4. Chemical and biological studies of Fusarenone (a mycotoxin produced by *Fusarium nivale*) and its analogues.
5. Electron microscopic analysis of hemorrhage induced by snake venom.
6. Studies on the fimbriae and hemagglutinin of *Bordetella pertussis*.
7. Studies on the standardization of animal sera for cell culture.

**REFERENCES**


ment of Virus Diagnosis and Epidemiology. In October, 1963, the Central Virus Diagnosis Laboratory was established as a virus reference and diagnostic laboratory. Later, National Serum Reference Bank (situated at Murayama) was transferred from the direct control of the Ministry of Health and Welfare to this Department as of April 1, 1975. In July, 1965, another new building was constructed at Murayama for the Department of Measles Virus which includes laboratory for the control of live and inactivated measles virus vaccines. In November, 1976, an annex building was constructed for control of rubella vaccine in the Department.

Since 1948, the branches of Hiroshima and Nagasaki had co-operated with the Atomic Bombs Causality Commission, sponsored by the National Academy of Science, National Research Council of the United States, but in April, 1975, this co-operative research organization was abolished as the result of agreement between the United States and Japanese Governments. Now its functions have been inherited by the Radiation Effect Research Foundation, which was established newly in the same place as a substituting organization.

The present organization and activities of the Institute

In general, the Institute has been assigned the following functions, responsibility and authorities according to the enactment pertaining to its establishment:

1) To conduct and co-ordinate research projects of national importance on the causative agents of infectious diseases and their prophylaxis and therapy, and various other projects necessary for public health and welfare.

2) To control, assay or test vaccines, sera and other biologic preparations, antibiotics, disinfectants, insecticides and antirodent drugs related to the prophylaxis, therapy, and diagnosis of diseases.

3) To produce vaccines and sera which are important on a national scale but are not suitable for production by private concerns.

At present the Institute is being organized as shown in Chart I to match its assignment. It has 15 departments, two laboratories, one library and the office of administration. The institute is also rendering various co-operation as listed in Chart II to international medical or research projects.

Chart I

The Organization of the National Institute of Health (1977)

Director-General..............Ken YANAGISAWA, M.D.
Deputy Director-General......Hideo FUKUMI, M.D.
The First Department of Bacteriology

Director: Koomi KANAI, M.D.

<table>
<thead>
<tr>
<th>Laboratory of Bacteriology</th>
<th>II</th>
<th>(Identification of enteric bacteria)</th>
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<tbody>
<tr>
<td>II</td>
<td>III</td>
<td>(Control of cholera and typhoid vaccines)</td>
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<tr>
<td>IV</td>
<td>IV</td>
<td>(Control of pertussis vaccine)</td>
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<td>&quot;&quot;</td>
<td>IV</td>
<td>(Production of plague vaccine)</td>
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<td>&quot;&quot;</td>
<td>&quot;&quot;</td>
<td>(Assay and examination of disinfectants)</td>
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<td>&quot;&quot;</td>
<td>&quot;&quot;</td>
<td>(Phage-type identification of typhoid and paratyphoid bacilli)</td>
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</tbody>
</table>

The Second Department of Bacteriology

Director: Ryosuke MURATA, M.D.

<table>
<thead>
<tr>
<th>Laboratory of Bacterial Toxins</th>
<th>Biochemistry</th>
<th>(Toxin production and role of toxin in pathogenesis)</th>
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<tbody>
<tr>
<td>Biochemistry</td>
<td>(Purification and mode of action of toxin of bacterial and animal origin)</td>
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<tr>
<td>Toxoids &amp; Antitoxins</td>
<td>(Production and control of toxoids, antitoxins and antivenins)</td>
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</tr>
<tr>
<td>Serology</td>
<td>(Serodiagnosis of syphilis and some allergic diseases)</td>
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<tr>
<td>Spirochaetes</td>
<td>(Leptospirosis and control of the vaccine and antiserum for leptospirosis)</td>
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Department of Virology and Rickettsiology

Director: Akira OYA, M.D.

