

**Annual
Report of the
Haffkine Institute**

1986-87



HAFFKINE INSTITUTE
PAREL, BOMBAY 400 012
INDIA

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CHAPTER I

INTRODUCTION

The year 1986-87 experienced similar financial problems as reported in the previous years. Efforts are underway for obtaining core grants from Government/Government funding bodies.

The research activities continued with the help of some grants received through research promoting organisations like Department of Science and Technology, Government of India; Indian Council of Medical Research and private commercial organisations. The following are the highlights of the various activities during the year under report.

Research.

The department of Bacteriology conducted genetic studies on industrially important bacterial culture and their phases.

The Biochemistry department in their investigation of the protective mechanism of *B. pertussis* extract in alloxan diabetic mice found a significant decrease in hyperglycaemia. In addition, both the recovery in SOD levels and decrease in lipid peroxidation in pancreas were significant indicating the protective effect of *B. Pertussis* in pancreas.

The Chemotherapy department in their search for Chemotherapeutic agents against malaria, fungal infection, tuberculosis and other bacterial infections synthesised numerous compounds and tested their *in Vitro* activity and some *in vivo* activity. Amongst them N-(2 Mercapto-4, 5-dichlorophenyl)-N-P-ethoxy phenyl thiourea exhibited antitubercular activity. Compounds of the 4, 6-diamino-1, 2-dihydro-1-(Substituted)-aryl-2', 2'-dialkyl or aryl S-triazines were synthesized and tested against *P.berghei* for anti-malarial activity. Two of the compounds showed 80-100% curative effect, both orally and subcutaneously in mice. Compounds of 5,6-Dichloro 2-substituted (thio) benzimidazoles showed promising antimalarial activity which are being further confirmed.

The Clinical Pathology and Immunology departments in their study of immune regulation in Salmonellosis have shown that the effects of interferon on immune response depended upon temporal relationship of interferon treatment with immunisation. Whereas interferon inducer given prior to immunisation enhanced the immune

response, the same given after immunisation suppressed. In their immunological studies in viral hepatitis they found that sizable adult population is susceptible to hepatitis B and that heterosexual mode of transmission is likely to be an important epidemiological factor in the community. The most important cause of fulminant viral hepatitis was found to be NANB hepatitis when samples of fulminant viral hepatitis cases were screened for markers.

To study the regulation of immune response to mycobacteria, the role of antigen presentation in generation of suppression of cell mediated immunity was studied. The study suggests that the difference in the immunogenicity between slow growers like *M. tuberculosis* H₃₇RV and rapid growers such as *M. vaccae* to be due to the inability of peritoneal cells to present rapid grower antigen efficiently.

The phytochemistry unit in their investigations with indigenous plants found that *pithecellobium duice* Roxb Benth leaves (chinch) and *Lasiosiphon eriocephalus* to possess considerable mosquito larvicidal activity.

The department of Virology studied the effect of PF dilution on sarcoma blockade in quail. It was found that with increase in PF dilution, there was gradient decrease in the blockade. Significant blockade of the sarcoma was observed upto the 1 : 64 dilution of PF. They also studied if PF is produced in the Japanese quail, on induction with rabies virus. Quails infected with RV-CVS subcutaneously, were bled after 24, 48 and 36 h. The plasma samples were tested for anti-RSV activity in quails. All the 3 plasma samples failed to inhibit sarcoma formation in quails. Antiviral spectrum of PF has been studied by earlier research workers. It was found that PF exhibited antiviral activity against the RNA viruses but not DNA viruses. This was confirmed in their experiment by studying the antiviral action of PF against untested RNA viruses (Newcastle disease, west Nile and coxsackie type B₂) and untested DNA viruses (Buffalo pox, inclusion body hepatitis and chick embryo lethal orphan virus). Blockade of NDV, WNV and coxsackie type B₂ by PF was observed but no blockade by PF could be demonstrated for the DNA viruses.

Activities of the WHO/NICD surveillance centre for viral hepatitis included survey and study of outbreaks of viral hepatitis in Bombay, Pune and Kolhapur districts hospitals. Routine survey of voluntary blood donors from Haffkine Bio-Pharmaceutical Blood Bank and multi-transfused cases from Haffkine transfusion service also was carried out. Outbreaks were also reported at Roha (Dist. Raigad), Gangapur (Dist. Nasik) and Khopoli (Dist. Raigad).

The Department of the Zoonoses investigated the possible induction of immunity in mice against angiostrongyliasis with UV irradiated larvae. Larvae exposed to U.V. irradiation for 5 or 5 minutes induced 91% and 97% protection against subsequent infection. They also studied the non-specific protection in experimental filariasis after exposure to *Setaria cervi* antigen alone and with Diphtheria-Tetanus, Tetanus, Diphtheria-Pertussis-Tetanus BCG vaccine, and polyvalent antsnake venom serum as adjuvant. The study showed varying degree of reduction in adult worm load and micro-filaremia.

Testing :

One of the prime functions of the Institute is to conduct various tests on products submitted by the Prohibition and Excise department of the Government of Maharashtra, and samples such as drugs, biologicals, food additives, disinfectants, pesticides, cosmetics, plastics etc. In all 5267 samples of various types were tested during the year under report.

Patient oriented services :

Clinical Pathology and biochemistry departments accept clinical samples from patients for investigations. In all 3344 samples were investigated in the two departments. Various hospitals, charitable and private organisations from Bombay, suburbs and other places utilised their services (Appendix IIIA).

Patients of various age groups are immunised against Cholera, Typhoid, Diphtheria, whooping cough, Rabies and poliomyelitis in the immunisation clinic against nominal charge. In all 1,531 patients attended the clinic and 1,513 patients immunised (Appendix IX).

The Immunohaematology department carried out 933 blood transfusions and 105 Rh titre and grouping tests (Appendix V).

Training programme :

The Institute offers various courses and training programmes for medical and paramedical personnel (Appendix XI). A list of students registered during 1986-87 for the different degrees/courses and students who have successfully completed their thesis and obtained their degrees are given in Appendix XIII and Appendix XIV. Appendix XV gives the list of recognised University teachers at the Institute.

Sponsoring Research Bodies :

The Department of Science and Technology, Indian Council of Medical Research, Government of India, Lady Tata Memorial Trust and the Central Council of Research in Ayurveda and Siddha system and Maharashtra Council on Science and Technology Education and Employment Department, Government of Maharashtra, Mantralaya, Bombay-400 032 financed some of the Research projects. The Institute is thankful and gratefully acknowledges their financial support.

Administrative Bodies :

The Governing Council presided over by the Hon'ble Minister for Public Health, Government of Maharashtra met once during the year under report. Apart from this the executive committee (Administration), and the Teachers' Council met several times to provide guidelines for the smooth functioning of the Institute.

CHAPTER II

GENERAL DEPARTMENTAL ACTIVITIES

Bacteriology :

Five students were registered for M.Sc. (Part II) in microbiology by papers. Three students secured first class and two second class. Five students were registered for M.Sc. (Part I), and all secured second class. Training programmes were also conducted for D.M.L.T., short-term training and Drug analysis students.

Routine testing activities were also carried out. Bacteriological analysis of various products were undertaken. Water samples were analysed and water filter tested. Lyophilization of cultures was also undertaken (Appendix I).

Biochemistry :

The regular training courses in M.Sc. Biochemistry (by papers Parts I and II, D.M.L.T. and short-term courses in biochemistry) were conducted. The department is recognised as one of the principal training centres for advanced biochemistry. Lectures on special topics were held for M.Sc. (Part I) students of Bombay University at Haffkine Institute during the second term of the year.

The department carried out clinical investigations of samples referred by various city hospitals, private practitioners and medical officers of the Institute. The total number of samples tested are shown in Appendix II.

Chemotherapy :

Four students are working for their Ph.D. degree in Medicinal chemistry. Three students are registered and working for their M.Pharm. degree in pharmaceutical chemistry. Two students have submitted their thesis for M.Pharm degree in pharmaceutical chemistry and one for Ph.D. degree to the Bombay University. Fifty compounds from other Institute were tested for *in vitro* anti-tubercular activity and 50 compounds were analysed for Carbon, Hydrogen and Nitrogen. Eleven patents for substituted maleimide

derivatives have been filed with the Patent Office, Government of India.

