are structured according to the existing facilities and needs of the region.

The full effect of the program can only be evaluated over a long period of time. Success should be judged essentially by the development in each center of a group of independently creative individuals who are contributing to fundamental scientific research and participating in the immunological aspects of the urgent problems of their own countries. A promising student should be brought as rapidly as possible to the Ph.D. level, perhaps sent abroad for additional training, and then allowed to pursue work on a more or less independent basis at one of the centers. After a period of years, his achievements might well be evaluated by an affirmative answer to the question: "On the basis of his accomplishments, would he be seriously considered for a tenure appointment in a major University anywhere in the world?" The key to the success of the center will be its ability to attract continuously the

brightest and most promising students and to encourage them to stay in immunology. One would hope that the centers will also produce the personnel for their own senior teaching staff and investigators in the future.

The WHO Immunology Unit, in addition to organizing the centers, has conducted a number of scientific group and expert committee meetings on problems important to the developing countries. Over the period 1962-1969, WHO awarded 65 fellowships and 52 research training grants in immunology. The Organization also has a number of reference centers for standardizing immunological reagents and a large number of collaborating immunological research laboratories.

The work of the centers at Ibadan and at Singapore will be considered in detail.

Ibadan: The center was established in mid-1964 and staffed by Dr. Ivan Riha from Czechoslovakia and Miss Ada E. Bezer from the United States. At various periods, short-term consultants have been sent to assist in teaching, to serve as outside examiners, and to advise on research. It has one laboratory plus two rooms in a temporary building, where the course is conducted. A four-month course has been given each year since 1965; the fifth course is now in progress. The number of students has ranged from four to eight. Some students have come from Senegal and Uganda. The 1968 group consisted of three medical graduates, one veterinary scientist, and two technicians, and the course was conducted by three WHO staff members and four visiting scientists. Dr. V. Houba from Czechoslovakia replaced Dr. Riha two years ago.

A description of the 1968 course is appended to this report.

Students were asked to prepare an outline of proposed future research projects to be presented in seminars and discussed at the end of the course.

Topics included immunological aspects of malaria, trypanasomiasis, and amebiasis; autoimmunity in heart disease; cutaneous streptothricosis in cattle; and fetal type of α-protein in hepatoma.

All six students passed the examinations and received certificates. The center has advised and collaborated with various other professors in the Medical School on problems of malarial nephrotic syndrome in children using immunoflourescent techniques, on estimation of immunoglobulin levels, on malarial immunity during pregnancy, and on heterophile antibodies in trypanosomiasis. A comprehensive proposal to study immunological factors in malarial infection was drawn up in mid-1969.

As of May 1970, a total of 21 students had taken the course; 16 of them passed, and 5 were dropped. Nine persons who had participated in earlier courses at the center were working on special problems in various departments at the University of Ibadan. Contact with 10 students has been lost. The war created many problems for the center, and it is expected that the situation will be much more stable, now that peace is restored.

Singapore: The center at Singapore began operation in January 1969 on the premises of the University of Singapore. It has 300 square feet of laboratory space, plus accommodations for laboratory animals. The center is guided by and ad hoc advisory committee, and Dr. David Nelson was its first head. In the two four-month courses that have been conducted so far, there were 16 participants from eight countries (Ceylon, China, Fiji, India, Indonesia, Philippines, Thailand, and Singapore); all but three had a doctoral degree. Each student was required to write two essays in the first course and one in the second, which was also presented orally as a seminar. The lectures in both courses were open to a wider group and were accepted as part

of the B.Sc. honors course. A number of consultants and visiting lecturers participated in the teaching program.

One of the participants in the first course is finishing his Ph.D. and is expected to return to the center. The center has been active and has been collaborating in research in three of the major problems of interest to the region: (1) nasopharyngeal carcinoma, which is reported to be 20 times as common among the Chinese as among Caucasians, (2) leprosy, (3) filariasis. Dr. Nelson has also been consulted on various other immunological problems.

Dr. Nelson is returning to Australia in July and will be succeeded by Dr. M. J. Simons.

