



ANNUAL REPORT
OF THE
HAFFKINE INSTITUTE
FOR THE YEAR
1975-76

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HAFFKINE INSTITUTE FOR TRAINING RESEARCH AND TESTING

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(At 31 March 1976)

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*Honourable Minister for Public Health, Government of Maharashtra,
Sachivalaya, Bombay-32.*

Vice-President

Dr. LEON D'SOUZA

*Honourable Minister of State for Public Health, Government of Maharashtra,
Sachivalaya, Bombay-32.*

Member-Secretary

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Director, Haffkine Institute, Parel, Bombay-12.

Members :

*Secretary, to Government of Maharashtra, Urban Development and Public Health
Department.*

Shri M. S. PALNITKAR

*Secretary to the Government of Maharashtra, Finance Department, Sachivalaya
Bombay-32.*

Shri V. PRABHAKAR

*Director-General of Health Services, Government of India, Nirman Bhavan,
New Delhi-11.*

Dr. P. P. GOEL

*Commissioner, Food and Drug Administration, Maharashtra State, Griha Nirman
Bhavan, Bandra (East), Bombay-51.*

Shri M. K. RANGNEKAR

*Director of Medical Education and Research, Government of Maharashtra, St. Georges
Hospital Compound, Bombay-1.*

Dr. G. S. MUTALIK

Director-General, Indian Council of Medical Research, Ansari Nagar, New Delhi-16.

Dr. C. GOPALAN

Vice-Chancellor, University of Bombay, Bombay-32.

Professor T. K. TOPE

Scientist Emeritus

Dr. C. G. PANDIT

450, Ganeshkhind Road, Pune 7

Trustee, Dorabji Tata Trust.

Professor R. CHOKSI

Bombay House, Homi Modi Street, Fort, Bombay 1

*Director of Health Services, Government of Maharashtra, St. Georges Hospital
Compound, Bombay-1.*

Dr. V. N. RAO

ACADEMIC COUNCIL

(At 31 March 1976)

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Members :

Shri M. K. RANGNEKAR

Dr. G. S. MUTALIK

Dr. S. S. GOTHOSKAR

Dr. (Smt.) S. M. VACHHA

Dr. M. B. BHIDE

Convener :

Dr. F. D. BHARUCHA

ADVISORY COUNCIL FOR RESEARCH*Chairman*

Dr. B. B. GAITONDE

Members :

Dr. C. G. PANDIT

Dr. V. N. RAO

Dr. K. SUNDARAM

Dr. K. K. G. MENON

Dr. NITYA NAND

Dr. M. B. SAHASRABUDDHE

Convener :

Dr. D. M. RENAPURKAR

EXECUTIVE COMMITTEE

(At 31 March 1976)

Chairman

Dr. B. B. GAITONDE

Members :

Dr. M. V. N. SHIRODKAR

Shri Y. V. THAKRE

Convener :

Dr. M. H. SHAH

STAFF OF THE HAFFKINE INSTITUTE

(At 31 March 1976)

ADMINISTRATION

Director :

B. B. GAITONDE, MD, MSc (MED), FASc

Honorary Administrative Officer :

Y. V. THAKRE, MA, LLB

Accounts Officer :

V. C. LIMAYE

LIBRARY

Librarian :

M. N. MANOHAR, BSc, Dip. Lit., Dip. in German language

BACTERIOLOGY

Senior Scientific Officer Class I :

S. V. GADRE, MSc, PhD

Senior Scientific Officer Class II :

D. S. CHITNIS, MSc

Junior Scientific Officer :

Shri R. P. BHAMARIA, MSc

BIOCHEMISTRY

Senior Scientific Officers Class I :

P. RAMAKRISHNAN, MSc, PhD

R. N. JOSHI, MSc

Junior Scientific Officers :

U. J. DUMASWALA, MSc, PhD

A. B. KULKARNI, MSc

CHEMOTHERAPY

Assistant Director :

M. H. SHAH, MSc, PhD

Senior Scientific Officers Class I :

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B. G. KHADSE, MSc, PhD

Senior Scientific Officer Class II :

BHARATI SHANKAR, MSc

Junior Scientific Officers :

M. R. PATEL, MSc

M. T. JAOKAR, MSc

CLINICAL PATHOLOGY

Senior Scientific Officer Class I :

S. MUKERJI, MBBS, MSc, PhD

Junior Scientific Officer :

J. P. MEHTA, MSc

Medical Officers (Maharashtra Medical Services Class II) :

Y. FERNANDES, MBBS, DPB

RANJANA A. DESHMUKH, MBBS

DIRECTOR'S RESEARCH CELL

Junior Scientific Officer :

S. S. JADHAV, M, Pharm

IMMUNOLOGY

Senior Scientific Officer Class II :

G. S. CHHATWAL, MSc, PhD

PHARMACOLOGY

Assistant Director :

M. B. BHIDE, MBBS, MD

Senior Scientific Officer Class I :

S. R. CHAVAN, MSc

Junior Scientific Officer :

S. T. NIKAM, MSc

RADIATION BIOLOGY

Senior Scientific Officer Class I :

N. G. CHANDERKAR, MBBS, BSc (Med)

Junior Scientific Officer : •

S. C. TALWALKAR, MSc

TESTING LABORATORY

Senior Scientific Officer Class I :

V. P. SHINDE, MSc, PhD

Junior Scientific Officers :

H. K. SONI, MSc

H. K. DALAL, BSc

S. S. JAIN, M. Pharm

TOXICOLOGY

Senior Scientific Officer Class I :

V. R. RAO, BVSc, AH, MVSc, PhD

Senior Scientific Officer Class II :

M. G. PHATAK, MSc

Junior Scientific Officer :

V. R. DABHOLKAR, MBBS

TRAINING

Senior Scientific Officer Class I :

F. D. BHARUCHA, BSc, DSc

VIROLOGY

Assistant Director :

M. V. N. SHIRODKAR, MBBS, AB, SCD, PBK

Senior Scientific Officer Class I :

H. J. MANSHARAMANI, MBBS

Senior Scientific Officer Class II :

V. H. APTE, MVSc

A. P. KULKARNI, MSc

Medical Officer

CHHAYA H. PANDIT, MBBS

ZOONOSIS*Senior Scientific Officers Class I :*

D. M. RENAPURKAR, MSc, PhD

W. N. GATLEWAR, MBBS, MSc, (Med), PhD

Senior Scientific Officer Class I :

M. K. BHOPALE, MSc, PhD

Junior Scientific Officers :

T. G. TARE, BSc

P. S. LONKAR, MVSc

CHAPTER-I

Introduction

"The science which alleviates suffering and conquers disease is the best means of achieving welfare of the people".

Haffkine Institute, forged ahead towards fulfilling the role assumed by it on the eve of its Platinum Jubilee Celebrations in 1974 and continued to strive for alleviation of the suffering. Established in 1899, the institute passed through many adaptive changes to meet the demands of the time. Initially named the Plague Research Laboratory and later on Bombay Bacteriological Laboratory, it was christened in the year 1929 as Haffkine Institute in memory of its illustrious founder, W. M. Haffkine.

The year 1975 proved another landmark in the history of the Haffkine Institute. This Institute was bifurcated into two autonomous bodies for taking over two different functions. Haffkine Bio-Pharmaceutical Corporation Limited was registered as a Public Limited Company to take over the production activities of the erstwhile Haffkine Institute. Haffkine Institute, registered as a Society under Societies Registration Act of 1860 and Public Trust Act 1950, was charged with the responsibility of continuing and strengthening the research, training and testing activities.

The new Haffkine Institute started functioning from September 1975. It was formally inaugurated by the Hon'ble Chief Minister of Maharashtra, Shri S. B. Chavan, on 13th November 1975. Various activities of the Institute today encompass research in tropical diseases, training of medical and paramedical personnel, providing facilities for post-graduate education in different disciplines of biomedical sciences, testing of drugs and chemicals referred by commercial organisations and other institutions and also offering advisory services to Government in matters of public health importance.

It is governed by the Governing Council consisting of fifteen members and presided over by the Hon'ble Minister for Public Health, Government of Maharashtra. The Chief Executive is the Director.

Research and training programmes are pursued through several departments such as : Bacteriology, Virology, Immunology, Clinical Pathology, Zoonosis (these form Division of Microbiology), Biochemistry, Pharmacology, Chemotherapy, Radiation Biology, Toxicology (these form Division of Biopharmaceutical Sciences) and a separate Division of Clinical Research with a ward of 25 beds. A special Director's Research Cell exists for carrying out research in problems of his own interest. A testing unit started functioning from September 1, 1975. The Unit has taken over the testing of biological and non-biological drugs referred to the Institute by different commercial organisations. This activity was hitherto carried out by the Pharmacology Department and interfered seriously with the research interests of the department.

The research programme of the Institute has been completely re-organised and research activities have been split up into four important categories, viz. (1) Project Research, (2) Production-oriented Research, (3) Epidemiological Research and (4) Basic Research in Biological Sciences. Presently, the Institute is involved in three important research projects viz. helminthiasis, snake venom research and research in infective hepatitis. Epidemiological research is directed towards the study of epidemiology of important communicable and parasitic diseases like Plague, cholera, typhoid, poliomyelitis, influenza, guineaworm, Filariasis etc. This year, the institute investigated into a suspected outbreak of plague in village Tapni of Nagpur District and laid fears of lay public at rest. In other epidemiological investigations also, the institute made impressionable contributions.

Production-oriented research at this Institute is aimed at improving the quality of biological products manufactured by this institute. Efforts to develop new technology with a view to reduce the cost of production and seek newer biological agents were continued. The main emphasis in this field was to improve the quality of vaccines, particularly the DPT and Cholera vaccine.

There was also an attempt to employ atomic radiation as a means for the preparation of toxoids and vaccines. This is the first time that radiation was used for the preparation of vaccines as a part of the policy of peaceful uses of atomic energy. Considerable progress was made in the direction of the preparation of a vaccine for serum hepatitis. Other notable achievements of the institute include the use of radio-labelled compounds for detecting bacterial contamination at a very early stage, study of leprosy, particularly with a view to estimating the extent of drug resistance and possibilities of overcoming it, study of immunological aspects of leprosy, seeking of indigenous compounds as pesticides and larvicides and preparation of new diagnostic reagents.

As a part of the import substitution programme of drugs and development of indigenous production technology, the synthesis of metronidazole and tetramisole was successfully achieved.

The training activities of this Institute were geared up to the present needs of the society. A number of new courses were planned, some of which were introduced during the year. The institute is recognised for preparing candidates for their M.Sc. and Ph. D. degrees. It also has recognition for M. D. degree in Pharmacology and Pathology. Apart from post-graduate degrees, the institute offers a one year Diploma Course of the University of Bombay in Medical Laboratory, Technology and a certificate course in Medical Laboratory Technology. It conducts Short-Term Training Courses, each of 3 months' duration in different fields. The courses conducted are in : Biochemistry, Clinical Pathology, Testing of Drugs, Preparation of Vaccines and Parenteral Solutions, Maintenance and Care of Laboratory Animals, Blood Banking, Entomology and Parasitology.

The testing unit carried out two principal investigations relating to the field evaluation of pesticides. These projects were sponsored by M/s. Voltas Ltd. and M/s. Bayer (India) Ltd. These projects have provided guidelines for the field testing of pesticides and insecticides for assessing their deleterious effects on the population.

The Institute has an excellent library with a multidisciplinary collection consisting of about 14,000 back volumes of journals and 6,200 books. It subscribes to over 300 national and international periodicals.