<table>
<thead>
<tr>
<th>Laboratory of Rickettsiology</th>
<th>Virology I</th>
<th>(Typhus, scrub typhus)</th>
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<tbody>
<tr>
<td>Virology I</td>
<td>II</td>
<td>(Herpesviruses)</td>
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<tr>
<td>&quot;&quot;</td>
<td>III</td>
<td>(Rabies and other Rhabdoviruses)</td>
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<tr>
<td>&quot;&quot;</td>
<td>IV</td>
<td>(Respiroviruses)</td>
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<td>&quot;&quot;</td>
<td>IV</td>
<td>(Arboviruses)</td>
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</tbody>
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Department of Enteroviruses

Director: Isamu TAGAYA, M.D.

<table>
<thead>
<tr>
<th>Laboratory I</th>
<th>II</th>
<th>(Tissue culture, simian viruses)</th>
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<tbody>
<tr>
<td>&quot;&quot;</td>
<td>III</td>
<td>(Polio vaccine control; tissue culture safety test)</td>
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<td>&quot;&quot;</td>
<td>IV</td>
<td>(Polio vaccine control; potency, monkey safety test)</td>
</tr>
<tr>
<td>&quot;&quot;</td>
<td>V</td>
<td>(Epidemiology and ecology of enteroviruses)</td>
</tr>
<tr>
<td>Poxvirus Laboratory</td>
<td></td>
<td>(Smallpox vaccine control, poxviruses)</td>
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</tbody>
</table>

Department of Measles Virus

Director: Akira SHISHIDO, M.D.

<table>
<thead>
<tr>
<th>Laboratory I</th>
<th>(Measles virus, mumps virus, measles vaccine control; potency test)</th>
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<tr>
<td>&quot;&quot;</td>
<td>II (Interferon, measles vaccine control; tissue culture safety test)</td>
</tr>
<tr>
<td>&quot;&quot;</td>
<td>III (Rous sarcoma virus, avian leukosis, measles vaccine control; monkey safety test)</td>
</tr>
</tbody>
</table>
Central Virus Diagnostic Laboratory
Director: Reisaku KONO, M.D.

Laboratory of Examination
Antigens and Antisera
National and WHO Serum Reference Bank

Department of Tuberculosis
Director: Toyoho MUROHASHI, M.D.

Department of General Biologics Control
Director: Masami KUROKAWA, M.D.

Department of Antibiotics
Director: Hamao UMEZAWA, M.D.

Department of Parasitology
Director: Shigeo HAYASHI, M.D.
Department of Medical Entomology
Director: Syoziro ASAHINA, Ph.D.
Laboratory of Medical Insects (Taxonomy, physiology, ecology and epidemiology)
  ,, Insecticides (Bioassay)
  ,, Pest Control (Resistance problem)

Department of Veterinary Science
Director: Kiyoshi IMAIZUMI, D.V.M.
Laboratory of Veterinary Public Health (Epidemiology of zoonoses and species-specificity of animal protein)
  ,, Experimental Animals I (Care and management of laboratory animals, supply of inbred animal strains)
  ,, ,, ,, II (Clinical and reproductive physiology of non-human primates, and quarantine and care)

Department of Biomedical Research on Foods
Director: Kageaki AIBARA, Ph.D.
Laboratory of Food Microbiology (Food microbiology, acute food poisoning)
  ,, Food Biology (Food toxicology, chronic diseases caused by foods)

Department of Pathology
Director: Yasuyuki EGASHIRA, M.D.
Laboratory of General Pathology (Pathogenesis of allergic diseases)
  ,, Cell Pathology (Cellular basis of immune responses)
  ,, Pathology of Infection I (Pathogenesis of bacterial diseases)
  ,, ,, ,, II (Pathogenesis of viral diseases, neurohistological test for polio, measles and rubella vaccines)