General Remarks: The problems of the "selection, care, and feeding" of potentially creative scientists are essentially different from those of mass education. Education and training must be on an almost individualized tutorial basis to inculcate the critical approach in analyzing data, in seeing fallacies in experimental design, in appreciating problems, and in seeking new types of solutions. Many of the processes of creative thought, while often intuitive, can perhaps be better conceptualized and thus aid persons to become more proficient in them. Creativity in science, when developed and nourished, can become a way of life for each individual scientist. The centers may thus have a role to play in the development of new and better educational techniques to bring this about.

R E F E R E N C E S

1. Research in Immunology: Report of Five Scientific Groups (1964) World Health Org. Tech. Rep. Sr 286.

2. WHO Immunology Research and Training Program, Report of WHO Expert Committee 28 Oct. to 1 Nov., 1968. IMM/69.3

3. WHO Executive Board, Forty-Fifth Session, Program Review: Immunology Agenda Item 210 12 Dec., 1969.

ANNEX 1

WHO REFERENCE CENTRES IN IMMUNOLOGY

WHO International Reference Centre for Immunoglobulins

Institut de Biochimie, Lausanne University, Switzerland

(Director: Dr D. S. Rowe)

WHO Regional Reference Centre for Immunoglobulins

National Cancer Institute, National Institutes of Health, Bethesda, Md, United States of America

(Director: Dr J. Fahey)

WHO International Reference Centre for Genetic Factors of Human Immunoglobulins

Centre départemental de Transfusion sanguine et de Génétique humaine, Bois-Guillaume, Seine-Maritime, France

(Director: Dr C. Ropartz)

WHO Regional Reference Centres for Genetic Factors of Human Immunoglobulins

Department of Medical Microbiology, University of Lund, Sweden

(Director: Professor R. Grubb)

Department of Biology, Western Reserve University, Cleveland, Ohio, United States of America

(Director: Professor A. G. Steinberg)

WHO International Reference Centre for the Serology of Autoimmune Disorders

Department of Immunology, Middlesex Hospital Medical School, London, England

(Director: Professor I. M. Roitt)

WHO Regional Reference Centres for the Serology of Autoimmune Disorders

Department of Bacteriology and Immunology, School of Medicine, Buffalo, N.Y., United States of America

(Director: Professor N. R. Rose)

Clinical Research Unit, Walter and Eliza Hall Institute of Medical Research, Royal Melbourne Hospital, Melbourne, Australia

(Director: Dr I. Mackay)

WHO International Reference Centre for Tumour-Specific Antigens

Division of Immunology and Oncology, Gamaleja Institute of Epidemiology and Microbiology, Moscow, USSR

(Director: Dr G. Abelev)

WHO International Reference Centre for Testing of Natural Resistance Factors

Department of Immunology, Institute of Epidemiology and Microbiology, Prague, Czechoslovakia

(Director: Dr J. Šterzl)

WHO International Reference Centre for the Use of Immunoglobulin Anti-D in the Prevention of Rh Sensitization

Medical Research Council, St Mary's Hospital Medical School, London, England

(Director: Dr N. Hughes-Jones)

PROGRAMME OF THE 1968 IMMUNOLOGY COURSE AT THE
WHO IMMUNOLOGY RESEARCH AND TRAINING CENTRE, IBADAN

Week	Theoretical instruction (a two-hour lecture followed by four hours of seminars)	Practical work
1[a]	Introduction to immunology	Organization of work in immunological laboratory; methods of protein estimation.
2	Antigens	Preparation of serum albumin and IgG; salting out techniques, TCA precipitation.
3	Antibody and Immunoglobulins 1	Preparation of serum albumin and IgG (continued).
4	Antibody and Immunoglobulins 2	Sephadex columns, DEAE chromatography.
5	Antibody formation	Preparation of serum albumin and IgG; concentration of proteins, freeze-drying, calculation of the yield.
6	Non-specific immunity and complement	Complement fixation, haemolysin estimation.
7	Cells involved in antibody formation	Preparation of antigens; injection and bleeding of laboratory animal; tests for purity on the antigens prepared; gel diffusion tests (Oudin, Preer, Ouchterlony techniques).
8	Immunoglobulins and their biological significance	Quantitative determination of precipitating antibody.
9	Immune paralysis	Quantitative determination of precipitating antibody (continued).
10	Antigen-antibody interaction	Agglutination, haemagglutination; titration of natural haemolysins, absorption of sera, passive agglutination, rheumatoid factor titration.
11	Significance of cross-reactivity and immune inhibition in immunity	Radioisotopes and their use in immunology; iodination of proteins; antigen-binding capacity of anti-HSA sera.
12	Hypersensitivity 1: anaphylaxis	Antigen-binding capacity estimation (continued); dissociation of antigen-antibody complexes; radioimmunoelectrophoresis on early and late antisera.
13	Hypersensitivity 2: reaction due to immune complexes	Radioimmunoelectrophoresis (continued); immunofluorescence; detection of HGG in mouse tissue; detection of anti-HGG-forming cells in mouse tissue.