Departments

Bacteriology

The Department of Bacteriology is involved in research on pertussis, typhoid, cholera, diphtheria and plague. Apart from research in these fields, extensive efforts are being continued to improve the quality of vaccines manufactured by Institute and to develop newer vaccines. The development of better methods of vaccine production and better vaccines are in process. A project on the use of C_{14} labelled glucose in sterility testing is progressing in collaboration with Radiation Medicine Centre, CRI.

The Department takes part in the postgraduate training and teaching programmes sponsored by the Institute. Post-graduate training courses are offered to students interested in undertaking specialised training in bacteriology.

Biochemistry

The Department of Biochemistry renders diagnostic service to city hospitals, private practitioners and the staff of the Haffkine Institute. This year, the department carried out 2173 tests (Appendix I). The department is currently involved in several important biochemical research projects like the study of hookworm antigens, rickets and vitamin D metabolism and isolation of insulin and other biological products from the glands and organs collected from slaughtered animals from Deonar Abattoir. The project on Isolation of Insulin has been sponsored by the Department of Science and Technology, Government of India.

The department offers facilities for post-graduate research programme and participates in the training programmes conducted by the Institute.

Chemotherapy

The Department of Chemotherapy undertakes to synthesise new compounds for their possible anthelmintic, antituberculosis, antileprosy and antiamoebic activity. This year, the department synthesised two hundred and fifteen compounds. These were characterised and subjected to preliminary screening.

Some new bicyclic compounds on the lines of tetramisole were synthesised and submitted for screening. Similarly, a number of new thiazoles,

thiadiazoles, imidazoles and piperazine derivatives were synthesised for screening them for various biological properties.

The Department also participated in DADDS depot injection trials carried out at Acworth Leprosy Hospital, Bombay and Richardson Leprosy Hospital, Miraj.

The Pilot Plant Committee of the Department held meetings at regular intervals. The laboratory investigations of two products, styrene oxide and metronidazole, were completed and six more are being investigated.

Clinical Pathology

The Department of Clinical Pathology is involved in routine clinicopathological investigations. It also undertakes histopathology investigations of the biopsy material received from various hospitals and other agencies (Appendix II). The research interests of the department relate to the study of typhoid carriers, venereal diseases, and the study of mycoses. The department is investigating problems relating to the epidemiology of antibiotic resistant strains of organisms in clinical conditions, serology and susceptibility to antibiotic agents. The department offers short-term training in clinical pathology and serology. It also participates in the DMLT training course.

Director's Research Cell

Director's Research Cell is conducting researches on pharmacology of scorpion venom, pharmacological and immunological studies on pertussis toxin, study of indigenous drugs as antifertility agents, mechanism of toxic effects following prolonged intake of contraceptive pill and the effect of protein malnutrition on the endocrine function in animals.

Immunology

The Department of Immunology is at present involved in venom research. Among the topics investigated are the biochemical aspects of snake venoms immunogenicity of snake venom, biochemistry and immunogenicity of scorpion venom. Apart from venom research, the Department is also busy in investigating immunological problems concerning leprosy and tetanus.

Pharmacology

The Department of Pharmacology was established at this Institute in 1924 to investigate Indian medicinal drugs. The Department undertook testing of drugs for detecting adulteration. This function has now been assigned to FDA. The Department was completely reorganised and streamlined to restrict its activities to intensive research in delineated problems.

The Department has a research project to investigate indigenous drugs. The Department has succeeded in locating an alkaloidal fraction in a plant coded Jagat I. This alkaloid exhibits neuromuscular blockade by depolarisation and is orally absorbed. The department has a project on leprosy,

supported by ICMR, to investigate drug resistance problem in leprosy and screen antileprotic agents. Central Council for Research in Indian Medicine and Homoeopathy is also lending its support to a project for investigating indigenous drugs. This Department has set up a joint research project with the Department of Zoonosis to screen several indigenous plants for their insecticidal and larvicidal properties.

Radiation Biology

The Department of Radiation Biology is one of the developing Departments of the Institute. It was set up as Radiation Biology Unit in the Year 1972. During this short period, this Department has made notable progress. The Department undertakes clinical diagnostic work on patients with thyroid disorders referred to it by various hospitals and practitioners. It is also collaborating with the Department of Virology in developing vaccine against strabias and hepatitis B. The department is also engaged in research on 'stress and adrenocortical functions and immune response in malnutrition'.

Toxicology

The Department of Toxicology started functioning from September 1, 1975. Since its establishment, it has been carrying out toxicity testing of various commercial products like drugs, insecticides, food additives, plastic containers etc. The Department is also actively participating in the training programmes sponsored by the Institute.

Virology

The Department of Virology has been and is, currently, very actively engaged in fundamental and applied aspects of research of the host-virus interaction with hepatitis B, Rous sarcoma, influenza, rabies and rubella viruses.

Since the isolation and adaptation of hepatitis B virus was hypothesized for the first time, in 1974, in a common laboratory animal model system, the newborn rabbit, maximal activity has been focussed on the investigations of the basic aspects of the host-virus interaction and studies on immunological, morphological, biochemical, pharmacological and radio-biological aspects. Efforts are being made towards the development of an inactivated and a live viral vaccine (*heterologous to man*) against hepatitis B.

The Department also investigated an epidemic of conjunctivitis which swept in whirlwind fashion across India in July-August, 1975 and isolated a chlamydia like organism from several cases. Also an outbreak of an influenza like illness aboard a ship in Bombay Harbour was investigated.

In addition to the regular M.Sc. and Ph. D. (by research) programmes, the Department conducts lectures and practicals in virology for the M.Sc. (by papers) students in Microbiology of the University of Bombay.

Zoonosis

Established in 1970, the Department of Zoonosis has four sections viz, Parasitology, Entomology, Herpetology and Epidemiology. The Department is engaged in research on important zoonotic diseases like plague, leptospirosis, parasitic diseases like soil transmitted nematode infections, dracunculiasis and filariasis.

Apart from research, the Department maintains colonies of fleas (*Xenopsylla cheopis* and *X. astia*), flies (*Musca domestica nebulosa*); cockroaches (*Periplaneta americana*), mosquitoes (*Culex fatigans*) and rodents.

The Department also keeps about 600-1,000 snakes and scorpions for collecting their venoms. The total number of snakes purchased and venom processed during the year is shown in Appendix IV.

The Department undertakes evaluation of commercial insecticides for their biological efficacy and evaluation of newer rodenticides. A project to screen several indigenous plants for their insecticidal and larvicidal activity in collaboration with the Department of Pharmacology has been recently launched.

Recently, the Department has started studies on insect development inhibitors and sex pheromones and on nematode pathogens of several vector insects, like cockroaches.

The Department receives many snakes, rodents, insects etc. for identification and renders advisory service to various institutes regarding identification and control of insects.

CHAPTER II

DEVELOPMENT IN TEACHING

Haffkine Institute is affiliated to the University of Bombay for post-graduate degree and diploma courses. The details pertaining to degree and diploma courses offered by the Institute are shown in Appendix VII. The Institute is recognised by the Universities of Bombay, Poona Nagpur, Baroda, Marathwada and the Konkan Krishi Vidyapeeth for post-graduate studies viz. M. Sc. and Ph. D. by research in various subjects. The National Council of Educational Research and Training, New Delhi, has recognised this Institution as a centre for guiding National Talent Scholars for M. Sc. courses. This year, the Institute was accorded recognition by the University Grants Commission, New Delhi, under Section 2(F) of the U.G.C. Act, 1956.

The Institute has an Academic Council of its own to decide about academic matters, curricula etc. Recently, a Teachers' Council has been constituted to go into the problems connected with research projects handled by students and help in their smooth progress. Dr. S. Mukherjee has been appointed as its convenor.

The Institute's post-graduate research programme envelopes fields of Applied Biology, Microbiology, Pharmacology, Biochemistry, Zoology, Immunology and other disciplines of biomedical sciences. The list of post-graduate teachers recognised by the University of Bombay is provided in Appendix IX. Following new teachers were recognised during the year under report in the subjects specified against them.

Dr. M. V. N. Shirodkar	..	Ph.D., Applied Biology and Microbiology
Dr. A. J. Baxi	..	Ph. D., Biochemistry
Dr. S. Mukherji	..	M. Sc., Microbiology

Sixty-nine students continued their work for post-graduate degree courses. Eighteen students were awarded post-graduate degrees in different subjects. The titles of their theses and other details are provided in Appendix XV.

The short-term training courses conducted by the Institute were very popular. In all, 95 students attended short term training courses in various fields. As will be seen from Appendix VI, short-term training course in Clinical Pathology attracted highest number of students.

Fourteen students successfully completed one-year diploma course in Medical Laboratory Technology. This course is sponsored by the University of Bombay. Another batch of fourteen successfully completed one year certificate training course in Medical Laboratory Technology conducted by the Institute.

CHAPTER III

RESEARCH PROGRESS

Biochemistry

Isolation of insulin and other biological products

Several lots of sheep pancreas collected from rabies—infected animals from Haffkine Institute were processed for the isolation of crude insulin on laboratory scale by employing various procedures. A modified process was employed for collecting glands in the shortest possible time. They were later subjected to storage at -40°C . Among the various procedures employed, the procedure of C. W. Pettings (Lilly Research Laboratories, Indiana) was found to give a comparatively better yield.

Earlier, many lots of bovine pancreas were also processed for isolation. It was difficult to get good glands from younger animals in a limited period. At present, attempts are being made to modify the procedure and to study insulin content of swine glands.

Rickets

In view of the fact that the liver is known to be the primary site for Vitamin D metabolism and its storage, 18 liver samples were analysed for their total Vitamin D content. This work was continued during the present year and twelve more samples were obtained from the J. J. Group of Hospitals for the estimation of total Vitamin D content (Appendix X).

It is known that the absorption of calcium from the intestine is regulated by the amount of calcium present in the lumen of the intestine, when adequate amount of Vitamin D is available. Hence, the regulatory mechanism underlying the absorption of dietary calcium was studied.

For understanding the mechanism, a study of adenyl cyclase, an enzyme responsible for the synthesis of $\bar{\text{C}}\text{AMP}$ in the intestinal brush border, can serve as an useful tool for the following reasons :—

- (i) $\bar{\text{C}}\text{AMP}$ is required for biosynthesis of protein ;
- (ii) Calcium, adenyl cyclase and prostaglandins are inter-related in the synthesis of cyclic AMP;
- (iii) Calcium can inhibit adenyl cyclase activity in many tissues.

In view of the above, experiments were planned, in which albino rats were divided into three groups as follows :—

Group I — Dietary Calcium ... less than 0.1 %

Group II — Dietary Calcium ... 0.6 %

Group III — Dietary Calcium ... 1.2 %

The adenyl cyclase activity in the brush border of the intestine was determined after the experimental period.

The adenylyl cyclase activity in the low dietary calcium group was high and that in the high dietary calcium group was low as compared to normal dietary calcium group, thus indicating that dietary calcium in high concentration decreases adenylyl cyclase activity in the intestinal brush border.

The effect of dietary calcium on lipid metabolism was also studied. Albino rats were arbitrarily divided into the three groups mentioned above and biochemical parameters were studied in the liver and serum.

In order to establish reliable criteria for earlier diagnosis of rickets, the disease was produced experimentally in animals by inducing either vitamin D deficiency or calcium deficiency, or both.