Clinical Pathology, Immunology :

The department of clinical pathology received specimens from various hospitals and agencies (Appendix IIIA) for investigation. The services offered covered general areas of cytology of the various body fluids, routine haematological examination, diagnostic serology, bacteriology, mycology and histopathological examination of biopsies (Appendix III).

The D.M.L.T. and short term training courses were conducted. The staff participated in the integrated Bombay University teaching programme for M.Sc. (Microbiology) M.D. (Pathology).

Human Pharmacology, Bioavailability and Radiation Biology Units :

During the year 1986-87 the Human pharmacology and bio-availability unit undertook routine testing of all incoming samples for blood absorption studies in human volunteers. The list of pharmaceuticals whose samples were accepted for the studies is given in Appendix IV. The Radiation biology unit carried out radio immunoassay of Tri-iodothyronine (T3), Thyroxin (T4) and Thyroid Stimulating Hormone (TSH) for the referred cases. Twenty referred cases were analysed.

Toxicology :

The Toxicology department was actively engaged during the period 1986-87 in toxicological evaluation of different types of pesticides, drugs, chemicals and cosmetics (Appendix VIII). These samples were referred by various industries. The department was also involved in training and teaching programme of Drug Analysis and Post graduate courses.

Virology :

Amongst the routine activities of the virology department, the immunisation clinic renders important public service. In all 1,531 patients attended the clinic during the period for vaccination. The vaccines administered and the number of patients vaccinated are given in Appendix IX. Presently vaccines like purified chick embryo cell rabies vaccine (PCEC), Human diploid cell vaccine (HDCV),

measles, mumps and rubella (MMR) and hepatitis B vaccines are also being given.

The clinical virology section of the department commenced working activity and the following diagnostic tests were performed. Four patients were tested for Rubella IgG and IgM antibodies by ELISA method. Three blood samples were tested for cytomegalovirus IgG antibody. Scrapings from lesions of 3 patients were processed for herpes simplex virus isolation in tissue culture.

Zoonoses :

The venomous animals unit building of the department was renovated to improve the facility for housing more animals and for public demonstration of venom extraction for visitors. Some of the chemotherapeutic agents synthesised by the Chemotherapy Department and Ayurvedic preparations were screened for anti-malarial activity in *in vivo* system. A number of commercial formulations and synthetic products were examined for their efficacy as vector control agents. Cholecalciferol, a new rodenticide, was evaluated for its rodenticidal activity against Indian species of commensal rats. A large number of snakes and scorpions were maintained for obtaining their venom and for research. The total quantity of venom produced and supplied to various organisations is shown in Appendix X.

Plague surveillance activity was continued. Out of 5,05,893 rodents received 94,229 were examined for plague. Susceptibility status of rats to experimental plague infection was assessed by carrying out experimental plague infection of rats by using a virulent strain of *Yersinia pestis* (195/p).

Academic Activities, Honours and Awards :

The Organon Research Centre, Calcutta invited Dr. B. G. Khadse, the Head of the Department of Chemotherapy to Calcutta on 28th to 30th September, 1986 to present a talk on the synthetic anthelmintic agents. Dr. B. G. Khadse alongwith his students attended the 38th Indian Pharmaceutical Science Congress held at Ahmedabad, 20th to 22nd December, 1986 and VIIth National Congress of Parasitology at Ravi Shankar University, Raipur on December 27th

Dr. V. Ramakrishna Rao, Head of the Department of Toxicology, as a W.H.O. adviser attended the International Programme on Chemical Safety, Task group on Environmental Health Criteria for Phosphine and selected metal phosphides at Geneva from 17-21 November, 1986.

Dr. R. Deshmukh, Medical Officer, incharge of the immunisation clinic attended the Association of Physicians of India conference at Hotel President, Bombay and delivered a lecture entitled "Recent advances in Antirabic vaccination".

CHAPTER III

RESEARCH PROGRESS
BACTERIOLOGY

1. Genetic recombination between enteric species with a view to obtain new strains with high academic and/or applied potential :

Various parameters governing transformation of *S. typhi*, Ty 21 a with pBr 322 DNA were studied in detail.

2. Genetic studies on industrially important bacterial cultures and their phages :

Attempts were made to isolate phage resistant mutants of *C. simplex*. Mechanism of resistance of *C. mediolanum* was investigated.

BIOCHEMISTRY

1. Biochemical studies on the mechanism of action of the hypoglycaemia causing factor (HCF) from bordete a pertussis :

The fact that *B. pertussis* preparations are able to attenuate the hyperglycaemia of alloxan diabetes seemed to indicate a probable protective role for the extract in pancreas against tissue damage due to alloxan. It is well known that alloxan-induced diabetes results from the generation and release of free radicals. These cause lipid peroxidation and other damaging effects like DNA strand breaks and inhibition of proinsulin synthesis in pancreatic islets. Alloxan is also known to inhibit the activity of the protective enzymes in tissue including superoxide dismutase (SOD) which forms the cell's first line of defence against oxidative damage.

Hence it was decided to investigate the protective effect of *B. pertussis* extract in alloxan diabetic mice. Several lots of albino mice were injected with known quantities of purified *B. pertussis* std. vaccine strain No. 25525) extract. This was followed by injection with a sublethal dose of alloxan given intravenously. At the end of 72 h a significant decrease in hyperglycaemia

was observed. In addition, there was a significant recovery in SOD levels together with significantly decreased lipid peroxidation indicating the protective effect of **B. pertussis** preparation in pancreas. It is noteworthy that this protective action is significantly different from that reported for several drugs and alcohols which only lower the hyperglycaemia of alloxan diabetes without any effect on the enzyme levels. This work has been accepted for publication. Studies are being undertaken to assess the overall protective effect of the **B. pertussis** preparation on other intracellular enzymes like glutathione peroxidase, catalase and glucose-6-phosphate dehydrogenase which are all involved in protection in the tissue against oxidative damage.

CHEMOTHERAPY

The principal activities in the Department are the synthesis and testing of biological properties of newly synthesized organic compounds. These compounds are tested for their antimalarial, Anthelmintic, Antifungal, Antibacterial and Antitubercular activities.

1) 5,6-Disubstituted-2-Alkylamino or arylamino benzothiazoles :

Some of the promising compounds from this series and reported in the previous annual report (1985-86) have been tested by *in vivo* procedure as anti T.B. agent, at Central Drug Research Institute, Lucknow, however they failed to show any favourable results, so this work was stopped.

2) N-(2-Mercapto-4,5-disubstituted-phenyl)

-N'-substituted phenyl thioureas :

New 40-50 novel thiourea derivatives were synthesized and tested for their antimalarial and antitubercular activities. Among these compounds one compound namely N-(2-mercapto-4,5-dichloro phenyl)-N'-p-ethoxy phenyl thiourea was tested thoroughly for its antitubercular activity. It exhibited highest activity i.e. 0.6 µg/ml conc.

3) 4,6-Diamino-1,2-dihydro-2,2-Alkyl :

or Aryl substituted s-Triazines :

Cycloguanil 4,6-diamino-1,2-dihydro-1-(p-chlorophenyl)-2,2-dimethyl-s-triazine is a known antimalarial.

In this line, new 4,6-diamino-1,2-dihydro-1-(substituted)-aryl-2,2-dialkyl or aryl *s*-triazines were synthesized and tested against *P. berghei* for antimalarial activity in the mouse model by Rane's test and by Peter's 4-day's test.

Out of 18 compounds synthesized, two compounds showed 80-100% curative effect at the dose of 5 mg/kg x 4 both orally and subcutaneously.

4 Synthesis and Antimalarial activity of some New 4,6-diamino 1,2-dihydro-1-(p-substituted -2,2-dimethyl-*s*-triazine hydrochloride :

Compounds with the *s*-triazine moiety as the basic nucleus have been synthesized and tested for their *in vivo* antimalarial action against rodent malarial strain *P. berghei* in mice.

