possible for more than a month or so if the colour bearing vegetation, responsible for photosynthesis, and the humble fungi, responsible for returning to the earth and atmosphere the dead animals and plants, were wiped out as suddenly. The photosynthesis makes food without which animals cannot live. The continuous accumulation of dead animals and plants would take up so much of land and sea that the living animals and plants would not be able to find a place anywhere. Whatever be the opinion of man on his own greatness, in the matter of large-scale protoplasmic transactions, he is like all other animals inferior to plants.

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Special Article

HISTORY OF KALA-AZAR IN INDIA*

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Introduction.—Kala-azar or the black fever was so named because in a large proportion of chronic cases there is a well-marked dark pigmentation of the skin. The word 'kala' may also have been used as signifying 'fatal' or 'deadly', because of the fact that the disease was fatal in almost all cases.

Early history.—Kala-azar is believed to have existed in Bengal for over a century now. Twining writing in 1835 described a condition that he called 'endemic cachexia of the tropical countries that are subject to paludal exhalations'. The disease he described under this title was certainly kala-azar so closely does the description fit in with the classical picture of kala-azar. It was in 1824-25, that there was an outbreak in Jessore of a fever that was characterized by relapses, progressive emaciation and enlargement of the spleen and the liver and the occurrence of certain complications that are frequently seen or almost exclusively occur in kala-azar. This outbreak led to an appalling mortality and no less than 75,000 people died in the division. From Jessore this disease spread to Nadia in 1832 as well as to the 24-Parganahs. It reached the Hooghly district in 1857 and in 1862 it reached the Burdwan district from the contiguous Nadia and the Hooghly districts. The disease reached Burdwan town in 1866. The description by Dr. French, the civil surgeon of Burdwan, of this fever may even to-day be regarded as an excellent clinical description of kala-azar. He traced the course of the progress of the disease from the time of the Jessore epidemic to the time of the Burdwan epidemic of the sixties of the last century.

The disease was introduced into the Dacca district in 1862 by the crew of a country boat who came from upcountry to the inland port of Jageer on the Dhaleswari river. All these men died of a low remittent fever of long duration. The disease spread to this town and thence to the village and towns of the district. In four years the once populous town of Jageer had ceased to exist. The mortality was so great that the dead were left in their houses or thrown into the 'beels' or rivers. There was an epidemic of this disease in North Bengal in 1872. In Bihar it was known to have existed in 1882 and there it was called 'kaladukh'.

The spread of the disease to Assam followed in the wake of the British conquest and the opening up of communications by road and steamer services with Bengal. The first outbreak was reported in 1875 from the Garo hills, where the local population called it 'sarkari bemari' or the British Government disease. Rogers was of the opinion that the Garo hill epidemic was caused by the direct extension of the disease from the Rangpur outbreak of 1872, the route being the newly opened trunk roads along the Brahmaputra river. The map (map 2, after Rogers) shows the spread of the disease into Assam during the last quarter of the last century. Kala-azar caused terrific havoc in Assam during the period; of the people affected over 95 per cent died and this led to a serious decimation of the population, over 25 per cent of the population dying in some districts.