Serum cholesterol level was found to have decreased in both groups, viz. Group I (low dietary calcium) and Group III (high dietary calcium), as compared to Group II (normal dietary calcium). In case of liver cholesterol, Group I has shown no significant difference, whereas in Group III, the level decreased significantly as compared to Group II. At the same time, animals of Group I showed significant decreased level of phospholipids, but in Group III, they did not show any significant change when compared with the levels in Group II (Appendix XI).

Chemotherapy

In the field of synthesis of organic compounds for possible therapeutic activity, the work reported previously was continued and some new problems were also taken in hand. All the newly synthesised compounds were tested for antituberculosis activity and many of them also for anti-parasitic activity.

The Department of Chemotherapy has undertaken process development work in respect of some drugs, the technology of which is not available indigenously and the demand for which is fulfilled only by import at present. Attempts were made to standardise the preparative methods for these drugs from indigenously available raw materials as far as possible.

A large number of compounds was synthesised and submitted for study of their anthelmintic activity *in vitro* against *A. lumbricoides* and *in vivo* against *N. dubius* and *H. nana*. In continuation of the synthesis of anthelmintic agents, some 2,6-dihalo-5-alkyloxyanilines were prepared and efforts were made to convert these anilines into corresponding isothiocyanate derivatives. However, a well-defined product could not be isolated and, hence, the substituted anilines were condensed with 2-chloro-3-isothiocyanato pyridine to obtain the corresponding pyridothiazoles. These were tested for anthelmintic activity against *H. nana* in mice in view of such activity exhibited by this group of compounds earlier in our laboratory.

Synthesis of the series of compounds on the lines of tetramisole, namely, 2, 6-disubstituted imidazo (2, 1-b) thiadiazoles, was continued

by introducing ethyl, propyl, hydroxyl or nitro group in the 2-position of the molecule in order to evaluate their activity with respect to these differently characterized substituents.

The synthesis of 5,6-dihydro-2,6-disubstituted imidazo (2,1-b) thiadiazoles, which are partially saturated, was taken in hand. One compound was synthesised, characterised and submitted for assessment of anthelmintic activity. A third series of bicyclic compounds of 2-substituted thiadiazole (3,2-a)-s-triazine-1,3-dione is also in hand for synthesis and evaluation.

The series of (5-nitro-1-methyl-2-imidazolidene)anilines and 2-mercaptol-aryl-imidazoles were synthesised as possible antiamebic agents. A few of these compounds showed antiamebic activity *in vitro* at a concentration of 5 to 20 $\mu\text{g/ml}$. Having got two compounds with asymmetric carbon atoms, like emetin, showing very promising antiamebic activity, some additional new compounds were also synthesised. In the place of piperazine, in the active compounds, some important amines like allylamine, 2,6-dichloro-aniline etc., were condensed to find out how far the piperazine part was responsible for the activity.

Antibacterial testing

In continuation of earlier work, a few additional azomethines were prepared by condensing the 4-(3'-amino-4'-methoxyphenyl) thiazoles and N-substituted-3-indolealdehydes and the resulting compounds were submitted for antituberculosis screening. Some of them showed *in vitro* antituberculosis activity up to 1 $\mu\text{g/ml}$.

Thiocarbanilides were prepared from *p*-alkoxy-phenyl-isothiocyanate and 2-(*p*-aminophenyl) thiazoles or 4-(*p*-aminophenyl)thiazoles. All these thiocarbanilides were submitted for antibacterial tests. One compound inhibited the growth of *M. tuberculosis* (H_{37}R_v) *in vitro* at a minimum concentration of 0.4 $\mu\text{g/ml}$.

Ten compounds of the series, namely, 2-(N^4 -substituted N^1 -piperazinyl)sulfonyl thiophene and nine compounds of 3-(N^4 -substituted- N^1 -piperazinyl)sulfonyl 5-nitrothiophene were synthesised. Three compounds showed antituberculosis activity at a concentration of 2 to 40 $\mu\text{g/ml}$ in *in vitro* screening.

Process development of drugs

5-Nitrofurfuraldehydediacetate is used as key intermediate for the manufacture of nitrofurans viz. nitrofurazone, nitrofurantoin and furazolidone. The process for preparation of 5-nitro-furfuraldehyde diacetate has been standardised up to 1.5 kg scale in laboratory. This is ready for further exploitation.

The process development of semicarbazide, which is the penultimate intermediate for nitrofurazone, was taken up.

Process development of dl-tetramisole

The scaling up of the process of dl-tetramisole, by making minor changes in the reaction conditions, such as temperature or conditions of isolation etc., was undertaken in order to make the process more economical. The first step was carried out at 1 Kg. scale.

The process of styrene oxide was standardised up to 5 kg. scale on pilot plant and is ready for commercial exploitation.

There are no reports in our country on indigenous manufacture of trimethoprim which has gained great importance recently. The scheme for process development for this drug was taken up.

The process for the preparation of the important diuretic drug in clinical practice, namely, frusemide was started.

Communicable Diseases and Microbiological Research

Anaerobic bacteria

Four-hundred and five samples of clinical (wounds and abscesses, post-operative) and non-clinical materials (operation theatre) were collected for the isolation of anaerobic bacteria. *Clostridia* (47), *Bacteroides* (19) and *Streptococci* (39) were isolated. Antibiotic sensitivity tests were carried out on 70 *Clostridium* and *Bacteroides* species. The antibiotics used were (i) colistin, (ii) neomycin, (iii) Methillion, (iv) chloromycetin, (v) penicillin, (vi) tetracycline, (vii) flagyl and (viii) erythromycin. Most of the strains were found to be sensitive to drugs mentioned at serial numbers iv, vi, vii and viii above.

Cholera carriers

(I.C.M.R. Project)

To study this problem, 4 villages of Thane district, falling under the jurisdiction of the Primary Health Centre, Virar, were selected. Stool samples of human beings, animals and water samples from tube-wells and ponds, were collected for culture

V. Cholerae Ogawa El tor phage (2) was isolated from one cholera case. This case, after discharge from the hospital, was found to contaminate water of an open well. Stool samples of 16 healthy human beings and of 3 animals, water samples collected from various sources i.e. ponds and open wells, yielded the growth of NAG vibrio (Appendix XII).

Fourteen human serum samples of NAG vibrio carriers showed presence of agglutinins against classical vibrio and two of the sera agglutinated with NAG vibrio. These findings suggested the possibility that pollution of water sources with *V. cholerae* is followed by the appearance of NAG vibrio.

Candida

Females suffering from muco-outaneous vaginal lesions were selected for the study. Three hundred and five vaginal swabs, were collected

and 33 candida strains were isolated. Biochemical and auxanographic-studies on these strains are being carried out. A polysaccharide antigen of *C. albicans* has been fractionated for skin test.

For animal pathogenicity test, white mice of different age and weight groups were injected with different concentrations (count) of the candida species to produce experimental granuloma and/or death in the animals.

Mycoplasma

Mycoplasma infection in children suffering from acute upper respiratory tract disease was studied.

One—hundred and fifty-three samples were collected for complement fixation test with *Mycoplasma pneumoniae* antigen and for cold haemagglutination test. The former as well as the latter were positive in 11 and 4 cases respectively. Laryngeal swabs were taken in 110 cases but mycoplasma was not isolated on culture.

Gonococci

Efforts to develop sensitive as well as simple serological techniques for the laboratory diagnosis of gonococci are being continued. Previously, an alkali extract of gonococci containing protein and sugar was found to cross react with other *Neisseria*. Subsequently, a phenol extract antigen of gonococci containing only sugar was found to be more specific in 150 gonococcal and 80 normal sera tested.

Typhoid

For detection of typhoid carriers, Vi haemagglutination test (Schubert, Edwards and Ramsey, J. Bact. 721, 648, 1959) was employed. Out of 46 typhoid cases, 19 reacted positively to the test (titre 1/100 and above) but their clots and stool specimens did not yield growth of any *Salmonella*. Two cases, whose clot cultures were positive for *S. typhi*, failed to give a positive reaction with the serological test, while 25 normal sera also behaved similarly. These findings indicated that Vi haemagglutination test is not of much value for the detection of typhoid carriers.

Plague

A study of distribution of rodents during different seasons in Greater Bombay showed that three principal types of rodents viz. *Rattus rattus*, *Bandicota bengalensis* and *Rattus norvegicus* were predominant throughout the year. There was no seasonal variation in their distribution. The flea index remained below one throughout the year.

Investigations into the rat fall reported from Tapni village in Nagpur District did not show any bacteriological or serological evidence of plague infection. *Rattus rattus* was observed to be the predominant rat species; *X. cheopis* constituted the predominant flea species. The area had a very high flea index. Fleas were found to be susceptible to BHC and resistant

to DDT. The rat fall subsided after spraying the area with BHC. No fresh cases were reported after the spraying.

Virus research

The most interesting advances made at the Department, in basic and applied aspects of the host-virus interaction in hepatitis B research were the confirmation of the hypothesis, advanced here in 1974-75, that HIBOMA and human hepatitis B virus (of which the former is a lapinized isolate) are identical, and that this adaptation of the human virus to the newborn rabbit, through 8 successive intrahepatic passages, had been accomplished *for the first time in a common laboratory animal*. The lines of evidence leading to this conclusion were morphological' (light and electron microscopy), classic virological (fulfilment of Koch's First Postulate by obtaining six isolates of HIBOMA from different patients), radiobiological (radioimmunoassay), immunological (specific virus neutralization tests) and biophysical (ultracentrifugation studies in sucrose density gradients and membrane filter passing experiments). The basic importance of the above is that, for the first time, a convenient, economical and readily available common laboratory animal model system has been described for the intensive study of hepatitis B virus from the virological, oncological, morphological, immunological, biochemical, pharmacological and radiobiological points of view. From the applied viewpoints, this system has provided a new source of hepatitis B virus and thus cleared the way for the development of the first inactivated and live virus vaccines against the globally ubiquitous and alarmingly increasing disease, hepatitis B in an *in vivo system heterologous to man*. A most interesting finding in the new model system is the clear demonstration that actinomycin-D completely protects newborn rabbits from the lethal action of HIBOMA-I virus, whereas rifampicin does not. This not only confirms the belief, now widely held, that hepatitis B is a DNA virus, but also opens up new vistas for the pharmacotherapeutics of hepatitis B. Similarly, the biophysical studies have been most fruitful, inasmuch as a partially purified preparation of HIBOMA virus has now become available, by which specific HBsAb is being produced in volumes adequate for basic and applied studies on hepatitis B virus. From the applied standpoint, the prospect of the local development of an RIA kit using antisera prepared from animals hyperimmunised with HIBOMA virus, in this Department, could lead to great advances in the indigenous availability of rapid and sensitive detection technology for hepatitis B antigen at our blood banks, surgical centres and in radiobiological research work, in general.

The host-virus interaction systems in viral oncology, *viz.* the West Nile-Rous and the rabies-Rous blockade systems, developed originally at this Department, continued to yield exciting results. Potent plasma factors (PF) have been demonstrated in both *in vivo* chick systems and the remarkable potency of the RV-induced PF (80-100 per cent of the birds totally tumour blocked), as an antiviral compound of high specificity, is being intensively investigated. (Appedix XIII).