The active compounds showed 80-100% elimination of parasitemia in mice 40 days post infection at a dose of 5 mg/kg x 4 by the Peters' test. One of the active compounds taken for preliminary acute toxicity study showed LD₅₀ of 190 mg/kg.

5 5,6-Dichloro-2-substituted (thio) benzimidazoles :

In this series new compounds are synthesized beginning from basic raw material available in the laboratory. These compounds were screened for antimalarial activity against *P. berghei* in mice.

5,6-Dichloro-2-(p-bromo benzyl)-thio-benzimidazole has shown antimalarial activity at 20 mg/kg body weight. Further investigations are in progress.

CLINICAL PATHOLOGY

Study of immune regulation in Salmonellosis :

Earlier we had reported that outcome of immunisation depended upon routes of immunisation and that different subsets of effector T cells were generated due to differences in the regulatory cells triggered by different routes. Further we had shown that these differences were due to differences in the presenting efficiency of antigen presenting cells (APC) encountering the antigen.

Employing treatment with interferon inducer such as poly I:C it was shown that the interferon improves the presenting

efficiency of APC. Further it was shown that the improvement in presenting efficiency was related to the duration of action of interferon on APC. We also showed that the effects of interferon on immune response depended upon the temporal relationship of interferon to immunisation; the interferon inducer given prior to immunisation enhanced the immune response, the same given after immunisation suppressed it. This project received a fellowship grant from I.C.M.R. The study has now been concluded.

2. Study of DTH eliciting antigen/s of *S. typhi* :

From the sonicate of *S. typhi* by repeated gel filtration chromatography, an antigenic preparation was obtained that could elicit DTH response. This preparation was found to be composed of several bands on isoelectrofocussing.

Isoelectrofocussing of the above preparation on several analytical media and combinations of ampholines was attempted. The DTH eliciting antigen was found to be present in the proteins with pI ranges of 6-8. However the bands were hazy and trails of adjoining bands merged with one another making purification difficult. This was identified to be due to polysaccharides present in the sonicate, which could not be separated from proteins by physicochemical methods.

The sonicate was then subjected to papain digestion before analytical electrofocussing. A great improvement has been observed. This approach is now being pursued for purification of the antigen.

3. Immunological and epidemiological studies in viral hepatitis :

1) Regulation of immune response to hepatitis B surface antigen (HBsAg) — role of anti-idiotypic response :

It has been observed that immune response to HBsAg is delayed in acute hepatitis till 3rd-4th week after the onset of the disease and is absent in chronic hepatitis B virus (HBV) carriers. Hence an investigation to study expansion of idiotype and anti-idiotypic network related to HBsAg was undertaken.

Though immune response to HBsAg was suppressed in early phase of acute hepatitis B and chronic HBV carriers, T cell response to anti-HBs idiotype was found to be well evolved as judged by

LM and LTT response to affinity purified human antibody to HBs Ag anti-HBs). In acute hepatitis B only one out of 50 cases studied showed anti-idiotypic antibody. Ten out of 38 chronic HBV carriers showed anti-idiotypic antibodies.

Immunological studies in chronic HBV carriers :

Markers of HBV infection, immune responses against them and levels of serum alanine aminotransferase (SALT) were studied in 38 chronic HBV carriers, in an attempt to correlate immune response with morbidity.

Out of 38 carriers 18 were asymptomatic carriers and 20 were cases of chronic liver disease (CLD). Significant relationship was observed between T cell response to hepatitis B 'e' antigen (HBe Ag and elevated SALT levels but only in HBeAg/HBV-DNA positive chronic asymptomatic carriers. No such relationship was observed in CLD cases, which could be because they were all cirrhotics and liver necrosis is multifactorial once cirrhosis sets in.

Lymphocyte infection by HBV and its consequences on immune response to HBV :

Peripheral blood lymphocyte DNA of 27 cases of acute hepatitis and 27 chronic HBV carriers was subjected to Dot-Blot DNA-hybridisation for detection of HBV genome. 17 cases of acute hepatitis and 11 cases of chronic HBV infection showed HBV-DNA in the lymphocyte.

PHYTOCHEMISTRY

The following plant material was collected from Pune, and Satara District.

- (1) **Pithecellobium dulce** Roxb Benth leaves (Chinch)
- (2) **Lantana camara** leaves (Tantan)
- (3) **Ixore coccinea** leaves (Banduk)
- (4) **Ficus bengalensis** leave (Vad)
- (5) **Pongamia pinnata** leaves (Karanj)
- (6) **Annona squamosa** leaves (Sitaphal)

Out of these plants **Pithecellobium dulce** leaves were powdered to uniform mesh, and extracted in soxhlet with hexane, ethyl-acetate and methanol.

Hexane extract was dried on water bath and evaluated for mosquito larvicidal activity with 0.01, 0.02, 0.03, and 0.04 percent concentration resulted in 88, 92, 100 and 100 percent mortality respectively. The same hexane extract was subjected to column chromatography using silica-gel. Elution was done with benzene.

benzene : methanol (90 : 10), benzene : methanol (80 : 20)
and

benzene : methanol (50 : 50).

Out of these benzene elute was dried on water bath and gummy material was crystallized using benzene acetone mixture. The gummy material was dissolved in benzene and acetone mixture by heating on water bath. It was then allowed to come to room temperature. It was observed that white crystalline material separated. This was filtered using whatmann Paper No. 1. The solid material was dried and evaluated for mosquito larvicidal activity.

It was noted that 0.004, 0.006, 0.008 and 0.01 percent concentration produced 88, 92, 100 and 100 percent mortality of mosquito larvae of *Culex pipiens fatigans*.

toxicological studies of petroleum ether extract of *Lasiosiphon oriocephalus*

Petroleum ether extract of *Lasiosiphon oriocephalus* Ramatha showed considerable mosquito larvicidal activity (0.004 percent concentration 100% mortality). Hence it was taken for toxicological study.

Acute toxicity study in mice :

Mice weighing between 18-20 gm were taken for this study. Petroleum ether extract was made suspension by using tween 80 and fed to mice with feeding needle. It was fed at dose level 40, 60, 80, 100, 120 mg/kg. to five mice and their physiological changes and mortality were observed for 7 days. First dose did not show any mortality whereas 20, 40, 60 and 100 percent mortality was observed with remaining doses.

RADIATION BIOLOGY UNIT

In vitro antiviral activity of Indigenous plants *P. niruræ* & *Elaeagnus*, supposed to have activity against Hepatitis viruses was studied.

The concentration of HBsAg in carrier plasma was detected by means of Radioimmunoassay and was subsequently allowed to react with extracts of above plants at various concentrations and at variable temperatures and intervals of incubation.

The concentration of virus (HBsAg) in sera samples such treated was estimated once again by Radioimmunoassay method. However the results did not show any reduction or inactivation in the concentration of HBsAg *in vitro*.

The studies are being continued further.

TOXICOLOGY

Teratogenic studies on Indigenous pesticide formulations :

Pesticides are generally used as formulations consisting of Technical grade material along with solvents, emulsifiers, stabilizers and other additives. Because of variation in percentage of technical grade material in different EC formulations, the levels of solvents and other additives also vary resulting in possible differences in toxicity. The available data regarding potential teratogenic hazard of the formulation to pregnant females is inadequate.

The present study was undertaken to evaluate the teratogenic effects of a widely used indigenously manufactured formulation Dimethoate 30 EC in rats. Dimethoate is also available as other concentration such as 40 EC. The teratogenic potential of different concentrations though widely used have not been fully evaluated. The study is in progress.

VIROLOGY

Research Activities :

Action of PF in heterologous system — (Japanese Quail):

Plasma factor (PF) has been shown to be active in heterologous human amnion cells against VSV and in mice against rabies and Coxsackie type B₂ viruses. Hence, the property of species specificity seems not to apply to PF, unlike the classical interferon. PF was further studied for its activity in the Japanese quail

(*Coturnix coturnix japonica*), against RSV. PF exhibited potent anti-RSV activity in quails. Two-fold serial dilutions of PF were prepared from 1 : 2 to 1 : 128, to study the effect of PF dilution on

sarcoma blockade in quail. With increase in PF dilution, gradient decrease in the blockade was observed. Significant blockade of the sarcoma was observed upto the 1 : 64 dilution of PF.