Department of Chemistry
Director: Yuzuru AKAMATSU, Ph.D.
Laboratory of Biochemistry (Lipid metabolism in bacteria)
  ,, Biophysics (Chromosomal replication in bacteria)
  ,, Chemotherapeutics (Mechanism of drug resistance in bacteria)
  ,, Biologics (Chemical control of biologics)

Department of Dental Research
Director: Shimpei ARAYA, M.D.
Laboratory of Biochemistry (Ecology of dental plaque)
  ,, Morphology (Destruction mechanism of the teeth)

Laboratory of Technology
Director: Hideo FUKUMI, M.D.
Laboratory of Radiation Biology (Radioisotope center)
  ,, Instrumental Analysis (Analytical instrumental center)
  ,, Culture media (Production and supply of culture media)
International Co-operation by the National Institute of Health

National Centers
- National Salmonella Center (WHO)
- National Shigella Center (WHO)
- National Center for Enteric Phage-typing (IAMS)
- National Influenza Center (WHO)
- National Blood Group Reference Center (WHO)

Regional Centers
- Collaborating Center for Virus Reference and Research (Enteroviruses) (WHO)
- Collaborating Center for Poxvirus Research (WHO)
- Collaborating Center for Respiro-viruses other than Influenza virus (WHO)
- Collaborating Center for Arbovirus Reference and Research (WHO)
- Collaborating Center for Standardization of Laboratory Procedures for the Diagnosis of Mycobacterial Diseases and for Bacteriological Research (WHO)
- Collaborating Center for Research and Reference Services for certain Immunological Biological Products (WHO)
- Collaborating Center for Defined Laboratory Animals (WHO)

Reference Laboratories
- Leptospirosis Reference Laboratory (WHO)
- Serum Reference Bank (WHO)

The U.S.-Japan Co-operative Medical Science Program

The present activities including the services being carried on in each of the departments or laboratories are as follows.

THE FIRST DEPARTMENT OF BACTERIOLOGY

The main research projects carried out in this department are:

1. Taxonomic and epidemiologic studies of Enterobacteriaceae and Vibrios.
2. Analytical studies on the mechanisms of intestinal infections by members of Enterobacteriaceae, especially Shigella.
4. Epidemiology of streptococcus infections. Infections with group A hemolytic streptococci are being studied mainly by sero-type identification, in connection with scarlet fever.
5. Studies on the mechanism of rheumatic fever in connection with group A streptococcus infection.
6. Studies on the isolation and characterization of the immunogenic substance of pertussis bacillus from the surface structure of the cell.
7. Studies on the mechanism of immunity in plague infection and its prevention by vaccination.
8. Studies on disinfectants, disinfection and sterilization methods.
9. Epidemiological studies on typhoid fever by phage typing of its causative agent.

In addition to the research projects listed above, the department is responsible for the control of bacterial vaccines and disinfectants as well as the production of plague vaccine. The department has served as the Salmonella Center and the National Shigella Center of WHO. The department has the responsibility of being the National Center of Enteric Phage Typing chosen by the International Association of Microbiological Societies.

THE SECOND DEPARTMENT OF BACTERIOLOGY

The main lines of research in this Department are concerned with bacterial toxins, snake venoms and antitoxins (including antivenins) as well as diseases caused by bacterial and animal toxins. Research on syphilis and leptospirosis are also included. The main research projects involved are as follows:
1. Toxin production by some pathogenic clostridia.
2. Purification and mode of action of bacterial toxins and toxic principles in snake venoms.
3. Biological activities of purified toxins and the role of toxins in the pathogenesis.
4. Biological activities of antitoxins.
5. Improvement of toxoids and antivenins to minimize unfavorable side reactions.
6. Improvement of serological tests for diagnosis of syphilis.
7. Studies on leptospirosis.
8. Improvement of the vaccines and antisera for the control of leptospirosis.