At the Virus Research Unit, a newly established section of the Department of Virology, in addition to the isolation of HIBOMA (II-VI), from different hepatitis B patients, the most interesting development has been the finding that the aetiological agent of epidemic conjunctivitis, which swept through Bombay and the rest of India in July, 1975, was, probably, *Chlamydia trachomatis*, and not a virus as had been believed elsewhere. In addition, the Unit investigated an outbreak of suspected influenza on board an Indian Navy vessel in Bombay Harbour. As a virological service to a neighbouring cancer hospital, the Unit isolated a strain of herpes simplex virus from a case of early carcinoma of the cervix.

Other viruses studied in the department included that of rabies. Work on the biochemical changes occurring in experimental rabies in mice confirmed that 5-hydroxytryptamine and noradrenaline are deeply involved in temperature regulation and the concentrations of the brain catecholamines showed a highly significant reduction from the normal levels.

Further studies in this direction continued. Efforts towards the ultimate goal of developing a better antirabic vaccine continued, in hamster kidney cell cultures, but the titres of rabies virus were found to be too low for suitable vaccine development and efforts continue.

Studies on rubella virus-produced cataracts *in ovo* in the chick embryo model developed in this department, continued and it was shown that only two strains of the virus produced cataracts, whilst two others did not. Earlier epidemiological studies on rubella in Bombay were continued.

Finally, a team of scientists was sent to Dhule District, Maharashtra, India, where an outbreak of a pox disease was reported in milkers of cows and buffaloes and in the animals. In the laboratory, pocks were produced on the chick CAM and these are being investigated from the point of view of buffalo pox or vaccinia aetiology.

Parasitic diseases and zoonosis

Filariasis

Maintenance of *L. carinii* culture in cotton rats and white rats was continued. One-hundred and twenty-two animals were infected and 99 infected animals were supplied to Pharmacology Department for drug evaluation.

Development of infection in *Culex p. fatigans* in the laboratory with *W. bancrofti*, using microfilaria carriers, was continued. Infective larvae of *W. bancrofti* were collected after dissecting mosquitoes. About 5,000 larvae have been collected so far.

A project has been undertaken to control filariasis by offering DEC treatment to microfilaria carriers. In all, 178 microfilaria carriers were

detected in 4 villages surveyed. They were given DEC treatment for twelve weeks with a dose of 6 mg/kg. once a week for 12 weeks in consonance with the recommendation of the WHO. The screening of microfilaria positive cases, with a view to assess the reduction in the number of microfilaria in the treated cases, is in progress.

Dracunculiasis

Studies on density of Cyclops were carried out in three villages of Kolaba District. The studies showed a range 15.0-20.0 of cyclops density per litre of water in November and December.

Soil transmitted nematodes

Strains of *Nematospirodes dubius* and *Hymenolepis nana* are being maintained for carrying out immunological studies and drug evaluation. An attempt is being made to establish *Necator americanus* culture in hamsters and in infant rabbits. Laboratory cultures of *Nippostrongylus brasiliensis* and *Ancylostoma caeylanicum* are being established.

Hookworm antigen

Hookworm larvae were collected by coproculture from stool samples of patients suffering from hookworm infection. These larvae were in the infective stage and, therefore, were best suited for antigenic studies.

Initially, stool samples were brought from Virar and since these were low in egg-load, sufficient larvae could not be obtained. Protein content as measured by Lowry's method was found to be low and electrophoresis on cellulose acetate paper gave diffused trailing.

Later, the stool samples were collected from J.J. Group of Hospitals. The egg-load was high and larval yield was satisfactory.

The following techniques were standardised :

- Zone electrophoresis using paper cellulose acetate gel strip ;
- Polyacrylamide gel electrophoresis ;
- Lowry's method for protein estimation;
- Gel filtration using Sephadex G-100.

Preliminary experiments for standardization of the above techniques with horse serum were satisfactory.

Total antigen or whole antigen was prepared by sonicating and lyophilizing the entire larvae. In another batch, the larvae, after sonication, were centrifuged. The supernatant was found to be soluble somatic antigen, while the sediment was found to be cuticular antigen.

Vector control and insecticide resistance

Various fractions of three indigenous plants viz. *Acorus calamus*, *Azadirachta indica* and *Ocimum sanctum* were screened for mosquito

larvicidal activity. Petroleum ether extracts of *Acorus calamus* and *Azadirachta indica* were observed to show antilarval activity. Further fractionation of petroleum ether extracts of these two plants is being carried out to identify the toxic principle.

Several species of nematodes were collected and identified from cockroaches. Attempts are being made to rear these nematode under laboratory conditions. Pathogenicity of several nematode parasites of cockroaches will be studied after the culture gets established. Recently, a project has been taken up to study sex pheromones of mosquito *Culex fatigans*. Some preliminary work has been done. This has shown the possibility of existence of male sex attractants in female mosquitoes.

Pharmacology

Indigenous Drug Research

The Department of Pharmacology has located an alkaloidal fraction exhibiting potent neuromuscular blockade by depolarisation and which is orally absorbed. The full elucidation of its structure will lead to a novel group of compounds useful as adjuvants in surgical anaesthesia, Parkinsonism and tetanus.

The alkaloid fraction from the plant "Jagat-I" exhibits neuromuscular blockade by depolarisation in chicks, cats, rabbits, guinea-pigs etc. The fraction is 10 times more active than curare. The blockade produced *in vivo* is immediate and reversible in a few minutes.

Insecticidal drugs

A collaborative research project was initiated to investigate the larvicidal/insecticidal principles from indigenous plants. Preliminary work was carried out on the following three plants viz. (i) *Acorus calamus*, (ii) *Azadirachta indica* and (iii) *Oscimum sanctum*.

Acorus calamus is popularly known as "Vekhand" in the local language, Marathi. It grows abundantly in Manipur and Naga hills. The powdered rhizome material was serially extracted in soxhlet with petroleum ether, ether, chloroform and alcohol. Different extracts were tested for mosquito larvicidal activity by the method recommended by WHO. The petroleum ether extract was further fractionated at reduced pressure and the fraction collected at 118°-124° c/6 mm. was found to be most active and comparable to pyrethrum extract.

Azadirachta indica (Marathi-Nimb)

Powdered leaves were extracted with petroleum ether, ether chloroform, alcohol and all such extracts were tested for larvicidal activity. Out of these extracts, petroleum ether extract was reported to have good activity as compared to pyrethrum extract. Qualitative analysis of this extract showed presence of steroids. Column chromatography of petroleum ether extract was carried out by using alumina column. The solvents

used for elution were : (1) petroleum ether, (2) petroleum ether : benzene (1 : 1); (3) benzene; (4) benzene : methanol (1 : 1); and (5) methanol. Five fractions were collected. Each fraction was put to TLC and spotted to find out number of steroids present in each fraction. Fraction (2) showed presence of three steroids. This fraction also showed juvenile hormone activity.

Ocimum sanctum (Marathi-Tulas)

Whole plant material was powdered and extracted with petroleum ether, ether, chloroform, alcohol and tested for larvicidal activity. Out of these extracts, petroleum ether and ether extract showed promising activity.

Oil from Hydnocarpus laurifolia

In a continued search for a new antileprotic drug, antileprotic activity of oil from *H. Laurifolia* was evaluated. The drug was tested by using mouse foot pad technique as described by Shepard. A quantity of 0.8 ml of the oil was mixed daily with the mouse food. The drug was also found effective in *M leprae* strains resistant to D.D.S.

Other indigenous drug research (C. C. R. I. M. H.)

N-M blocking activity was located in a coded plant CBS and local anaesthetic activity in the coded plant.

Screening of synthetic compounds

About 50 compounds were screened for their antileprosy, antifilarial, anthelmintic and antiamoebic activity. Out of these, three compounds were found to be active in helmenthic infections. One compound (R-2768) exhibited potentiating activity of metronidazole.

The level of drug resistance in *M. leprae* to DDS was evaluated and two cases were found to be drug resistant.

Marine toxicology

During the year, collaboration was developed with Marine Research Centre of Konkan Krishi Vidyapeeth for the supply of poisonous snakes from Ratnagiri. A Rapport was also developed with local fishermen. A pure fraction of toxin from *E. schistosa*, was separated. This fraction has lower molecular weight than that described by others. The details of the work done are as follows :

Studies on Enhydrina schistosa

The venom was separated into four major proteins by CM cellulose column chromatography. The most toxic fraction was further purified by Sephadex gel filtration. The fraction was found to be homogenous by polyacrylamide disc gel electrophoresis and Sephadex gel filtration. Antisera against the fractions were prepared in rabbits.

Biochemical studies

Enzyme activities were determined in the crude venom. Following enzymes were detected : phospholipase A, phosphodiesterase, alkaline phosphomonoesterase, 5'-nucleotidase, choline esterase and proteolytic activity.

*Studies on *Hydrophis cyanocinctus**

The venom from *H. cyanocinctus* showed d-tubocurarine like action on N-M junction. It was irreversible and not antagonised by anti-cholinesterases. After CM cellulose column, a fraction with reversible activity was isolated.

Director's Research cell

Pharmacological and immunological studies on pertussis toxin

Crude pertussis toxin, as well as 22 different fractions obtained after subjecting it to starch block electrophoresis, were studied individually for their pharmacological, immunological and other toxic actions. It is already reported that pertussis toxin is capable of producing β -adrenergic blockade, histamine sensitization, hypoglycemia and some neurological disorders in children. In addition to these reported activities, it was found that pertussis toxin can also cause severe hypothermia leading to death. When individual purified fractions (15 anionic and 7 cationic) were studied for their pharmacological, immunological and other toxic actions, it was found that any individual fraction could not evoke any pharmacological response. But it was surprising to see that four anionic and 2 cationic fractions, which were unable to produce hypoglycemia, hypersensitivity, β -adrenergic blockade or hypothermia, could as successfully immunise the animals as pertussis vaccine. The animals were tested as per official method described in I. P.

Along with the detailed study of individual fractions, the exact mechanism of action of histamine sensitization after administration of pertussis toxin was studied. In these investigations, the possibility of any change occurring in the histamine levels of mast cells was ruled out by testing histamine contents of mast cells in control and pertussis toxin pretreated animals. *In vitro* assay of histamine was performed on isolated guinea-pig ileum. Further, histaminase activity in the liver and intestine of rats pretreated with pertussis toxin was studied. It was found that histaminase activity in the intestine remained unchanged, whereas in the liver it showed significant reduction.

β -adrenergic blockade reported to be caused by pertussis vaccine thus far had not been demonstrated by any worker in an *in vitro* model. This effect in isolated rabbit aortic strip and in guinea-pig tracheal chain was demonstrated in the experiments carried out at this Institute. It was also found that the cAMP levels in the liver of pertussis-treated rats were significantly lowered. cyclic cAMP levels were estimated by using radioimmunoassay technique.

Scorpion venom

The crude venom was purified using CMC cellulose column. Each fraction was studied for its pharmacological action. It was interesting to note that out of seven fractions, only two contained histamine. One fraction contained serotonin, two were potent CNS stimulants and two were totally inactive.

Study of antifertility components of an indigeneous plant (code LF-1)

The alcoholic extract of the plant LF-1 was tested for estrogenic and anti-estrogenic activity. Brief chemistry was also done. The alcoholic extract was fractionated on chromatographic neutral alumina using benzene, alcohol and water. The benzene and alcohol elutes were evaporated to dryness and dosage forms were prepared by making suspensions with gum acacia. The benzene fraction, when administered for 3 days after mating, exhibited 60% antifertility activity at a dose level of 400 mg/Kg body weight in mice. The alcoholic fraction, when administered for 3 days after mating exhibited 100% activity at a dose level of 400 mg/Kg body weight in mice. The water soluble portion of alcoholic extract, when administered for 3 days after mating, exhibited 60% antifertility activity at a dose level of 400 mg/Kg. body weight in mice. The extract was also tested qualitatively for flavonoids, alkaloids, saponins, tannins, resins, glycosides, steroids and reducing sugars, etc. It was positive for reducing sugars, steroids (or saponins) and tannins.