Next, it was felt necessary to study if PF is produced in the Japanese quail, on induction with rabies virus. Quails injected with RV-VCS subcutaneously, in the wing web tissue, were bled after 24, 48 and 96 h. The plasma samples were tested for anti-RSV activity in quails. All the 3 plasma samples failed to inhibit sarcoma formation in quails.

Antiviral spectrum of PF :

Previous research workers have studied the antiviral spectrum of PF against some RNS (Influenza, Sendai, Rous sarcoma and vesicular stomatitis), and some DNA (Vaccinia, Fowl pox and Herpes) viruses. They reported that PF exhibited antiviral activity against the RNA viruses studied, the DNA ones being unaffected.

To lend further supporting evidence to the findings of previous workers, the antiviral action of PF against an additional number of these, hitherto untested, RNA viruses (Newcastle disease, West Nile and Cocksackie type B₂) and three, hitherto untested DNA viruses (Buffalo pox, Inclusion body hepatitis and chick embryo lethal orphan virus) was studied.

Statistically significant ($p < 0.001$) blockade of NDV, WNV and Cocksackie type B₂ viruses was observed on simultaneous inoculation of these viruses with PF. On the other hand, BPV, BHV and CELO viruses showed no statistically significant and demonstrable blockade by PF. These results support the work done by previous researchers on the RNA-restricted and unique antiviral spectrum of PF.

Anti-West Nile Virus (WNV) activity of plasma factor (PF) in mice :

Experiments to see effect of PF on WNV in a heterologous system was done. Simultaneous inoculation of WNV and PF was given intracerebrally in 2 day mice. The PF used was undiluted and crude. It was seen that the overall mortality between day 0-21 is 28.5% in experimental group and 93.3% in control group. A significant difference between the two groups was thus established ($p < 0.001$).

Purification of PF :

5 ml of PF was given a 30% cut i.e. to 5 ml of PF, 0.85 g of $(\text{NH}_4)_2\text{SO}_4$ was added. This was then ultracentrifuged at 20,000 RPM at 4°C for $\frac{1}{2}$ hour. The pellet solution as well as the supernatants solution were desited by passing them through a column of G-25. The protein contents of crude PF, the pellet and supernatant were checked. The PF contains 5.08 mg/ml, pellet contains 0.540 mg/ml, and supernatant contains 0.330 mg/ml.

To check the activity of all the fractions, they were brought to the same concentration. The pellet showed 92% reduction as against 42% reduction of pocks when tested against BS-RSV.

Activities of the WHO/NICD Surveillance Centre for Viral hepatitis :

During the current year, the study of viral hepatitis was confined mainly to selected areas of reported outbreaks, as well as to hospitalised cases at Bombay, Pune and Kolhapur districts, respectively.

The outbreaks were reported at Roha (Dist. Raigad), Gangapur (Dist. Nasik) and Khopoli (Dist. Raigad) in the months of March 1987, December 1986 and June 1987, respectively. They were found to be due to contaminated well water supply in rural areas causing infection by the feco-oral route.

Besides, a routine survey of voluntary blood donors from the Haffkine Bio-Pharmaceutical Blood Bank and multi-transfused cases from our blood transfusion service, was also carried out.

An overall recent incidence of the viral hepatitis situation from all over Maharashtra State has been presented in Appendix-IXA. It summarises the incidence of viral hepatitis outbreaks in Maharashtra during the period of April-August (1986-1987). The period so selected covers water shortages in most of the districts, along with commencement of the rainy season, wherein chances of contamination of potable water are maximal. Usually, during this period, there is a peak in the incidence of water-borne diseases all over the State. The figures mentioned here are compiled from the reports of the Directorate of Health Services from all 40 districts of Maharashtra from urban, as well as rural areas.

Further, comparative data from the current, as well as the preceding year have also been presented to assess the magnitude of the problem faced by the State Health Authorities due to the increasing trend of viral hepatitis.

In 1987, the incidence of attacks of viral hepatitis in the State showed a significant rise (891) in rural areas, which is phenomenal and almost 8 times as compared to last year (133). This can be attributed to the present scarcity of water and drought affecting rather the rural setup than the urban, where the incidence shows a marginal increase. Once again, the highest incidence in both the years is between July-August, which covers about 50% of the total number of cases, confirming the contamination of well water with seasonal rains.

Appendix-IXB summarises mortality, in urban and rural Maharashtra, due to viral hepatitis. For the years 1986 and 1987, the period covered is between April to August, when the incidence of viral hepatitis was at its peak.

The incidence of viral hepatitis, in 1987, showed a 4-fold increase in rural areas, along with corresponding increase in the mortality trend.

The overall incidence of mortality in viral hepatitis cases is approximately 5% and there is not much variation in the given April-August 1987 incidence.

Appendix-IX(C) presents a summary of marker studies at the three locales mentioned earlier.

Gangapur (Nasik District) :

The village is 10 km away from one of our sentinel Centres situated at the Civil Hospital, Nasik and 200 km away from Bombay city.

Out of 40 samples of serum collected from cases for the study, 6 (15%) showed presence of HBsAg by ELISA, while 5 of the samples (12.5%) showed presence of anti-HAV antibodies. The majority (75%) of the cases, therefore, fall into the category of non-A non-B hepatitis. This was comparable to our findings for an outbreak reported during last year.

Roha (District Raigad) :

An outbreak occurred in the residential colony of a chemical factory. More than 200 persons had an attack of acute viral hepatitis.

Roha, a coastal place, is situated nearly 100 km from Bombay and has a predominantly industrial population.

In our study, 9% of the collected samples showed the presence of HBsAg, with only one individual showing HAV antibodies. Since 5-10% is the prevalent carrier rate in the population in Maharashtra, which we had reported earlier, it may be concluded that the infection was non-A non-B in origin.

Through our proper decontamination measures following identification of the source, the outbreak was brought under control.

Khopoli (District Raigad):

It is situated about 100 km. away from Bombay.

An outbreak occurred in one of their industrial estates, the possible course of which was water from a contaminated storage tank.

Since none of the samples was positive for either HAV or HBV, the outbreak was of non-A non-B origin.

Pune and Kolhapur :

The representative samples were collected from acute viral hepatitis hospitalised cases, in both of these urban areas. As many as 50% of the samples showed presence of HBsAg by ELISA with nearly 15% possessing anti-HBs, as well. Only 4% of the samples showed presence of anti-HAV, by ELISA.

Since the sample size showed a high prevalence of HBV further investigation is in progress to rule out spread of infection through injectibles, or other similar routes.

Voluntary Blood Donors :

These were mainly from the urban areas in and around Bombay City proper. It shows an HBsAg carrier rate of 2.6% in healthy voluntary blood donors, as against 4.8% which we have reported already from prison blood donors.

Mut transfused Cases :

A total of 26 thalassaemic children were screened for markers of viral hepatitis infection. These children had received transfusions from the donors mentioned above.

As many as 23% of the cases were positive for HBsAg, 15% having developed antibodies against HBV and 7.6% showing demonstrable antibodies against HAV.

ZOONOSES

Plague :

In all 5,05,893 rats were received from different wards of Greater Bombay. Out of 5,05,893 rats received, 94,229 rats were examined for evidence of plague. None of the rats showed evidence of presence of *Y. pestis* infection. Besides these rodents, serum samples of 1,080 rats were also examined for presence of antibodies to F₁ antigen of *Y. pestis*. These studies also did not produce any evidence of presence of antibodies to *Y. pestis* organisms thereby indicating absence of *Y. pestis* infection in the rodent population of Greater Bombay. Assessment of susceptibility status of various types of rodents to experimental plague infection revealed that while *R. norvegicus* continues to reveal resistance to experimental plague infection, there is considerable lowering in the resistance status of *R. rattus*. *Bandicota bengalensis*, on the other hand, continues to remain susceptible to plague.