[a] Three days only.

Week	Theoretical instruction (a two-hour lecture followed by four hours of seminars)	Practical work
14	Hypersensitivity 3: delayed type	Hypersensitivity; active anaphylaxis, passive cutaneous anaphylaxis, detection of antibody-forming cells by local haemolysis in gel.
15	Immunopathology	Characterization of the antisera produced in rabbits and guinea-pigs immunized with antigens prepared by the students.
16	Infection and immune reactions[a]	Characterization of antisera (continued); detection of antigen-antibody complexes in tissue sections by immunofluorescence.

The last four days of the course were taken up by free discussion and eight hours of seminars. A written, practical, and oral examination was conducted by an external examiner.

[a] No seminars.

ANNEX 3

PROGRAMME OF THE 1968 IMMUNOLOGY COURSE AT THE WHO IMMUNOLOGY RESEARCH AND TRAINING CENTRE, SÃO PAULO

Month	Theoretical lectures	Practical work
1	English conversation and composition (4 h/day).	None.
2 (first half)	Physical and chemical methods currently used in immunology (10 h). Introduction to basic immunology (8 h).	Determination of pH; buffers and indicators; visible light and UV spectrophotometry; fractionation of serum proteins; estimation of proteins by UV spectrophotometry, biuret, ninhydrin, and Folin-Ciocalteu reagents; micro-Kjeldahl; column chromatography; gel-filtration; paper chromatography of oligosaccharides and peptides; fingerprinting.
2 (second half)	Principles and applications of immunofluorescence (10 h).	Fluorescent labelling; characterization and standardization of labelled antibodies; quantification of IF staining; demonstration of antibodies to Streptococcus and Treponema; demonstration of nuclear antibodies; special projects.
3	The precipitin reaction (6 h). Protein structure and protein biosynthesis (4 h). Theories of antibody formation (2 h). Structure and biological properties of immunoglobulins (2 h). Genetic aspects of antibody production (2 h). Complement components and their functions (2 h). Complement fixation (6 h).	Immunization of laboratory animals; quantitative estimation of antibody by method of Heidelberger and Kendall and methods of greater sensitivity; optimum proportion methods; Ramon flocculation; in vivo titration of antitoxins and antivenoms; quantitative CF methods; the macromethod of Mayer et al. and micromethod of Wasserman & Levine; quantitative conglutination; immuno-adherence; special projects.
4 (first half)	Purification and characterization of proteins and carbohydrates (6 h). Immunochemical analysis by gel-precipitation (6 h).	Extraction and purification of pneumococcus polysaccharide and dextran; quantitative determination of methylpentose, glucosamine, and acetyl-hexosamine; preparation of isomaltose oligosaccharides from dextran; cold ethanol fractionation of serum proteins; preparation of crystalline egg albumin; preparation of azo- and DNP-proteins; immunodiffusion methods; special projects.
4 (second half)	Enzymes (6 h). Hapten-antibody interaction; inhibition reactions (6 h).	Immunoelectrophoresis of human serum, normal and pathological; immunoelectrophoretic characterization of enzymes in pancreas extracts and snake venoms; equilibrium dialysis; quantitative inhibition with oligosaccharides; passive haemagglutination with tanned and BDB red cells; Coombs' test; special projects.