Oral contraceptive hormones and neurotransmitters

The study of the effect of oral contraceptive hormones on the metabolism of neurotransmitters in brain did not reveal any significant change in the levels of neurotransmitters, such as noradrenaline, dopamine and serotonin in different parts of the brain. Therefore, a study of the pattern of pyridoxal phosphate levels in the brain as well as the liver tissue of the animals was undertaken. Earlier reports indicated that pyridoxal phosphate is otherwise very closely related to the neurotransmitter metabolism in brain. However, studies undertaken here indicated no change in the pyridoxal phosphate level in the brain as well as in the liver tissues.

Thereafter, experiments were conducted to study the role of tryptophan content in the diet of experimental rats simultaneously treated with oral contraceptive hormones. Animals were given standard diet (free of tryptophan) and their tryptophan intake was controlled by feeding a known amount of tryptophan orally. It was found that the serotonin contents of the brain of animals treated with oral contraceptives decreased considerably as compared to those of the control group.

Production-oriented research

Production of diphtheria toxin in submerged cultures.

A toxin titre of about 140 Lf per ml has now been attained in shake flask cultures using CN 2,000 variant of PW 8 Weissensee strain of *C. diphtheriae* in a medium based on papain digest of beef.

Studies in tetanus toxin production

In order to boost tetanus toxin yields at this Institute, factors governing toxin production were studied using Massachusetts's medium. The most important finding was that a change in surface area to volume ratio raised the toxin titres from about 60-70 Lf/ml. to 100-110 Lf/ml. However, this change in ratio was not very practical for large-scale toxin production. The optimum ratio allows only 900 ml. medium in a 5 litre beaker as against 3 litre medium in a 5 litre beaker currently employed by the production Department.

It was also interesting to note that conditions of aeration and agitation of the culture, when altered, raised the titre from 60-70 Lf/ml. to 90-100 Lf/ml.

Use of labelled glucose for determining antibiotic sensitivity

Antibiotic sensitivity of different organisms, viz. *S. aureus*, *E. coli* was assessed by using labelled glucose. This was assessed for antibiotics like ampicillin, chloromycetin, gentamycin, tetracycline, streptomycin, polymyxin, nitrofurantoin.

Labelled glucose was incorporated into the medium to which a known number of organisms of the above mentioned strains was added. Antibiotic doses of known concentrations were also incorporated into the medium. The vials were incubated at 37° C and 14 Co₂ counts were recorded after 3 hours. Antibiotics, which were found active, are given below serially :—

<i>S. aureus</i>	erythromycin	gentamycin	tetracycline
<i>E. coli</i>	chloramycetin	gentamycin	tetracycline
	polymyxin	nitrofurantoin	
<i>P. vulgaris</i>	sulphonamide	chloromycetin	kanamycin
	gentamycin		

Studies in typhoid vaccine

Experiment on neutralisation test of 'O' serum with Vi+ve and Vi-ve strains was repeated. Dilutions taken were 1 : 4, 1 : 8, 1 : 16, 1 : 32, 1 : 128 and 1 : 512.

Results showed that 'O' serum neutralizes Vi+ve strain completely and Vi-ve strain partially. But Vi serum does not neutralise either Vi+ve strain or Vi-ve strain. It is seen that Vi antibodies are not involved in neutralisation of the factor responsible for skin reaction.

For further confirmation, Ty₂ whole serum was tested for neutralization with Vi±ve as well as Vi-ve strains. It neutralised both the strains.

Radiation biology

Studies on immune response in mal-nutrition

Humoral and cellular immune responses were studied in groups of under-nourished and malnourished individuals after their exposure to antigens. The antigens used were cholera, tetanus and triple vaccines. Studies show that cellular immune response is affected, depending upon the degree of malnutrition present in the individual. However, the humoral immune response does not show any significant variation from the normal in under-nourished cases.

Adrenocortical function in protein malnutrition

Experiments were carried out to see whether the stress of protein deprivation, in any way, altered the psychomotor behaviour of animals. Rats were initially trained in the pole climbing apparatus. The training was continued till the animals produced consistent response to conditioned and unconditioned stimuli. The animals were later exposed to cold stress at -10°C . It was observed that protein deficient animals did not show any changed response to conditioned stimulus as compared to that produced by the normal rats during four weeks of treatment. Similar findings were achieved when rats were exposed to the stress of gamma irradiation. The combination of chronic stress and acute stress resulted in a significant rise in the plasma corticosterone levels in the normal and protein deficient groups ; however, there was no difference in the rise in the two groups. These results indicate that the stress of malnutrition does not alter the psychomotor behaviour of the animals.

CHAPTER IV

TESTING

The testing of various pharmaceutical products, biological materials, clinical samples, water, disinfectants and food samples was previously carried out by different departments of this Institute. In order to co-ordinate all the testing activities of the Institute, an independent Testing Unit was established on 1st September 1975. The main function of this unit is to analyse a variety of samples such as drugs for their purity by pharmacopoeial tests, foodstuffs for their nutritional value and others for bioavailability of antibiotics etc.

The Testing Unit is recognised by the Food and Drug Administration, Government of Maharashtra, as an approved laboratory for testing pharmaceutical drugs, cosmetics etc. Activities of the unit during the current year are narrated below :

Prohibition and excise Section

The Prohibition and Excise Department, Maharashtra State, had sent toddy, Indian made foreign liquors, ganja, opium and bhang for analysis. The details of the samples analysed are provided in Appendix XIV.

Commercial samples for purity

Recently, the Haffkine Institute has been recognised by M/s. State Pharmaceuticals Corporation of Sri Lanka (Ceylon) as an approved laboratory for testing commercial pharmaceuticals and cosmetics. They have also approved the Institute as the inspecting authority for the purpose of issuing certificates of quality, quantity and loading of drugs to be exported from India to Sri Lanka. The samples received from commercial pharmaceutical firms were analysed according to the pharmaceutical procedure and Indian Standard Specifications.

Bioavailability of drugs

The Unit undertook bioavailability studies of antibiotics and other drugs by administering them orally. Antibiotics such as tetracycline, oxytetracycline, doxycycline, chloramphenicol, oleandomycin, ampicillin were tested for blood absorption.

Special studies

Food samples : A sample of imported U. S. A. wheat contaminated with weed seeds was analysed. The contaminated weed seeds were identified to be *Vicia* species and found non-toxic to the extent of 350 to 700 seeds/Kg. of wheat grain (i.e. about 10 g of seeds/Kg).

Hazards to public health due to air and water pollution

Haffkine Institute Team consisting of a Medical Officer and a Scientist visited Sangvi and Yeoli villages, Taluka Bhore, during the period 9th to 11th October 1975, in connection with the complaints from people living in

the neighbouring areas of Arlabs Limited. Investigations showed that there was no danger to health of the people of Sangvi and Yeoli villages due to effluents and gases let off by the Arlabs Ltd. However acidic fumes of gases accompanying smoke let off in the air without chimney arrangement by the factory could cause irritational coughing and sneezing in the people of Sangvi village.

Project work on pesticides

The Testing Unit undertook project work to test the tolerability of an organophosphorus pesticide (Zolone 35% EC) to human beings, cattle, goat and fowl, when used as an aerial spray application during the period 11th December 1975 to 29th December 1975. The conclusion following the field trial was that human volunteers (even when exposed thrice), cattle, goat and fowls exposed to the aerial spray of Zolone 35% EC at a concentration of 750 ml per acre, did not show any pesticide induced toxicity during the course of investigation.

In March 1976, three projects were assigned by M/s. Bayer (India) Limited, Bombay, to conduct studies on toxic hazards induced by their organophosphorus pesticide, Methyl parathion preparations, namely Metacid 50 and Folidal 2% dust. The field trials were conducted in Guntur and Prakasam Districts (Andhra Pradesh) during the period from 6th March 1976 to 28th March 1976. Results are being analysed.

CHAPTER V

LIBRARY

During the year, six meetings of the Library Committee were held to discuss matters pertaining to reorganisation of the library. The Committee members made useful suggestions for the improvement of the Library.

The Library participated in the international exchange programme sponsored by World Health Organization and obtained 85 issues of different journals to complete the volumes. During the year, 47 books were donated by the World Health Organization, CIBA of India Ltd. and others.

From January 1976, Library started subscribing to a new journal, viz. *Sabouraudia*.

The Library continued to participate in the Inter-library Loan Service. The extension of working hours from 5 p.m. to 7. p.m. was continued during the year. In addition to this, from January 1976, the Library is being kept open on Saturdays also from 9 a.m. to 5 p.m.

Collection of reprints

Collection of reprints and references on cholera and plague was brought up-to-date. Recently, similar work has been taken up on typhoid and it is in progress.

A few off-prints on the life of Dr. Haffkine were received and added to the Haffkine Biography Division during the year.

CHAPTER VI

SUMMARY AND OUTLOOK FOR FUTURE

The process of reorganisation has given an impetus to research activities of the Institute. Several new projects have been introduced and many new ones are being contemplated.

The institute has made remarkable strides in research in communicable diseases. Plague research has shown that though there is no endemic plague, the surveillance against this disease should continue. Guinea-worm research was mainly concentrated on intermediate host cyclops and the screening of several cyclopocidal agents. Several plant based mosquito larvicidal agents were screened for larvicidal properties against *C. fatigans*.

The synthesis of antiparasitic, antibacterial and antituberculosis agents was continued with fervour. Some of these compounds have given promising results in *in vitro* and *in vivo* screening.

Ceaseless attempts are on to develop new antifertility agents. The new antifertility agent LF now awaits human trials. The study of contraceptive hormones and their effect on metabolism progressed very well.

Research on venoms, animal and microbial toxins made a considerable advance. A cobra venom 'Toxoid' has been developed. Biochemical studies with various fractions of venoms were continued. Studies on diphtheria and tetanus toxins progressed very well.

The institute proposes to introduce several new departments for strengthening its research activities. It will very soon have a fully developed Department of Parasitology. Some of the new departments established recently *viz.*, Radiation Biology Unit, Department of Toxicology and Human Pharmacology, Clinical Research Division are getting ready for participating in our goal of serving the poor and alleviating the suffering. A unit for malaria research is being set up.

Several new training programmes are proposed to be introduced. Testing facilities are being expanded. A project to develop radioimmunoassay kits is being launched.

These are some of the major developments of the year 1975-76. Outlook for future appears bright when we glance through our achievements.

Appendix I

DEPARTMENT OF BIOCHEMISTRY

Routine biochemical and other special tests carried out during the year

Name of the test	No. of tests
<i>Blood Serum—</i>	
Amylase	19
Acid phosphatase	2
Alkaline phosphatase	71
Bilirubin	121
Calcium	6
Chlorides	20
Cholesterol	102
Creatinine	8
Icteric index	55
Non-protein nitrogen	7
Phosphorus (inorganic)	2
Proteins—Total	88
Proteins—Albumin	73
Proteins—Globulins	73
Sugar	404
Thymol turbidity	62
Urea nitrogen	84
Uric acid	12
Van den Bergh	27
	1,235
<i>Urine and Stool—</i>	
Acetone bodies	2
Albumin	3
Bile salts and pigments	172
Calcium	1
Occult blood (urine)	1
Porphyryne	2
Sugar	176
Urobilinogen	1
Total	358

Appendix I—contd.