The Department serves as the Leptospirosis Reference Laboratory of WHO and as a WHO Collaborating Laboratory for Research and Reference Services for certain immunological and biological products. The Department is responsible for control of various toxoids and antitoxins, of the vaccine and antiserum for leptospirosis and of the reagents for serodiagnosis of syphilis. The Department is also responsible for production of Schick Test Toxin (diphtheria).

DEPARTMENT OF VIROLOGY AND RICKETTSIOLOGY

The department is concerned with research and some duties related to arboviruses, respiratory viruses, rabies, herpesviruses and rickettsiae. The main research projects and duties of the department are as follows:
1. Laboratory diagnosis of scrub typhus and assay of typhus vaccine.
2. Biochemical studies on the interaction between arbovirus and host cells. Studies on structure of Japanese encephalitis virus, studies on macromolecular synthesis in the infected cells, and studies on its mutants of arboviruses.

3. Biological studies on rabies virus employing mainly chick embryo and BHK-21 cell cultures, studies of sub-unit structure of rabies virus, applicability of tissue culture for production of rabies vaccine, and assay of brain-type-rabies vaccine for human use.

4. Epidemiological studies on influenza and other respiratory viruses, assay of influenza vaccine.


7. Studies on human diploid cell culture.

WHO Collaborating Centers for Virus Reference and Research (respiratory viruses and arboviruses) are located in this department. National surveys on the epidemiology of influenza and Japanese encephalitis are being carried out in close cooperation with the Division of Health Intelligence and Disease Surveillance of the Ministry of Health and Welfare and the prefectural health institutes.

Department of Enteroviruses

The main lines of research of the department are related to enteroviruses, poxviruses, viral hepatitis, non-bacterial acute gastroenteritis, herpes simplex virus, SV40 and oncogenic human adenoviruses. The work includes reference activities on enteroviruses and orthopoxviruses. The main research projects are as follows:

1. Poliovirus:
   Studies on the improvement of type 3 virus for use as live vaccine.

2. Echo- and coxsackieviruses:
   Serological characterization of some enterovirus strains with reference to neutralization by the reference antiserum.
   Genetic studies on some mutants of coxsackie- and echoviruses.
   Humoral and cellular immunity in enterovirus infections.

3. Poxviruses:
   Studies on viral components of vaccinia virus.
   Studies on the polypeptides of orthopoxvirus virions.
   Studies on the white poxvirus in mastomys natalensis.
   Comparative studies of variola virus strains.
   Studies on the heat-labile substance inhibitory to poxviruses present in normal animal sera.

4. Viral hepatitis:
   Studies on HB antigens.
   Studies on HA virus.
5. Non-bacterial acute gastroenteritis:
   Studies on epidemic vomiting and diarrhoea among primary school children.
   Studies on epidemic infantile winter diarrhoea.
6. SV 40:
   Studies on the defectiveness and oncogenicity of SV 40.
   Rescue of viral genome from transformed cells.
7. Adenovirus:
   Studies on DNA synthesis by adenovirus infected cells.
   Since 1962 the department has been assigned by WHO as one of the Regional Reference Centers for Enteroviruses and has collaborated with WHO by reporting the isolation of enteroviruses. In 1974 the title was changed to the WHO Collaborating Center for Virus Reference and Research (Enteroviruses). In 1968 the department was assigned as a WHO Collaborating Laboratory for Smallpox, and in 1974 the name was changed to the WHO Collaborating Center for Poxvirus Research. The department is also concerned with the control of live oral poliovaccine and smallpox vaccine.