Parasita :

In vitro cultivation of *Plasmodium vivax* and *P. falciparum*. In addition to RPMI 1640 complete medium 9 other tissue culture media were used for evaluating their suitability for *in vitro* cultivation of *Plasmodium vivax* and *P. falciparum*. These included the media like Gerbera medium, Nutrient mixture F₁₀, Eagle's MEM, White's medium, Nitsch medium etc. Of the various tissue culture media employed for the cultivation of malarial parasites Gerbera, Nitsch and White's medium supported the multiplication of parasites *in vitro*. The growth in these media was comparable to the growth obtained with RPMI 1640 medium. It was possible to maintain parasite strains for four weeks with these media. Suitability of these media for long term cultivation of plasmodia is being further evaluated.

In order to find out a strain which could produce higher parasite multiplication *in vitro*, 11 new strains of *P. vivax* and *P. falciparum* were established in the laboratory. However, none of the strains of *P. vivax* and *P. falciparum* produced parasitaemia higher than 5% *in vitro* and our search for the ideal strain continues.

Screening of antimalarial agents :

All 90 compounds synthesised at the Department of Chemotherapy were screened for antimalarial activity in *P. berghei*-mouse model system. Out of 90 compounds, 9 compounds revealed activity comparable to chloroquine. Further studies with these compounds are in progress.

Angiostrongyliasis :

Effect of UV irradiation, spleen cells and MLN cells on protective immunity in mice :

The UV irradiated larvae of *Angiostrongylus cantonensis* were used for the possible induction of immunity in mice against angiostrongyliasis. A single oral dose of 100 infective UV-irradiated larvae exposed for 5 or 15 minutes induced 91% and 97% protection against subsequent infection. Adoptive protection against *A. cantonensis* could also be transferred by spleen and mesenteric lymph node cells obtained from vaccinated mice.

Larvicidal effect of perbendazole on experimental infection of *Angiostrongylus cantonensis* in mice :

Perbendazole was given orally and subcutaneously to mice infected with *A. cantonensis* at different stages of infection. The subcutaneous route of administration was more effective than the oral one. On the 5th day after infection, the drug perbendazole had a higher efficacy than on the 10th day post infection. This finding shows that perbendazole had complete larvicidal effect at early stages of infection.

Filariasis :

Non specific protective studies in filariasis :

Many workers have investigated prospects for development of a vaccine against filariasis by using living, irradiated/attenuated microfilariae and adult worm homogenates, and have shown that

It may be possible to suppress filarial infections by these vaccines. In the present study, exposure of cotton rats to *Setaria cervi* antigen before their challenge with *Litomosoides carinii* infection conferred 'protection' against *L. carinii* infection. *S. cervi* antigen alone gave only 17.17% worm reduction, but with FCA and FICA, there was 33.33% and 12.67% worm reduction respectively. The use of *S. cervi* antigen with Diphtheria-Tetanus, Tetanus, Diphtheria-Pertussis-Tetanus and BCG vaccines as well as polyvalent anti-snake venom serum as adjuvants showed varying degree of reduction in adult wormload and microfilaremia. BCG and DT vaccines acted as excellent adjuvants and brought about 93.7% and 91.33% worm reduction and a significant decrease in m counts viz. 50.8 mg/cmm and 55.3 mf/cmm respectively. The other vaccines however, did not prove as successful as BCG and DT vaccines in inducing non-specific type of protection.

Hookworm infection:

The study of effector mechanisms responsible for immunity in *Ancylostoma ceylanicum*-hamster model system has been useful in providing valuable information on vaccine development. This study was therefore pursued in our laboratory. Hamsters were immunised with UV-irradiated larvae followed by the normal larval infection. Another experiment was set up with adult worm antigen emulsified with FICA and FCA adjuvants (x 4). Serum transferred from hyper immune hamsters provided a significant degree of protection against *A. ceylanicum* in mature recipient hamsters. Immune serum pools treated were effective. However the level of protection, as measured by challenge worm recoveries, ranged from 50 to 90%. Protection did not increase consistently with increasing volumes of immune serum, although as little as 5.0 ml/100 g of body weight afforded consistent protection against challenge infection. The specificity of the protection was suggested by the removal of this activity by absorption with heat killed larvae which have been shown to induce protection by immunization. Immunoglobulin-G obtained from the sera pool by means of ammonium sulphate treatment followed by DEAE ion exchange chromatography showed significant protection against *A. ceylanicum* infection in hamsters. *In vitro* sensitization of infective larvae with hamsters antibody failed to alter *in vivo* viability. Further observations are continued.

Research on venomous animals :**A. Snakes :**

The studies on the following aspects of snake biology are in progress.

1. Survivability of different types of snakes under laboratory conditions.
2. Studies on out put of venom of **Echis carinatus** and its toxicity.
3. Comparative studies on the yield of venom from snakes (Cobra, Krait, R. Viper and Echis) of different length groups at different intervals in captivity.

B. Scorpions :**Rearing of young black scorpions in captivity :**

Black scorpions, born on 23.8.1982, were reared in captivity in the scorpion cages. There were two sheddings. Four scorpions were found dead during the year. No courtship or mating was observed. An attempt is being made to mate these scorpions under laboratory conditions. For this purpose a cage with a new medium is being prepared to maintain the scorpions.

CHAPTER IV

GENERAL ACTIVITIES

Library :

The Library has a collection of books on biomedical sciences and related fields. It collects and provides information to scientists, and students in the field of Biochemistry, Communicable diseases, Immunology, Pharmacology, Zoonoses, Virology etc. of this Institute as well as to the institutions all over India.

The library remains open to readers on all working days except on Saturdays, Sundays and all Public Holidays.

There are 8,478 books in the library. The number of books added during the year were 498 out of which 158 were received as gifts from different organisations. About 332 books were purchased from the Grant-in-aid received from UGC (Rs. 2,00,000/- received in December, 1985-86).

The journals subscription for the year was divided amongst two agents by equal amounts of the total subscriptions. Total number of journals subscribed were 139. Total number of bound volumes in the library are 18,340. About 62 volumes were bound during the year.

Facilities :

1) Library provides reprographic facilities to its staff and outside readers. The library received xerox requisitions for approximately 11,370 pages during the year.

2) **Inter library loan:** The library borrowed 74 journals from neighbouring libraries for its staff and loaned 190 journals to other libraries in the city.

3) **Visitors:** About 3,003 outsiders visited the library for reference.

APPENDIX I
BACTERIOLOGY

Tests	Number
1. Supply and lyophilization of culture	46
2. Biocides including disinfectants and antiseptics ..	65
3. Filter candles	57
4. Gelatin samples	6
5. Beverages samples	79
6. Water samples	70
7. Eye drop samples	2
8. Culture identification	1
Total	326

APPENDIX II
BIOCHEMISTRY

Name of the body fluid	No. of tests
Blood	248
Urine	58
Special tests	142
TOTAL	448

APPENDIX III
CLINICAL PATHOLOGY

Tests						Number
A.	Histopathology	..	..	..	..	422
B.	Haematology	..	..	..	..	1003
C.	Cytology for malignant cells	..	..	..	..	12
D.	Clinical Pathology					
	Urine for routine examination	..	..	..	..	286
	Stool for routine examination	..	..	..	..	170
	Semen examination	..	..	..	..	4
	C.S.F. routine cell count	..	..	..	..	1
	Immunological Pregnancy Tests	..	..	..	..	205
	Biological (Rat Test) Pregnancy Tests	..	..	..	..	3
E.	Bacteriology					
	Direct smear for Tubercle Bacilli	..	..	..	..	1
	Culture for Tubercle Bacilli	..	..	..	..	71
	Animal inoculation for Tubercle Bacilli	..	..	..	..	12
	Smear and Culture for C. diphtheriae	..	..	..	..	8
	Culture of Theatre swabs for Anaerobes	..	..	..	..	128
	Urine culture	..	..	..	..	144
	Pus culture	..	..	..	..	50
	Sputum culture	..	..	..	..	35
	Stool culture	..	..	..	..	5
	Stool culture (Cholera)	..	..	..	..	1
	Blood culture	..	..	..	..	2
	Antibiotic Sensitivity Tests	..	..	..	..	155
	Plural fluid culture	..	..	..	..	2
	Synovial fluid	..	..	..	..	2
	Aspirated fluid culture	..	..	..	..	6
	Ear swab culture	..	..	..	..	1
	C.S.F. culture	..	..	..	..	3
	Conjunctivitis swab	..	..	..	..	10
	Throat swab culture	..	..	..	..	4
	Abdominal tapping fluid culture	..	..	..	..	1
	Ascitic fluid culture	..	..	..	..	1
F	Serology					
	Widal tests	..	..	..	..	86
	Weil Felix Tests	..	..	..	..	18
	Brucellosis Tests	..	..	..	..	20
	V.D.R.L. Tests	..	..	..	..	13
	Paul Bunnell Tests	..	..	..	..	11
TOTAL						2896