Name of the test	No. of tests
<i>Cerebro-spinal Fluid (C.S.F.) and other body fluids—</i>	
C.S.F. chlorides	6
C.S.F. Proteins	10
C.S.F. Sugar	6
S.M. Test	5
Total	27
<i>Special Tests (Clinical)—</i>	
Catecholamines (urine)	5
Gastric analysis	12
Glucose Tolerance Test	26
Iron (serum)	1
Kidney function test	1
17-Ketosteroides (urine)	17
Lange's Colloidal Gold Curve (C.S.F.)	65
Lipids (serum)	2
Potassium (serum)	19
Protein-bound iodine (serum)	30
Protein by paper electrophoresis (serum)	22
Sodium (serum)	22
S.G.O.T.	135
S.G.P.T.	138
Triglycerides (serum)	2
Urinary calculi	8
Vinyl Mandelic Acid (urine)	11
Total	516
<i>Food Analysis—</i>	
Moisture	4
Proteins	4
Ash	4
Fat	4
Carbohydrates	4
Calories	4
Total	24

Appendix I—contd.

Name of the test	No. of tests
<i>Animal Sera/Blood—</i>	
Sugar	6
Bilirubin	3
S.G.O.T.	2
S.G.P.T.	2
Total	
<i>Summary—</i>	
Blood serum	1,235
Urine and Stool	358
C.S.F. and other body fluids	27
Special tests (clinical)	516
Food analysis	24
Animal blood and sera samples	13
Grand—Total	

Appendix II

CLINICAL PATHOLOGY

Routine investigations carried out during the year are enumerated below :

	No. of samples
A. <i>Histo-pathology</i>—	
Specimens received	1,548
Blocks prepared from the specimens	2,686
B. <i>Haematology</i>—	
Haemoglobin estimations	430
Total R.B.C. Count	410
Total W.B.C. Count	441
Differential W.B.C. Count	449
P.C.V. Estimations	13
E.S.R. Estimations	202
Prothrombin Time	7
Platelet count	6
Bleeding Time	7
Clotting Time	7
C. <i>Clinical Microscopy</i>—	
Urine for routine examination	307
Stools for routine examination	288
Semen examinations	11
C.S.F. for cytological examination	2
Other puncture fluids for cytological examination	7
Pregnancy Tests (Qualitative)	1,174
Pregnancy Tests (Quantitative)	168
D. <i>Bacteriology</i>—	
Blood cultures routine	6
Blood cultures for enteric organisms	320
Urine cultures for routine examination	159
Urine cultures for enteric organisms	59
Stool cultures, routine	12
Stool cultures for enteric organisms	115
Throat swabs for diphtheria and other organisms	120
Anaerobic cultures of operation theatre material	389
Toxin neutralisation tests	389
Animal pathogenicity tests	389
Smear for Acid Fast Bacilli	89

Appendix II—contd.

	No. of samples
Concentration of A.F.B. materials	71
Culture of specimens for tuberculosis	71
Guinea-pig inoculation tests for T.B.	21
Smears for Gonorrhoea	1,512
Cultures for Gonorrhoea	998
Miscellaneous cultural examinations	69
Antibiotic sensitivity tests	557
Antibiotic sensitivity tests for Gonorrhoea	355
Autovaccines	27
E. <i>Serology</i> —	
Widal tests	320
Weil-Felix Tests	320
Tests for Brucellosis	320
Paul Bunnell Tests	18
Vi Haemagglutination Tests	250
Gonococcal Haemagglutination Tests	450
V.D.R.L. Tests	328
Wassermann Tests	2
Rose Wealer Tests	565
Kahn Tests	16
Grand—Total	14,932

Appendix III

RADIATION BIOLOGY

Thyroid function studies on patients referred to this Institute were carried out during the year. The details are given below :

131

(a) I uptake studies :

(i) Total patients referred	89
(ii) Detected hyperthyroid	32
(iii) Detected hypothyroid	14
(iv) Detected euthyroid	43

(b) Thyroxine suppression test :

(i) Total cases diagnosed	8
(ii) Total patients tested	4
(iii) Detected hyperthyroid	2
(iv) Detected euthyroid	2

Appendix IV

SNAKE AND SCORPION VENOM PROCESSING

In all, 270·92 gms. of venom was processed and 343·10 gms. of venom was supplied for the manufacture of antivenin and for research during the year. Quantities of various types of venoms processed and supplied are shown below :

Snake Venom	<i>Quantity of venom processed</i>	<i>Quantity of venom supplied</i>
	gms.	gms.
Cobra	117·82	168·29
Krait	52·12	38·10
Russell's Viper	71·03	107·23
Echis	29·95	29·48
Grand Total.	270·92	343·10

The quantity of scorpion venoms processed and supplied is shown below

Scorpion venom	<i>Quantity of venom processed</i>	<i>Quantity of venom supplied</i>
	gms.	gms.
Black scorpion (<i>Palamnaeus gravimanus</i>)	4·19	8·96
Red Scorpion (<i>Buthus tamulus</i>)	3·04	1·00

Appendix V

STATISTICS RELATING TO STUDENTS

Students enrolled at the institute during the year 1975-76

	Higher Degree (M.D., Ph.D.)	No.
M.D.		
Pharmacology		1
Ph.D.		
Applied Biology		6
Biochemistry		5
Microbiology		9
Organic Chemistry		1
M.Sc.		
Applied Biology		4
Biochemistry		11
Microbiology		17
Organic Chemistry		8
Zoology		2
M. Pharm.		4
Other Courses		
Diploma in Medical Laboratory Technology		14
Institute's MLT Course		14
Total		96

Appendix VI

SHORT-TERM TRAINING COURSES

Ninety-five students attended short-term training courses during the year. Details of subjects offered and the number of students attending these courses are recorded here.

Clinical Pathology	22
Biochemistry	18
Testing of Drugs	18
Preparation of vaccines and parenteral solutions (Bacteriology and Media)	14
Blood Banking	20
Animal House	3

Appendix VII

DEGREE COURSES OFFERED

- M.Sc. : Microbiology, Biochemistry, Zoology, Organic Chemistry,
Applied Biology
- Ph.D. : Microbiology, Biochemistry, Zoology, Organic Chemistry,
Applied Biology and Pharmacology
- M.Pharm. : Pharmacology and Pharmaceutical Chemistry
- M.D. : Pathology and Pharmacology

DIPLOMA

- DMLT : Diploma in Medical Laboratory Technology

Appendix VIII

TRAINEES AND RESEARCH FELLOWSHIPS AND SCHOLARSHIPS

Trainees admitted :

Medical Laboratory Technology Course (M.L.T.)	14
Diploma in Medical Laboratory Technology (D.M.L.T.)	14
Short-term Training Courses	95

Number of Research Fellowships and Scholarships :

Government of India Research Training Scholarships	4
Government of Maharashtra Senior Research Fellowships	7
Government of Maharashtra Junior Research Fellowships	8
Government of Maharashtra Senior Research Scholarship	1
Government of Maharashtra Research Scholarships	3

Appendix IX

POST-GRADUATE TEACHERS

The following post-graduate teachers are recognised by the University of Bombay :

Name	Qualifications
Dr. B. B. Gaitonde	MD, MSc. (Med), FASc
Dr. M. B. Bhide	MD
Dr. F. L. Saldanha	MSc, PhD, FIC (Cal.)
Dr. A. J. Baxi	MSc, PhD
Dr. D. M. Renapurkar	MSc, PhD
Shri Y. S. Nimbkar	MSc, Dip Bac. (Manchester)
Dr. M. H. Shah	MSc, PhD
Dr. P. Y. Dighe	MSc, PhD
Dr. K. H. Dave	MD, DPB
Dr. S. S. Sabnis	MSc, PhD.
Dr. M. V. N. Shirodkar	MBBS, AB, ScD, PBk

Appendix X

VITAMIN-D CONTENT IN LIVER OF CHILDREN OF DIFFERENT AGE GROUPS

Age Group	Vitamin D/100 gm. wet Liver
Below 3 months	60.7 / μ gm (Range 23.8 to 116.3 / μ gm)
4 to 6 months	70.8 / μ gm (70.0 / μ gm)
7 to 9 months	Nil
10 to 12 months	69.7 / μ gm (Range 52.3 to 88.0 / μ gm)
13 to 18 months	56.98 / μ gm (Range 51.5 to 62.2 / μ gm)
19 to 24 months	Nil
25 months and above	81.1 / μ gm (46.2 to 110.8 / μ gm)

Appendix XI

BIOCHEMICAL PARAMETERS OF THE RAT SERUM AND RAT LIVERS AFTER THE EXPERIMENTAL PERIOD

	Group I (Low calcium)	Group II (Normal calcium)	Group III (High calcium)
Total serum Ca mgm/100 ml.	7.4	8.16	8.54
Serum alk. phosphatase Bodansky unit	2.9	2.55	4.56
Serum cholesterol mgm/100 ml.	107.6	126.9	85.5
Liver cholesterol	257.5	249.6	186.2
Liver phospholipids	3.503	5.746	5.686
Adenyl cyclase activity in brush border of the intestine PM/10 min. at 37°C/mgm of protein.	28.5	9.16	3.48

Research on Rickets (*See* page 13)

Appendix XII

CHOLERA STUDIES—NO. OF SAMPLES SCREENED

Samples	Nos.	Organisms isolated	
		<i>V. cholerae</i>	N.A.G. Vibrio
A. <i>Stool</i> —			
Human	2763	1	16
Animal	47	..	3
B. <i>Water</i> —			
Tube well	12	..	1
Open well	43	1	6
Ponds	2	..	1
Total . . .		2	27

Cholera carrier studies (*See* page 16)

Appendix XIII

RSV TUMOUR BLOCKADE IN CHICKS BY FORTY-EIGHT HOUR PF

Inoculum		Tumour-free chicks/ Total inoculated — Day 21 Post — RSV		Tumour-free chicks per cent — Day 21 Post — RSV	
Exp.	Control	Exp.	Control	Exp.	Control
PF(H)+RSV ^a	NP(H) ^d +RSV	8/10	0/13	80	0
PF(H) ^b +RSV	RSV	36/36	0/12	100	0
PF(A) ^c +RSV	RSV	1/19	0/11	5	0

a=RSV dose $10^{3.0}$ chick CAM PkFU/ml.

b=plasma factor in heparin

c=plasma factor in Alsever's solution

d=normal plasma in heparin

Appendix XIV

TESTING OF PROHIBITION AND EXCISE SAMPLES AND COMMERCIAL SAMPLES

Samples	No. tested
Prohibition and Excise	18
Toddy	180
Foreign liquors	599
Rectified spirit	6
Opium	4
Ganja	34
Bhang	13
Commercial samples	880
Bioavailability of drugs	17
	1,751

Appendix XV

HIGHER DEGREES AND OTHER RESEARCH PROJECTS

M.Sc.

Synthesis of furan derivatives incorporating piperazine ring as possible antimicrobial agents Shri V. S. KHOT.

Synthesis of thiazole derivatives of possible therapeutic value Shri B. R. COLAH.

Synthesis of 1, 3, 4 oxadiazoles and related compounds as possible antitubercular agents Shri V. S. TAMORE.

Role of Bandicoots in rabies epidemiology Smt. S. R. NAIR.