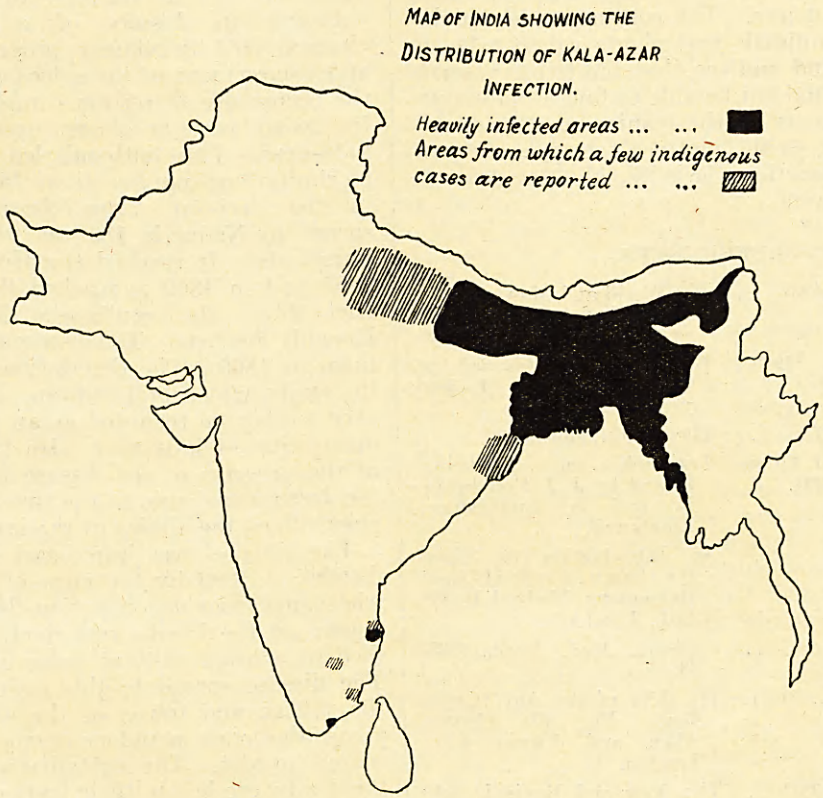
That kala-azar was prevalent in other parts of India, *viz,* the Madras Presidency and the United Provinces, was recognized after the discovery of the parasite in 1903 (*see* map 1).

Previous to the discovery of the parasite, several hypotheses were put forward by different

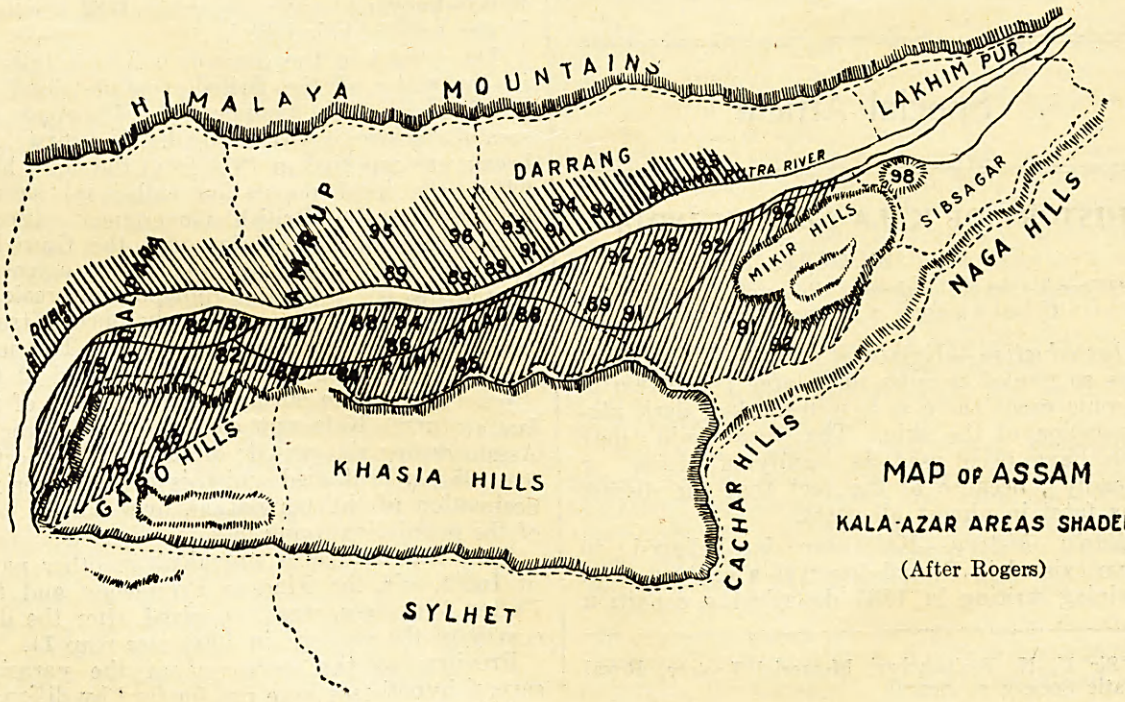
*Sir U. N. Brahmachari Memorial Lecture, Royal Asiatic Society of Bengal.

workers. Some interesting examples of the dangers of partial correlation were displayed when Giles (1892) finding the hookworm ova in the stools of every case affirmed the disease to be ankylostomiasis and later Rogers (1897) and then Ross (1899) concluded that it was a severe form of malaria for a parallel reason. Both these infections will be found in almost 100

Map 1.