APPENDIX III A
CLINICAL PATHOLOGY

Hospitals and Agencies making use of the service of
Clinical Pathology Department

Bombay Area	From Maharashtra
Cama and Albless Hospital	Civil Hospital, Thana
St George's Hospital	Civil Hospital, Alibag, Raigad
Jagannam Hospital	General Hospital, Sawantwadi
Central Railway Hospital	I.S.P. Hospital, Nasik
B Y.L. Nair Charitable Hospital	Public Health Centre, Buldhana
K E.M. Hospital	Civil Hospital, Akola
M G.M. Hospital	District Hospital for Women, Akola
L T.M.G. Hospital	Primary Health Centre, Jalgaon
E S.I.S. Hospitals	General Hospital, Osmanabad
K B. Bhabha Hospitals	Civil Hospital, Dhulia
Kasturba Hospital for Infectious Diseases	Civil Hospital, Nasik
J J. Group of Hospitals	
Police Hospital	
Fertilizer Corporation of India	
B J. Wadia Hospital for Children	
Greater Bombay Municipal Dispensaries.	

APPENDIX IV
HUMAN PHARMACOLOGY AND BIOAVAILABILITY

Name of the Company	Product
Indian Drug & Pharmaceuticals Ltd.	.. Tetracycline caps. Ampicillin caps.
Ranbaxy Laboratory	.. Rifampicin Caps.
Novus Pharma	.. Rifampicin Caps.
Lupin Laboratory	.. Ampicillin syrups Sulpha TMP
H. Jules Pharma	.. Sulpha TMP
Kopran Pharma	.. Rifamp Caps.
Ranbaxy Laboratories	.. Ampicillin syrup Tetra caps.
Trimph Pharma	.. Ampicillin Caps.
Hamlin Pharma	.. Ampicillin Caps.
Harris Pharma	.. Tetracyclin Caps.
Bushal Laboratory	.. Ampicillin Caps.
Kab Pharma	.. Erythro Syrup. Doxy caps.
P & B Lab.	.. Sulpha TMP Syrup.
Hindustan Antibiotics	.. Rifampicin caps.
Concept Pharma	.. Sulpha TMP Cap. Amoxycillin Cap. Rifampicin Syrup.
Meher Pharma	.. Rifampicin Caps. Amp. Cap. Syrup. Sulpha TMP Tab. Syrup. Erythro Tab. Syrup.
Sarvodaya Laboratory	.. Rifampicin cap. Ampicillin cap. Tetra cap. Sulpha TMP Tab.
C.C.I. Pharma	.. Sulpha TMP Syrup.
Lupin Laboratory	.. Erythro syrup.

APPENDIX V
IMMUNOHAEMATOLOGY

Tests	Number
Transfusion	933
Rh Titre and grouping	105
Total :	1,038

APPENDIX VI

LIBRARY

The following figures indicate the working of the library during the year 1986-87

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
3003	835	190	74

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.
498	612	139	43	4

APPENDIX VII
TESTING

Tests	Number
Prohibition & Excise Testing	
(1) Indian made Foreign Liquors	2404
(2) Beer	896
(3) Toddy	1144
(4) Ganja	49
(5) Bhang	9
(6) Charas	1
Total :	4503
Commercial Testing	
(1) Pyrogen	64
(2) Assay	68
(3) Germicidal value	77
(4) Sterility	33
(5) Potency of Toxoids	5
(6) Potency of Anti tetanus Toxoid	6
(7) Physical Tests	56
(8) Other Chemical Tests	50
(9) Miscellaneous	3
Total :	362

APPENDIX VIII
TOXICOLOGY

Sr. No.	Classification of sample	Number tested	Toxicity parameter
1.	Drugs	2	Acute oral toxicity, LD ₅₀
		2	Acute intra-venous toxicity.
2.	Cosmetics	2	Primary skin irritation.
		1	Mucous membrane irritation.
3.	Chemicals	9	Acute oral toxicity.
		1	Acute dermal toxicity.
		1	Toxicity to fish, LC ₅₀
		7	Primary skin irritation.
		2	Mucous membrane irritation.
4.	Pesticides	4	Acute oral toxicity.
		4	Acute dermal toxicity.
		2	Toxicity to fish, LC ₅₀
		2	Primary skin irritation.
		3	Mucous membrane irritation.

APPENDIX VIIIA

TOXICOLOGY

Sr. No.	Sample	LD ₅₀	Fiducial limits/ Remarks
A. Acute oral toxicity in mice :			
1.	Sidfloce 440	10,000 mg/kg	— —
2.	Solcolloid-CBF	>5,000 mg/kg	— —
3.	Vim	>10,000 mg/kg	— —
4.	Rin	>10,000 mg/kg	— —
5.	Setlyte	>5,000 mg/kg	— —
6.	Texavyl/DMC2	>15,000 mg/kg	— —
7.	Polyethylene glycol 1450	>15,000 mg/kg	— —
8.	Adhesive Dendrite LA-85	4.5 ml/kg	3.629-5.580 ml/kg
9.	Welfloc	>15,000 mg/kg	— —
0.	Arozin 60% w/w	409.5 mg/kg	369.0 - 454.5 mg/kg
	Isoproturon	2640 mg/kg	2181.6 -3194.4 mg/kg
B. Acute Intra-venous Toxicity in mice :			
	Aristo-neural	0.72 ml/kg	0.65- 0.79 ml/kg
2.	Amino acid injection	>50 ml/kg	— —
C. Acute oral Toxicity in rats :			
	Solcolloid-CBF	>5,000 mg/kg	— —
2.	Polyethylene glycol 1450	>15,000 mg/kg	— —
3.	Arozin 60% w/w	1260 mg/kg	992 -1600 mg/kg
4.	Isoproturon	3400 mg/kg	2295.4 -4454.0 mg/kg
D. Acute dermal toxicity in rabbits :			
	Solcolloid-CBF	>10,000 mg/kg	— —
2.	Arozin 60% w/w	3780 mg/kg	3203.0 -4460 mg/kg
3.	Isoproturon	>10,000 mg/kg	— —
4.	Malathion 50 EC	2360.92 mg/kg	2101.96-2644.22 mg/kg
5.	Dimethoate 30 EC	1644.80 mg/kg	1303.89-1940.86 mg/kg
E. Primary skin irritation study in rabbits :			
1.	Scapol-LES	— —	mild skin irritation
2.	Lustrol G.P.	— —	no irritation
3.	Detergent powder	— —	mild skin irritation
4.	Vim	— —	mild skin irritation
5.	Rin	— —	mild skin irritation
6.	Castrol perfecto, 125	— —	mild skin irritation
7.	Isoproturon	— —	mild skin irritation
8.	Fem instobleach	— —	mild skin irritation

Sr No	Sample	LD ₅₀	Fiducial limits/ Remarks
9	Fem soft gentle soap or hands.	— —	mild skin irritation
0	Dimethicon	— —	mild skin irritation
	Arozin 60% w/w	— —	mild skin irritation
F	Mucous membrane irriation study in rabbits :	—	—
	Solcolloid-CBF	— —	mild irritation
2	Sca pol LES	— —	mild irritation
3	Fem soft gentle soap for hands.	— —	mild irritation
4	Phenthoate 50% EC	— —	mild irritation
5	soproturon	— —	mild irritation
6	Arozin 60% w/w	— —	mild irritation
G	Acute toxicity in fish :		
	Gel-EL (M)		96 hrs LC ₅₀ — 860 ppm
2	Odocide		96 hrs LC ₅₀ — 9.3 ppm
3	Polycide		96 hrs LC ₅₀ — 2.5 ppm

APPENDIX IX

VIROLOGY

Vaccine administered	Number of patients
Ant'rabie	1118
Cho'era	14
Typhoid	5
Meas'es	3
T'p'e	146
O'a'polio	197
Tetanus	28
P'ague	2
	TOTAL : 1513

APPENDIX IXA
VIROLOGY
Comparative Incidence* of attacks of Viral Hepatitis in Maharashtra
1986-87
April-August

AREA	MONTH — 1987						MONTH — 1986					
	Apr.	May	June	July	Aug.	Apr. to Aug.	Apr.	May	June	July	Aug.	Apr. to Aug.
RURAL	167	106	101	223	294	891	76	6	23	24	4	133
URBAN	160	207	229	191	259	1046	145	139	224	270	388	1156
TOTAL :	327	313	330	414	553	1937	221	145	247	294	392	1299

* Aggregate number from all the districts.