Studies in Plague Kum. M. SHANTA.

A study of the role of human patients and rabies infected rats in transmission of rabies Kum. S. G. BHOPATKAR.

Studies in Diphtheria Kum. MEENA R. BHADARKAR.

Ph.D.

Synthesis of 1, 2, 3, 4 tetrahydropyrimidines as possible chemotherapeutic agents Shri B. N. PALANDE.

Synthesis of pyrimidine compounds of possible biological and medicinal interest Shri K. Y. MAHAJAN.

Efficacy of Cholera Vaccines in experimental models Smt. SUSY CHERIAN.

Studies on immune response in mice in presence of steroid hormones and adjuvants Shri M. P. NAIK.

Biochemical studies on the venoms of Indian Elapid snakes Shri G. S. CHHATWAL.

Biochemical studies in Indian snake venoms ; particularly in Russell's Viper Venom. Shri R. C. KANKONKAR.

Biochemical and immunological study of human fibrinogen and cryoprecipitate (AHF factor VIII) Shri P. R. DICHWALKAR.

Oral contraceptive steroids and carbohydrate metabolism in rabbits Shri H. J. KULKARNI.

Epidemiological studies on Bancroftian filariasis Dr. W. N. GATLEWAR.

Peripheral autonomic transmission in the isolated rat stomach fundus and its modification by S-Methoxyindole compounds Shri A. Y. NIMBKAR.

Research projects under fellowships and scholarships.

Production of tetanus toxin Shri D. N. SHROFF.

Synthesis of Frusemide—a diuretic Kum. I. J. BANERJI.

Biochemical changes in experimental rabies Kum. R. M. BARIDE.

Studies on Rickets Shri H. S. VED.

Synthesis and development of anthelmintic compounds Shri P. P. DALVI.

Biological and immunological actions of Pertussis Toxins Shri S. S. JADHAV.

Cobra Venom Toxoid Dr. (Smt.) S. R. KANKONKAR

Biochemical and immunological studies of scorpion venom (Black and Red) Dr. (Smt.) S. R. KANKONKAR

HIGHER DEGREES AND OTHER RESEARCH PROJECTS—Contd

Immunological studies on leprosy Kum. S. W. AWACHAT.

Antifertility studies on *Lygodium flexuosum* Shri V. B. BABNE.

Studies in cotton rat filariasis Kum. S. C. RAMAMURTHI.

Studies on the characterisation of HIBOMA virus Shri J. M. DESHPANDE.

Fractionation and purification of antigenic fractions of hook-worm larvae and studying their immunodiagnostic value Kum. L. S. KULKARNI.

Synthesis of organic compounds of possible therapeutic value Shri C. B. NERURKAR.

Studies on antifertility activity of an indigenous drug and mechanism of action of IUCD Shri R. T. MAHAJAN.

Synthesis of thiazolyl derivatives of possible therapeutic value Shri B. R. COLAH

Sensitivity of *N. gonorrhoea* to antimicrobial agents Shri N. T. JOSHI.

Synthesis of thiazolyl derivatives of possible therapeutic value (antituberculosis agents) Shri A. M. PATIL

Preparation of oral toxoid and study of its immunological aspects Shri D. R. ASHTEKAR

Epidemiological survey of *Bordetella pertussis* Kum. S. R. KOLHEKAR.

Study of *Mycoplasma* Shri S. A. ANGADI.

Study of anaerobic cultures Kum. S. R. SALVEKAR.

Appendix XVI

WORKING OF THE LIBRARY

The following figures indicate the working of the library during the year.—

Number of outside readers visiting the library	Number of books and periodicals issued to our staff	Number of periodicals issued under inter-library loan service	Books and periodicals obtained for our staff from other libraries
6316	1662	196	62

Additions to library

Number of books added during the year	Number of volumes bound	Number of current periodicals subscribed	Current periodicals received free of charge	Number of reports received from scientific Institutions
198	436	218	159	69

Appendix XVII

PAPERS SENT FOR PUBLICATION

BANDISODE, M.S. and GAITONDE, B.B. : *Ascaris lumbricoides* : Mechanism of action of thiabendazole.

Indian Journal of Medical Research

BHIDE, M.B., NAIK, P.Y. and GHOOI, R.B. : Comparative studies on the pharmacological evaluation of vasicine and vasicinone.

Bulletin of Haffkine Institute

BHIDE, M.B., NAIK, P.Y., MAHAJANI, S.S. and GHOOI, R.B. : Studies on the anti-asthmatic activity of Mesua ferrea.

Bulletin of Haffkine Institute

CHAUDHARI, D.T., SABNIS, S.S. and DELIWALA, C.V. : Potential anticancer agents III Schiff bases derived from 4 [N,N-bis-(3-chloropropyl) amino] benzaldehydes

Bulletin of Haffkine Institute

CHAUDHARI, D.T., and SABNIS, S.S. : Potential anticancer agents, IV : Schiff bases derived from 4-[N,N-bis-3-(methylsulphonyl)-oxypropy, amino] benzaldehydes

Bulletin of Haffkine Institute

CHAUDHARI, D.T., SABNIS, S.S., PATEL (Smt.), M.R. and DELIWALA, C.V. : Synthesis and study of 4-(*p*-aminophenyl) thiazoles for *in vitro* antitubercular activity and as useful chemotherapeutic intermediates.

Bulletin of Haffkine Institute

CHAVAN, S.R., BHAT (Kum.), V.M., RENAPURKAR, D.M. and BHIDE, M.B. : A new larvicide from Acorus calamus Linn. (Areceae)

Bulletin of Haffkine Institute

COLAH, B.R., SABNIS, S.S., VAIDYA (Kum.), N.D. and BHIDE, M.B. : Synthesis of thiazolyl derivatives of possible therapeutic value (Anti-inflammatory agents). I

Bulletin of Haffkine Institute

DAVE (Smt.), J.K., FERNANDES (Smt.), Y. and GAWAND (Kum.), S.C. : Fluorescent Staining for Mycobacterium tuberculosis in tissue sections. Comparison with Fite Faraco procedure.

Bulletin of Haffkine Institute

GAITONDE, B.B., BHIDE, M.B. and JOSHI, R.S. : Studies on the interaction of piperazine and sennosides on isolated rat colon.

Bulletin of Haffkine Institute

GAITONDE, B. B. and JOGLEKAR, S. N. : Mechanism of neurotoxicity of cardiotonic glycosides.

British Journal of Pharmacology

GANAPATI, R., NAIK, S. S., SHAH, M. H., SHIRSAT (Kum.), L. S. and GAITONDE, B. B. : Clinical trial of DADDS in lepromatous leprosy.

Leprosy in India.

GHOOI, R. B. and BHIDE, M. B. : Effect of disodium cromoglycate on the formation of bradykinin.

Bulletin of Haffkine Institute

Appendix XVII—contd.

KANKONKAR (Smt.), SHARDA, KANKONKAR, R. C. and GAITONDE, B. B. : Immunogenic response to cobra venom toxoid prepared by Gamma-Radiation (Part-II).

Bulletin of Haffkine Institute

KHADSE, B. G., PATEL (Smt.), M. R. and SHAH, M. H. : New piperazine derivatives as antibacterial agents.

Bulletin of Haffkine Institute

KHADSE, B. G., SHAH, M. H., BHIDE, M. B. and BHAT (Kum.) V. M. : Synthesis and study of 2-heterocyclic aminopyrido (3, 2-d)—thiazoles as possible anthelmintic agents.

Bulletin of Haffkine Institute

KHADSE, B. G., SHAH, M. H., DELIWALA, C. V., BHIDE, M. B. and BHAT (Kum.), V. M. : Synthesis and study of 2-arylamino pyrido (3, 2-d)-thiazoles as possible anthelmintic agents.

Bulletin of Haffkine Institute

KHADSE, B. G., SHAH, M. H., DELIWALA, C. V., BHIDE, M. B. and PATHAK (Kum.) S. R. : Synthesis and study of 2- [4'-aryl-2'-thiazolylamino], pyrido (3, 2-d) thiazoles and 2-[p-(2' substituted-4' thiazolyl) arylamino] pyrido (3, 2-d) thiazoles as possible anthelmintic agents.

Bulletin of Haffkine Institute

KINI, R. P., PATEL (Smt.), M. R. and SHAH, M. H. ; Substituted salicylanilides and their antimicrobial activity.

Bulletin of Haffkine Institute

MUKERJI, S., DHABUWALA, J. B., FERNANDES (Smt.), Y., BHIDE (Kum.), S. N. and MURTHI (Smt), P. : Problem of typhoid and paratyphoid fever in Bombay.

Bulletin of Haffkine Institute

PATIL, A. M., KIRKE (Kum.), P. A. and CHAUDHARI, D. T : Synthesis and study of 4-(3-amino-4-methoxy-phenyl)-thiazoles for *in vitro* antituberculosis activity and as useful chemotherapeutic intermediates.

Bulletin of Haffkine Institute

RENAPURKAR, D. M., SARMA (Smt.), L. V., MENON (Kum.), SUSHILA and SANT, M. V. : Sérological studies in plague.

Bulletin of Haffkine Institute

SHEKAWAT, D. R., CHAUDHARI, D. T. and SABNIS, S. S. : potential anticancer agents —VI : acidhydrazones from p-(3-azaspiro, [5 : 5] undec-3-yl) benzaldehydes.

Bulletin of Haffkine Institute

VED, H. S., SHINDE, V. P. and AMBEGAONKAR. S. D., : Nutritive value of " Sukhadi " — A supplementary food.

Bulletin of Haffkine Institute

Appendix XVIII

PAPERS PUBLISHED

- BHIDE, M. B. and GHOOI, R. B. : " Letter to the Editor " in connection with the article " Atropine, sodium chromoglycate and thymoxamine in PGF₂ induced bronchoconstriction in extrinsic asthma ".
British Medical Journal, 1975, 3, 769.
- CHAUDHARI, D. T., SABNIS, S. S. and DELIWALA, C. V. : Potential anticancer agent—I. Schiff bases from benzaldehyde dimethanesulphonates.
Bulletin of Haffkine Institute, 1975, 3, 20-26.
- CHAUDHARI, D. T., SABNIS, S. S. and DELIWALA, C. V. : Potential anticancer agents—II. Schiff bases from benzaldehyde dimethanesulphonates.
Bulletin of Haffkine Institute, 1975, 3, 81-90.
- CHITNIS, D. S., DAVE (Smt.), J. K. and SANT, M. V. : Urinary Tract Infections—II. R-factors among urinary pathogens.
Bulletin of Haffkine Institute, 1975, 3, 44-48.
- DAVE (Smt.), J. K. and FERNANDES (Smt.) Y. : Adenomyosis Uteri—A study of 150 cases.
Bulletin of Haffkine Institute, 1975, 3, 159-163.
- GAITONDE, B.B., JOGLEKAR, S. N., NABAR, S.D. and KULKARNI, H. J. : Oestrogenic activity of *Pueraria tuberosa* (Vidharikand).
Bulletin of Haffkine Institute, 1975, 3, 53-56.
- GAITONDE, B.B. and KANKONKAR (Smt.), SHARDA, R. : Preparation of cobra (*Naja naja*) venom toxoid using gamma-radiations (Part-I).
Bulletin of Haffkine Institute, 1975, 3, 111-113.
- GAITONDE, B. B. and MAHAJANI, S. S. : Studies on the mode of anthelmintic action of tetramisole.
Bulletin of Haffkine Institute, 1975, 3, 33-37.
- GATLEWAR, W. N. and SANT, M. V. : Evaluation of Sawada's filarial antigen.
Bulletin of Haffkine Institute, 1975, 3, 102-106.
- IYER, S. NATARAJAN and GAITONDE, B. B. : *Giardia lamblia* — A simple method of cultivation.
Bulletin of Haffkine Institute, 1975, 3, 114-118.
- KHADSE, B. G., SHAH, M. H. and DELIWALA, C. V. : Synthesis and study of 2-(N⁴ substituted—N¹—piperazinyl) pyrido (3, 2-d) thiazoles, 5-nitro-2-(N⁴-substituted—N¹—piperazinyl) benzthiazoles and allied compounds as possible anthelmintic agents.
Bulletin of Haffkine Institute, 1975, 3, 27-32.
- KULKARNI, S. K., BAPAT, J. P., BAXI, J., KULKARNI, K. V., CHANDERKAR, N. G. and GAITONDE, B.B. : Evaluation of radio-immuno detection method for hepatitis B (Australia) antigen.
Bulletin of Haffkine Institute, 1975, 3, 107-110.