DEPARTMENT OF MEASLES VIRUS

Research work in the department is mainly directed towards investigation of the biological properties and pathogenesis of measles, mumps and rubella viruses. Immunological and epidemiological studies on measles, mumps and rubella infection are also in progress. Studies are being made on Rous sarcoma virus infection, and on interferon induction by some viruses and rickettsiae. The main research projects are as follows:
1. Studies on neurotropic properties of measles virus with special reference to pathogenesis of subacute sclerosing panencephalitis (SSPE) and multiple sclerosis.
2. Immunological comparisons among measles, distemper and rinderpest viruses.
3. Immunological studies on mumps infection.
4. Immunological studies on Rous sarcoma virus infection in Japanese quails with special reference to tumor immunity.
5. Studies on the mechanism of induction of interferon on virus infection.
6. Studies on congenital anomalies in experimental animals induced by rubella infection.
   The department is responsible for control of live attenuated measles and rubella virus vaccines. It is also responsible for control of gamma globulin for measles antibody.

CENTRAL VIRUS DIAGNOSTIC LABORATORY

The laboratory serves as a virus reference and diagnostic laboratory for prefectural health institutes and hospital laboratories of the whole country. An-
other duty is to prepare and supply reagents for diagnosis of virus infections to the above laboratories.

In National and WHO Serum Reference Bank the assigned activities are to co-operate with epidemiological surveillance of important infections by the Ministry by standardizing the laboratory methods used in the whole country and to store sera collected in prefectures for this purpose and to serve as a national serum bank. The main research projects in this laboratory are as follows:

1. Studies on epidemiology of virus diseases including those of echo, 4, 6, coxsackie A 16 and rubella in the past. Etiological studies on epidemics suspected of viral etiology are one of main concerns if such event occurs. For example the etiological agent of a new type of conjunctivitis having been pandemic in Asia and Africa in 1971 was discovered and identified as a new picornavirus in this laboratory.

2. Immunology of virus infections.

This laboratory was once engaged in studies on local resistance of the alimentary tract and the role of various classes of immunoglobulins in virus infections. The recent interest directs to immunological events in chronic and persistent virus infections.


Experimental vertical transmission of rubella virus in rabbits was achieved in this laboratory. Co-operative studies on field trials of rubella vaccine have been carried out with Department of Measles Virus.

4. Studies on acute hemorrhagic conjunctivitis (AHC) virus.

As mentioned above, this laboratory is now being engaged in characterization of AHC virus and its global epidemiology.

5. Studies on interferon.

Purification of animal and human interferon, interferon production with attenuated live vaccine and biological characterization of interferon are the subjects of studies.

6. Improvement of the method for diagnosis of virus infections.

7. Improvement of reagents for diagnosis of virus infections.

DEPARTMENT OF TUBERCULOSIS

In this department, research is in progress on the following subjects:

1. The mechanism of delayed hypersensitivity in tuberculosis.

Studies on the purification of the pharmacologically-active substances, MIF and SRF, released from lymphoid cells on immunological stimulation.


Studies on the host-parasite interactions on subcellular and molecular levels, with particular emphasis on the association between bacilli and the phagolysosomal system of the host cells.

Various kinds of malignant tumors in mice and guinea pigs are being treated with BCG vaccine with promising results.

4. Genetic studies on mycobacteria.
   Studies on transfection, conjugation, DNA-damage by UV-irradiation and repair by photoreactivation, and genetic mapping by mutants in synchronous culture cells.

5. The biological significance of the surface structure of mycobacterial cells.
   Chemical analysis of the phage receptor of the cell surface and investigation into fimbriae.

6. Cultivation of *M. leprae* and *M. lepraemurium*.
   Successful cultivation of *M. leprae* in cell-free semi-synthetic liquid, semi-liquid agar and solid agar media.

7. Pathogenicity of atypical mycobacteria.
   The endemic condition and pathogenesis of atypical mycobacteria isolated from specimens obtained from sporadic cases in this country are examined.

8. Comparative studies on various substrain of BCG.
   The allergenicity and immunogenicity of BCG are under strict examination and comparison is being made of various substrains maintained in representative institutes in other countries.

   Phage typing of *M. tuberculosis* is being carried out in an international scale.

    Studies are in progress on the precise relationship of cross resistance to some anti-tuberculous antibiotics (streptomycin, kanamycin, viomycin, capreomycin, lividomycin and tuberactinomycin).