APPENDIX IXB
VIROLOGY
Incidence of deaths of Viral Hepatitis in Maharashtra (1986-87)
December 1986 — April 1987

Area	Dec.	Jan.	Feb.	Mar.	Apr.	Dec. to Apr.
RURAL	8	6	4	2	9	29
URBAN	8	7	10	7	10	42
Total*	16	13	14	9	19	71

* Aggregate number from all the districts.

APPENDIX IXC

VIROLOGY

Markers of Viral Hepatitis in selected Sera (OUTBREAKS IN MAHARASHTRA) 1986-87

AREA		Number Sera Tested	HBsAg ELISA	Anti-HBs ELISA	HAV IgM ELISA
PLACE	DISTRICT				
**GANGAPUR	(NASIK)	40	6(15%)	Not done	5(12.5)
**ROHA	(RAIGAD)	53	5(9.0%)	Not done	1(1.8)
**KHOPOLI	(RAIGAD)	30	0(0.0%)	Not done	0(0.0)
*PUNE	(PUNE)	25	13(52.0%)	4(16.0)	1(4.0)
*KOLHAPUR	(KOLHAPUR)	38	20(52.6%)	5(13.1)	2(5.2)
BOMBAY	(Voluntary Donors)	113	3(2.6%)	23(20.3)	Not done
BOMBAY	(Thalassemic cases)	26	6(23.0%)	4(15.3)	2(7.6)

* Hospitalized Cases

** Out Patient Department Cases

APPENDIX X
ZONNOSES ~

Snakes	No. procured	Venom produced (g)	Venom supplied (g)
Cob a	165	35.80	109.18
K a t	67	8.82	7.56
R v per	46	3.13	45.67
Ech s	429	7.63	0.10
Tota :	707	55.38	162.51
Scorpions :			
Red scorpions	7518	3.43	6.75
Back scorpions	71	—	—
Tota :	7589	3.43	6.75

APPENDIX XA
ZONNOSES

Statistics of visitors to snake farm :

1	Students	..	..	..	..	2696
2	Staff of Scientific Institutions	..	..	..	..	18
3	D'stinguished visitors	..	..	..	..	60
4	Foreigners	..	..	..	..	15
5	Thursday visitors	..	..	..	..	1216
6	Others	..	..	..	..	159
Total :						4164

There were 35 enquiries regarding identification of snakes from hospitals and individuals.

APPENDIX XI

POST-GRADUATE COURSES OFFERED

M.Sc.	—	Microbiology, Biochemistry, Zoology, Organic Chemistry, Applied Biology.
M.Sc. (By papers)	—	Microbiology, Biochemistry.
Ph.D.	—	Microbiology, Biochemistry, Zoology, Organic Chemistry.
M. Pharm	—	Pharmacology and Pharmaceutical Organic Chemistry.
M. Phil	—	Microbiology
M.D.	—	Pathology, Pharmacology and Microbiology.
D.M.L.T.	—	Diploma in Medical Laboratory Technology.
D.A.	—	Certificate Course in Drug Analysis — Short-term Training Course.

APPENDIX XII

TRAINEES ADMITTED

M.Sc. by papers	..	..	..	..	..	..	11
Diploma in Medical Laboratory Technology (DMLT)	..	..					18
Course in Drug Analysis	..	..	..	..	..		6
Short Term Training Course	..	..	..	..	..		12

Research Fellowship and Scholarship

Jr. Research Fellowship (Platinum Jubilee)	..	..	..	Nil
Jr. Research Scholarship (Chinchwad land)	..	..	..	Nil

APPENDIX XIII

List of students who registered during the year 1986-87
for M.Sc., Ph.D., M. Pharm, M. Phil and M.D.

M.Sc.		Ph.D.	
	Shri J.R. Samuel	(1)	Dr. (Mrs.) R.A. Deshmukh
2	Kum. R.N. Bhise	(2)	Shri K.E. Shroff
3	Kum. S. Jayashree		
4	Mrs. M.U. Pradhan		
5	Mrs. S.S. Rege		
M. Pharm		M. Phil	
	Shri S.M. Patil	(1)	Smt. A.A. Ohol
2	Shri V.R. Lokhande	(2)	Smt. J.K. Phadnis
		(3)	Smt. L.R. Phadke
		(4)	Shri S.N. Jagdand
M.D.			
	Dr. V.R. Sing		

APPENDIX XIV

Degree awards during the year 1986-87

Name of Candidate	Subject	Topic
1 Smt. S.R. Ghooi	Ph.D. Applied Biology	Neuro muscular blocking agent from Indian <i>Dioscorea</i> <i>Hispida</i> .
2 Kum. M.L. Ramaiya	Ph.D. Applied Biology	Studies on cultivation of <i>Plasmodium berghei</i> <i>in vitro</i> .
3 Shri M.G. Phatak	Ph.D. Pharmacology (Medicine)	Pharmacokinetic studies in experimental protein malnutrition.
4 Kum. C.N. Desai	M. Pharm	Chemotherapy of Tuberculosis: synthesis and study of organic compounds as possible Anti-Tubercular agents.

APPENDIX XV

POST-GRADUATE TEACHERS

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

Name	Qualifications
Dr. M.V.N. Shirodkar	M.B.B.S., A.B., Sc.D. (Johns Hopkins) P.B.K. (U.S.A.)
Dr. R.S. Kamat	M.D.
Dr. K.H. Dave	M.D., D.P.B.
Dr. D.M. Renapurkar	M.Sc., Ph.D., FMAS
Dr. V.R. Rao	M.V.Sc., Ph.D.
Dr. P. Ramakrishnan	M.Sc., Ph.D.
Dr. S.V. Gadre	M.Sc., Ph.D.
Dr. B.G. Khadse	M.Sc., Ph.D.
Dr. M.K. Bhopale	M.Sc., Ph.D.
Dr. R.P. Bhamaria	M.Sc., Ph.D.
Dr. S.R. Chavan	M.Sc., Ph.D.
Dr. S.T. Nikam	M.Sc., Ph.D.
Dr. B.D. Sathe	M.Sc., Ph.D.
Dr. (Mrs.) A.C. Desai	M.Sc., Ph.D.
Dr. D.P. Buduk	M.V. Sc., Ph.D.
Dr. (Mrs.) V.R. Kamath	M.Sc., Ph.D.
Dr. N.G. Chanderkar	M.B.B.S., B.Sc. (Med) Path. & Bact., M.D., Ph.D.

APPENDIX XVI

Papers presented at National and International Conferences

Indian Pharmaceutical Conference held at Ahmedabad on 20-22nd
December, 1986.

"Synthesis and Evaluation of 4,6-diamino 1,2-dihydro-1-(substituted phenyl) 2',2'-dialkyl or aryl s-triazine hydrochloride as antimalarial agents. Khety, Zarine; Khadse, B.G.; Renapurkar, D.M. and Kamath, V.R.

"Synthesis and Evaluation of 4,6-diamino 1,2-dihydro 1-(substituted hetero-aryl) 2',2'-dimethyl s-triazine hydrochloride as antimalarial agents. Khety, Zarine; Bhirud, S.B.; Khadse, B.G.; Renapurkar, D.M. and Kamath, V.R.

"Synthesis and study of 2-substituted-4-(1-biphenyl)-thiazole as anti-tuberculosis agents. Desai, C.N.; Bobade, A.S. and Khadse, B.G.