Appendix XVIII—contd.

MANSHARAMANI, H. J. : *In ovo* cataract-induction by rubella virus.

Bulletin of Haffkine Institute, 1975, 3, 164-166.

NERURKAR, C. B. and CHAUDHARI, D. T. : Synthesis of 2-(*p*-aminophenyl) thiazoles as useful chemotherapeutic intermediates.

Bulletin of Haffkine Institute, 1975, 3, 57-60.

SALDANHA, F. L. and BOMAN, T. J. : Studies on folic acid and liver regeneration.

Bulletin of Haffkine Institute, 1975, 3, 137-142.

SALDANHA, F. L., SANT, M. V., JHALA, H. I. and NIMBKAR, Y. S. : Ecological studies on *V. cholerae* and *P. vulgaris*.

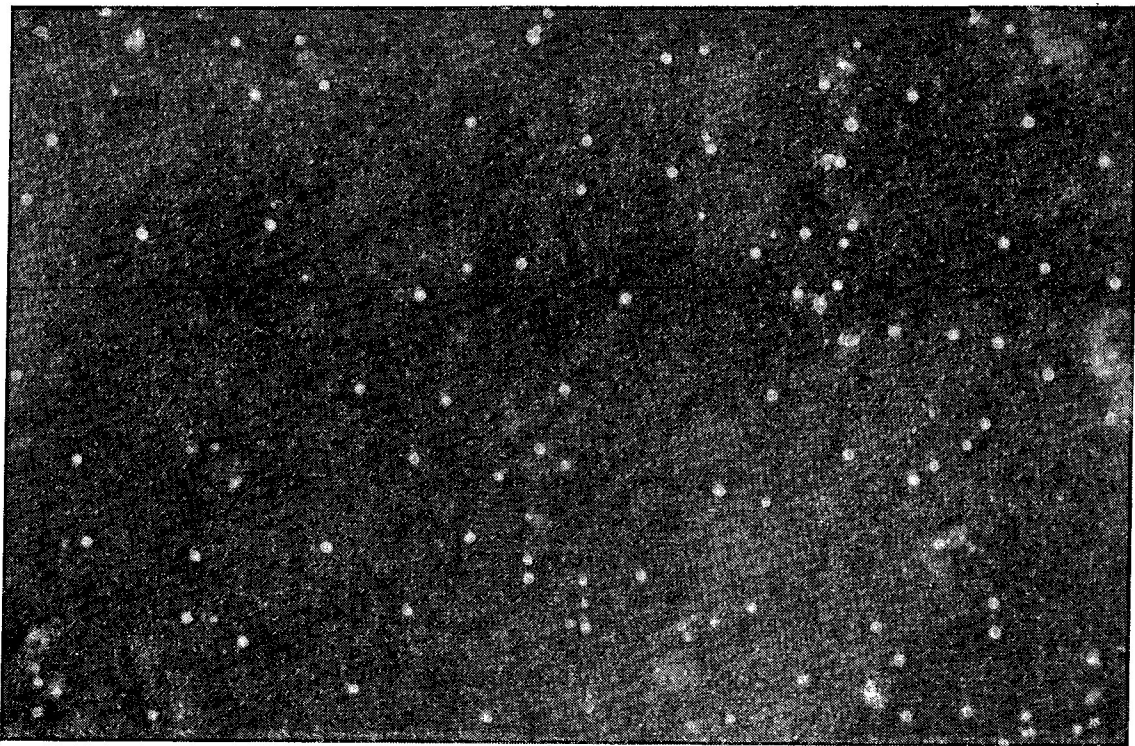
Bulletin of Haffkine Institute, 1975, 3, 38-43.

SALDANHA, F. L., SANT, M. V., JHALA, H. I. and NIMBKAR, Y. S., : Studies on bacterial interaction between *V. cholerae* and *Strep. faecalis*.

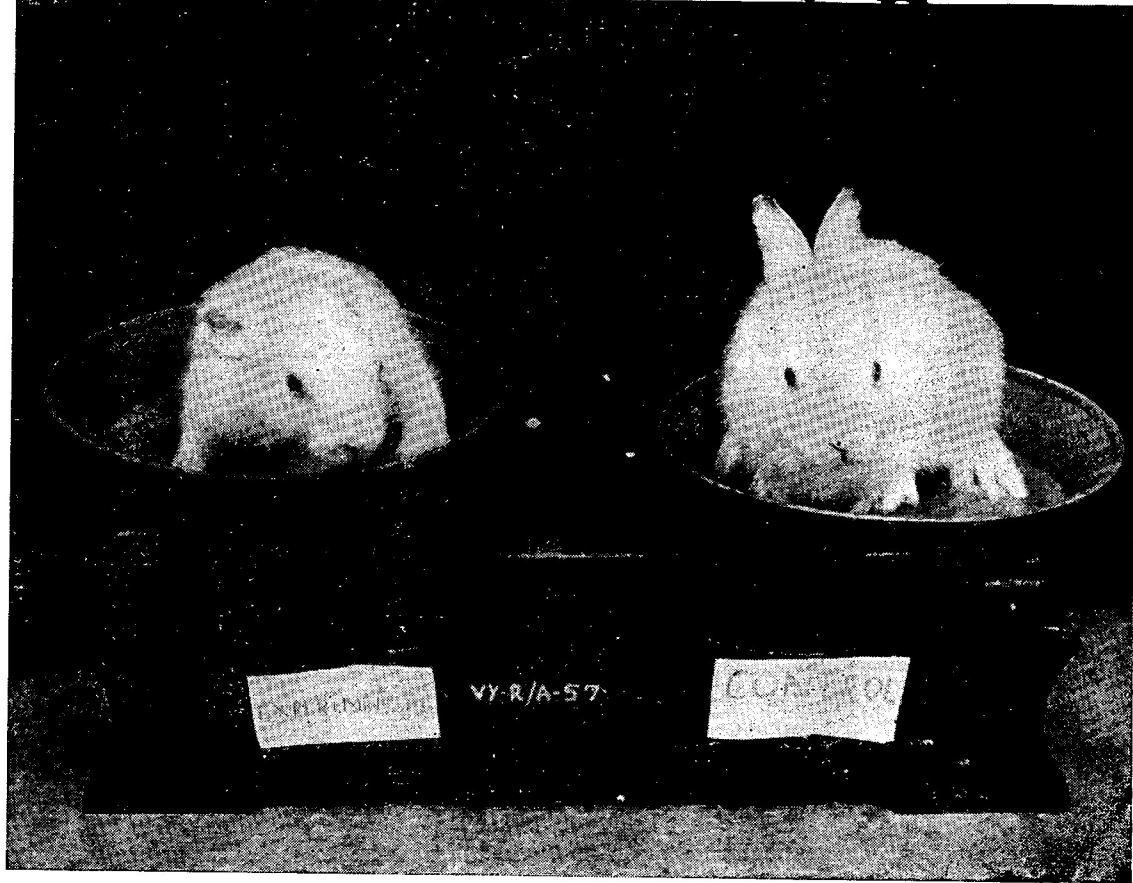
Bulletin of Haffkine Institute, 1975, 3, 91-96.

SHINDE, V. P., AMBEGAONKAR, S. D. and NIMBKAR, Y. S. : A simple commercial method of preparation of the casein hydrolysate medium for the cultivation of cholera-genic vibrios.

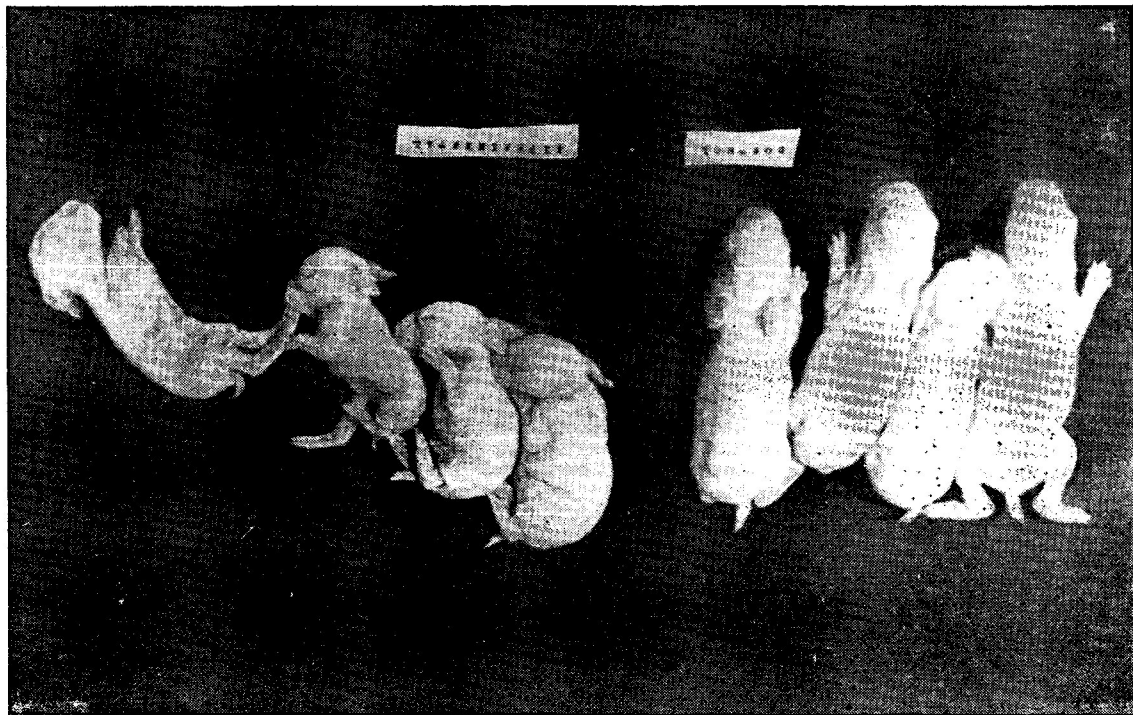
Bulletin of Haffkine Institute, 1975, 3, 119-127.



Electronmicrograph of Hiboma-I showing 20 nanometer virus particles (magnification 1,29,000)



Chronic experiment—experimental animal stunted (runting) due to Chronic Hiboma-I Hepatitis. Inactivated virus-injected healthy control. Both animals 45 days of age, inoculated at three days of age.



Experimental and control groups of infant rabbits clearly showing the severe disease produced in the virus-injected experimental animals.