11. Studies on the active principle of tuberculin.

12. Studies on sarcoidosis.
    Preparation and distribution of the Kveim antigen.
    This department is the control and reference center for biological products for prevention and treatment of tuberculosis. Tuberculin standardization, BCG vaccine assay, screening and confirmation of antituberculous drugs and classification of mycobacteria are the main activities in this connection. The department serves as the WHO Collaborating Center for standardization of laboratory procedures for the diagnosis of mycobacterial diseases and for bacteriological research to identify and examine the biological properties of mycobacterial strains isolated in the Western Pacific area.

**DEPARTMENT OF GENERAL BIOLOGICS CONTROL**

The main research projects are as follows:

1. Immunological assay of blood-clotting factors in human plasma and its preparations.
3. Anticomplementary activity of human IgG preparations.
4. Immunological methods for preparing reagents for HBs antigen detection.
5. Culture media and conditions in sterility tests for bacteria, fungi and mycoplasma.
8. Leukopenia-inducing substance(s) of influenza virus and its vaccine.
9. Biological properties of histamine-sensitizing factor (HSF) and lymphocytosis promoting factor (LPF) of *Bordetella pertussis*.
10. Biological properties of bacterial endotoxins and pathogenesis of shock due to bacterial vaccines.

Besides undertaking the research projects listed above and carrying out routine work on control of blood products, and checks on the sterility, pyrogenicity, freedom from abnormal toxicity of immunological products and toxicities of killed vaccines not performed in other departments, the department was assigned by WHO as National Reference Center for Blood Grouping since 1970.

**DEPARTMENT OF ANTIBIOTICS**

The Department of Antibiotics carries out research and routine work on antibiotics. The main research is on the discovery of new antibiotics including anticancer antibiotics, genetical studies on strains producing antibiotics and the mode of action, biosynthesis and chemical structure of antibiotics. Studies are also in progress on biologically active substances produced by micro-organisms, the derivatives of antibiotics, methods of assay of antibiotics, and the main topics of cancer research as listed below.

1. Research on new antibiotics and biologically active substances produced by micro-organisms.
   Screening production, isolation and purification of new antibiotics and biologically active substances including enzyme inhibitors and research on chemical, physical and biological characteristics of these antibiotics are in progress.
2. Genetical research on streptomyces.
   With a view to improving production of antibiotics by streptomyces and for taxonomical purposes the following studies are in progress:
   1) Introduction of DNA into streptomyces by transduction or transformation.
   2) Investigation of the plasmids involving secondary-metabolite production.
   3) DNA-DNA hybridization.
The mode of action of antibiotics is being studied at cellular, subcellular and molecular levels.

   The following research is in progress in relation to the screening and development of new anticancer drugs:
   1) From the cancer side: The relationship between the malignancy of cancer and the structure, antigen, nucleic acid, etc. of cancer cells.
   2) From the host side: The alteration of the host by cancer, etc.
   3) Immunology of cancer.

5. Research on the biosynthesis of antibiotics.
   Studies are in progress on the biosynthesis of antibiotics, not only for academic interest, but also for their production and for synthesis of their derivatives.

6. Chemical transformation of antibiotics.
   Research is in progress on the synthesis of derivatives of antibiotics, particularly of those active against drug-resistant strains of micro-organisms.

7. Improvement and development of methods for examination of antibiotics.
   Routine work includes isolation and identification of soil micro-organisms and maintenance of strains of micro-organisms and tumors. The department is also responsible for the national assay of commercial antibiotics and the preparations of master and working standards for antibiotic assay. In addition, the department collaborates with WHO in making International Standards for antibiotics.