APPENDIX XVII

Papers Published 1986-87

V.M. Rangnekar, Bhamaria, R.P. and Khadse, B.G. "Synthesis of N-Aryl/heteroaryl/substituted methyl-x-(p-substituted anilino) succinimides as anti-tubercular Agents. *Indian J. Chemistry*, 25B, March, 1986, pp 342-344.

Ashtekar, D.R., Fernandes, F., Khadse, B.G. and Shirodkar, M.V.N. "A rapid method for the evaluation of new antitubercular agents". *Chemotherapy*, 33, 22-27 (1987).

Naik, Satish, D., Khadse, Barsu, G. and Ambaye Ramkrishna, Y. "Synthesis and anticancer activity of Pyrolidine-2,5-dione-N-mustards". *I.R.C.S.*, 15: 27 (1987).

Vijayalaxmi R. Kamath, Sushila Menon, M.K. Bhopale and D.M. Renapurkar. "Experimental Chemotherapy of *Angiostrongylus cantonensis* infection in mice with flubendazole and levamisole and their combination". *Folia Parasitologica*, 84, 87-92, 1987.

A.J. Almeida, M.K. Bhopale and D.M. Renapurkar. "Evaluation of *Setaria cervi* antigen in the immunodiagnosis of human filariasis". *Bratislavské lekárske Listy*, 87, 641-8, 1987.

Vijayalaxmi R. Kamath, R.P. Hemkar and D.M. Renapurkar. "Laboratory evaluation of rodenticidal activity of cholecalciferol against Indian species of commensal rats. *Pestology*, X (6) 22-25, 1986.

S. Bapna and D.M. Renapurkar. "Laboratory evaluation of cyclopicidal activity of cypermethrin". *Current Science*, 55, 632, 1986.

Chirmule N.B., Deo M.G., Shirodkar M.V.N., Deshmukh R., Chanderkar N.G. ICRC — vaccine induced changes in *M-leprae* specific cell mediated immunity in langur monkeys. (*Presbytis — entellus*). *Int. J. Leprosy* 1986 — (In press).

Ranjana Deshmukh and M.V.N. Shirodkar 1986, Prions: Life without coils. *Science Age* August 1986, 23-27.

M.V.N. Shirodkar, N.G. Chanderkar, R.A. Deshmukh, C.H. Pandit, A.P. Kulkarni, A.B. Kulkarni, Sandhya Sathe, J.M. Deshpande, R.D. Bapat, S.G. Kinare and S.N. Marathe.

A Non Human Primate model for HBV-induced hepatitis-further implications. Proceedings of Indo-US workshop on Viruses and Human cancer. Dec. '86. Amala cancer Research Centre, Trichur, Kerala, India.

R. A. Deshmukh, N.G. Chanderkar, G.B. Akerkar, R. Rayande, B.R. Bhate, and M.V.N. Shirodkar. National Institute of communicable Diseases. Annual review meeting report of the programme officers of viral hepatitis surveillance centres. Sept., 25-26, 1986; pp 47-50.

D.M. Renapurkar. "Prevalence and distribution of commensal rats and rat fleas in Maharashtra State. Part II: Rat and rat flea survey of Maharashtra". *Pestology*, 10: 8, 22-25, 1986.

APPENDIX XVII (continued)

D.M. Renapurkar. "Prevalence and distribution of commensal rats and rat fleas in Maharashtra State. Part III: Rat and flea survey of Western Maharashtra region". *Pestology*, 10: 9, 22-27, 1986.

R.S. Kamat, C. Pandit, S.A. Kamat. Hepatitis B "epidemiology and prevention". *Indian Practitioner*, 40: 777, 1987.

Papers in Press :

Khadse, B.G., Lokhande, S.R., Bhamaria, R.P. and Prabhu, S.R. "Synthesis and Antitubercular studies of 4-(5-Nitro-2-furyl/2-pyrazinyl/1-adamantyl)-2-(substituted aryl/alkyl amino) thiazole". *Ind. J. Chem.*

George, A., Rath S., Ghosh, S.N., and Kamat, R.S. "Route related variation in the immunogenicity of killed *S. enteritidis* vaccine; role of antigen presenting cells". *Immunology* (in press).

Ramakrishnan, P. and Kala, Anita. "*Bordetella pertussis* extract increases superoxide dismutase levels and reduces the diabetogenic effect of alloxan in mice". *Medical Science Research* (Elsevier Pub. UK), Vol. 15, 1987.

A. George, R. Nair, S. Rath, S. Ghosh and R.S. Kamat. "Regulation of immune response in experimental *S. enteritidis* infection in mice". *J. Med. Microbiology* (1987) (in press).

B.J. Mohite, S. Rath, V. Bal, S.A. Kamat, S.N. Marathe, A.J. Zuckerman, and R.S. Kamat. "Mechanism of liver cell necrosis in acute type B. hepatitis: role for T cell response to Hepatitis B surface antigen." *J. Med. Virology* (1987) (in press).

APPENDIX XVIII

Papers sent for Publication

Prabhu, S.R. Lokhande, S.R., Bhamaria, R.P. and Khadse, B.G. "Synthesis and Antitubercular study of 2-substituted alkyl and 2-substituted aryl amino-4-(3'-nitro-4'-(N-pyrrolidino/N4'-methyl-N1'-piperazinyl) phenyl/ thiazoles as a possible antituberculosis agents". *Mirror*.

"Synthesis and study of N-(2-Mercapto-4,5-disubstituted-phenyl)-N'-substituted-phenyl thioureas as a possible antituberculosis agents." *Indian J. of Pharmaceutical Science*.

"Protection against *Plasmodium berghei* rats by immunisation with adult worm homogenate of *Setaria cervi*". *Current Science*.

M.L. Ramaiya, Vijayalaxmi R. Kamath and D.M. Renapurkar. Long term *in vitro* cultivation of *Plasmodium berghei*". *International Journal of Parasitology*.

D.M. Renapurkar. "Distribution and susceptibility of *Xenopsylla astia* to insecticides in Maharashtra State, India." *Insect Science and its application*.

APPENDIX XVIII (Continued)

Renapurkar, D.M. "**Suncus murinus**: Observations on ecology, distribution, status to plague in Bombay". **J. Hyg. Epid. Micro.**

"**Bandicota bengalensis**: observations on ecology, distribution, status to plague in Bombay". **Proceedings of Indian Academy of Sciences, Bangalore.**

Renapurkar, D.M. "Observations on commensal rats and their status to plague in Bombay". **J. Hyg. Epid. Micro.**

Renapurkar, D.M. "Some observations on ecology and distribution of the rat flea *Xenopsylla brasillensis*. **Insect Science and its application.**

Renapurkar, D.M. "Distribution and susceptibility of *X. cheopsis* to insecticides in Maharashtra State, India". **Medical and Veterinary Entomology.**

D.M. Renapurkar. "The cockroach Problem". **Pest management.**

Vijayalaxmi R. Kamath and D.M. Renapurkar. Comparative bioassays of ***Bacillus thuringiensis* var *israelensis*** (H-14) formulations against *Culex-fatigans* larvae in laboratory condition. **Bull. Haffkine Institute.**

V.R. Kamath, Sushila Menon and D.M. Renapurkar. "Larvicidal effect of perbendazole on experimental infection of ***Angiostrongylus cantonensis***." **Chemotherapy, 1987.**

V.R. Kamath and D.M. Renapurkar. "Effect of ***Ancylostoma ceylanicum*** on the subsequent infection with ***Plasmodium berghei*** with hamsters and mice". **Indian J. of Malariology.**

Saroj Bapna, D.M. Renapurkar, S.R. Chavan. "Cyclopical activity of three indigenous plant extracts. **Insect Science and its Application.**

S.R. Chavan, S.T. Nikam. "Mosquito larvicidal activity of essential oil from ***Michelia — Champaka*** — flowers". **Pestology.**

S.R. Chavan, S.T. Nikam. "Investigation of alkanes from ***Azadirachta indica***. A Juss, Neem leaves and their mosquito larvicidal activity". **Pesticides.**