Department of Parasitology

The main research projects in the four laboratories are as follows:
1. The identification of the causative agents of human parasitic diseases for parasitological diagnosis.
2. Fine structural and cytochemical studies on Toxoplasma gondii and other protozoa.
3. Taxonomical studies on Anisakidae and other helminths.
4. Epidemiological studies on clonorchiasis and paragonimiasis.
5. Ecological studies on avian schistosome.
6. Studies on the epidemiology and control of filariasis and onchocerciasis.
8. Analysis and improvement of antigens for immunodiagnosis of schistosomiasis and other human parasitic diseases.
9. Studies on the patho-physiology of clonorchiasis and schistosomiasis in relation to the chemotherapy.
10. In vitro cultivation of protozoan parasites and trematodes.
11. Biological studies on molluscuscan hosts and molluscidicides.
   Routine work is carried on identification of parasites, preparation of hel-
mirth antigens for immunological diagnosis, examination of new antihelmintics, and laboratory- and field-tests on the lethal properties of new compounds against molluscan hosts.

**DEPARTMENT OF MEDICAL ENTOMOLOGY**

Current projects of the Department are as follows:
1. Taxonomic studies on cockroaches and flies of the Pacific area.
2. Studies in chironomid midges and other nuisances.
3. Epidemiology of Japanese encephalitis and other arboviruses with special emphasis on biology of vector mosquitoes and transmission mechanism (in co-operation with Arbovirus Laboratory).
4. Ecology of flies with special reference to their dispersal.
7. Studies in faunal fluctuation affected by pesticide application.
8. Methodological research and official bioassay services for the insecticides of public health importance used in this country.

**DEPARTMENT OF VETERINARY SCIENCE**

The research activities of the department are concerned with two fields, veterinary public health and laboratory animals, both of which are included in veterinary science and closely related to medical science. The main research subjects involved are as follows:
1. Veterinary public health.
   1) Epidemiological investigation on such zoonoses as toxoplasmosis, salmonellosis and listeriosis.
   2) Studies on species-specificity of animal protein with special reference to serological differentiation of animal meats.
2. Laboratory animals and nonhuman primates.
   1) Disease control.
      Diagnostic, epizootic and prophylactic investigations on diseases common in laboratory animals and nonhuman primates.
   2) Breeding.
      Studies on the reproductive physiology of cynomolgus monkeys.
      Breeding of carnivores for laboratory use.
      Development of inbred and mutant strains of mice for biomedical research.
   3) Clinico-physiological studies on the process of adjustment of wild nonhuman primates to laboratory conditions.
   4) Production and maintenance of SPF, gnotobiote and germ-free animals.
      Studies on biological differences between these animals and conventional ones.
The routine work of the department includes quarantine and conditioning of small laboratory animals and nonhuman primates, safety tests for the freedom of *Bacillus anthracis* in smallpox vaccine, serological diagnosis of human brucellosis, serological differentiation of animal meats and sero-typing of *Listeria monocytogenes*.

**DEPARTMENT OF BIOMEDICAL RESEARCH ON FOODS**

Microbiological, biological, biochemical and toxicological studies are in progress on etiology and mechanism of acute and chronic diseases caused by foods.

1. Studies on mycotoxins.
   2) Studies on bioassay systems for mycotoxins in foods with chicken embryos and animal cell cultures.
   3) Studies on the metabolic fate of mycotoxins in rats and mice.
   4) Studies on decomposition of Aflatoxin B1 by microflora of the rat intestine.

2. Studies on carcinogenic N-nitroso compounds.
   1) Gaschromatographical analysis of N-nitrosamine and its related compounds.
   2) Investigation of N-nitroso compounds in commercially processed sea foods.

3. Toxicity induced by processing.
   Studies on toxic substances produced in edible oil by irradiation with ultraviolet rays and purification and identification of such toxic components.

4. Studies on methods of testing food for being irradiated with $\gamma$-ray.

5. Studies on transformation of microflora in foodstuffs by irradiation.

6. Influence of foodstuffs on the intestinal microflora of human and experimental animals.

**DEPARTMENT OF PATHOLOGY**

The current activities of Department of Pathology are mainly directed to research in the fields of infection, immunity and allergy. Much emphasis is laid on the studies on the cellular mechanism of the immune responses. The research projects are as follows:

1. Studies on the correlation between humoral and cellular immunity.
2. Studies on the effects of immunologic adjuvant.
4. Experimental allergic and viral encephalitis.
5. Electron microscopic studies on virus infection.
6. Viral tumor as an infectious disease.
This department is responsible also for histopathological examinations for safety of several vaccines such as live poliomyelitis and measles vaccines.

**DEPARTMENT OF CHEMISTRY**

The main research projects of this department are as follows:
1. **Biomembranes.**
   Biochemical studies on the role of lipids in biological membrane.
   Lipid metabolism in bacteria and mammalian cells.
2. **Mechanism of drug resistance of bacteria.**
   Studies on the mechanism of drug resistance of *E. coli* carrying the R factor.
3. **Replication of bacterial chromosomes.**
4. **Improvement of chemical assays for standardization of vaccines, sera and antibiotics.**
   Routine work includes control of chemical ingredients of vaccines and antibiotics.

**DEPARTMENT OF DENTAL RESEARCH**

The main research projects are as follows:
1. **Destruction mechanism of the tooth by dental caries explored by the methods of:**
   1) microscopic movies of destruction of thin sections caused by various solutions,
   2) radiomicrography and electron microscopy,
   3) chemical and biochemical analysis.
2. **Studies on caries susceptibility in relation to structural and chemical nature of tooth enamel.**
3. **Prevention of dental caries and periodontal disease on a basis of biochemical analysis of dental plaque microbe nature.**
4. **Survey for strontium-90, a fission product formed in atomic explosions, in calcified tissues, especially deciduous teeth collected from Japanese children since 1962 (in co-operation with the Laboratory of Radiation Biology).**

**LABORATORY OF TECHNOLOGY**

The laboratory serves as the control center of such equipment and supplies as radioisotopes, analytical instruments, culture media and others, for general use for biological studies in this institute. The laboratory also carries out research work on the topics as follows:
1. **Investigation of tritium labelling on bioactive substances and contaminated waste disposal.**
2. **Survey of human deciduous teeth for strontium contents.**
REVIEW

THE PRESENT STATUS OF THE NATIONAL INSTITUTE OF
HEALTH IN 1977, THE THIRTIETH YEAR SINCE ITS
FOUNDATION

KEN YANAGISAWA

Director-General, National Institute of Health, Shinagawa-ku, Tokyo

(Received: November 1, 1976)

Foundation of the Institute and its development in the past 30 years

The foundation of the National Institute of Health, which is now 30 year's old, dates back to May 21, 1947. Its establishment was due to the national necessity to have a central institute which carries out research contributing to national health and welfare. At the time when it was established under the Ministry of Health and Welfare, the urgent problem was control of epidemic and endemic diseases which were prevalent all over the country just after the war and restoration of good sanitary condition as quickly as possible. The activities of the institute, therefore, have primarily been concentrated on research on communicable diseases including their etiology, immunology, epidemiology, prophylaxis and therapy and on assay of biological products and antibiotics. About 10 years had passed since its foundation when the institute devoted itself to its original purpose of fundamental medical research.

At the foundation, sharing the space, facilities and personnel of the Institute for Infectious Diseases of the Tokyo University was arranged for the Institute. Therefore, re- and new organization of the departments and laboratories of the Institute and construction of the buildings for laboratories and offices had been conducted step by step, and finally in 1960, 13 years after the foundation, the establishment of the Institute was completed at the present place (Shinagawa-ku, Tokyo) (Yanagisawa, 1967).

As to branch laboratories of the Institute, at first, the Hiroshima and Nagasaki Laboratories became branches of the Institute in 1948 (Maki and Nagai, 1967). In 1961, the branch laboratories for polio vaccine assay and the monkey quarantine house were built at Murayama, about 40 km distant from the main Institute. In April, 1963, a new building was completed at Murayama to contain laboratories for live oral polio vaccine control and for the work of the Depart-