Map 2.



per cent of the inhabitants of some districts of Assam (Napier, 1943).

Recent history. Researches on kala-azar during the twentieth century.—The discovery of the parasite independently and almost simultaneously by Leishman who found it in the spleen of a British soldier who had contracted kala-azar at Dum Dum near Calcutta and subsequently died in England, and by Donovan in Madras in the biopsy material from the spleen of patients suffering from kala-azar, was followed by great advances in knowledge of the various aspects of kala-azar.

Protozoology.—The parasite, *Leishmania donovani* itself, was studied first; and in 1904 Rogers and later G. C. Chatterjee cultivated the parasite in artificial medium and described the flagellate form that develops on culture of the oval form from the spleen or the peripheral blood. Further studies by various protozoologists in India, *viz,* Christophers, R. Row, Shortt, Mackie, Knowles, B. M. Das Gupta, J. C. Ray and others, provided comprehensive knowledge on the morphology, cultural characters and other protozoological features of this parasite.

Pathology.—The morbid changes in the body caused in kala-azar were first studied by Christophers in 1904. Of the later studies of the pathology of kala-azar in India, that of M. N. De deserves special mention because of the important contributions made to this subject.

Clinical features.—The clinical picture of the disease was further clarified by the work of Rogers, Muir, U. N. Brahmachari, Napier and others. A peculiar cutaneous sequel to kala-azar was first described by U. N. Brahmachari in 1922. He called this condition 'dermal leishmanoid'. This condition (post-kala-azar dermal leishmaniasis) was further studied by Shortt and Brahmachari, Acton and Napier, Knowles and B. M. Das Gupta, Smith, C. R. Das Gupta and other workers of the Calcutta School of Tropical Medicine.

Epidemiology.—Epidemiological studies of considerable interest on kala-azar in India were also carried out by different workers during the first thirty years of the present century. In the nineteen twenties outstanding contributions were made by the workers at the School of Tropical Medicine, Calcutta, headed by Napier, and by the Kala-azar Commission of India.

Diagnosis.—The first of the diagnostic serum tests, a globulin precipitation test, was described by U. N. Brahmachari in 1917. This test has proved of value in North China but in Bengal where there is so much malaria this test has not proved to be very specific. About 1921 various workers noted that in kala-azar the blood serum when treated with formalin gave a peculiar reaction. This became the basis of Napier's aldehyde test for kala-azar. This test has proved to be of great value in the diagnosis of chronic kala-azar. In 1927 Chopra, J. C. Gupta and David first described the antimony test. Subsequently Napier standardized the technique of this test too. This test is of value in the diagnosis of cases of kala-azar with small splenic enlargement and of duration of over two months. In 1936 a South American worker first noticed that a positive complement fixation reaction was obtained with the Witebsky, Klingenstein and Kuhn (WKK) antigen in leishmaniasis. This finding was confirmed by Greval, Lowe and their associates (Greval, Lowe and Bose, 1939, Lowe and Greval, 1939) for Indian kala-azar. In 1939 Greval, Sen Gupta and Napier developed a technique of complement fixation test of high degree of 'specificity' and sensitiveness for kala-azar using the WKK antigen. Dharmendra next showed that similar antigen could be prepared from various acid-fast saprophytic bacilli and this gave a positive reaction with kala-azar serum. The test was further worked out by Sen Gupta (1944) and a modified technique was described by him next year (Sen Gupta, 1945). This test has proved to be of great value in the diagnosis of kala-azar and positive indication of kala-azar is usually obtained as early as the third week of illness.

The methods of demonstration of the parasite were developed soon after the discovery of the parasite; and techniques of demonstration of these in the peripheral blood, splenic puncture material, by cultural methods, etc., were described. The important recent advances were Napier's invention of a special spleen puncture syringe and the adoption of the Salah Pattern sternum puncture needle for sternal biopsy in suspected cases of kala-azar. With the former the parasite could be demonstrated in about 95 per cent of cases and with the latter in about 85 to 90 per cent.

Treatment.—Previous to the introduction of the specific treatment for kala-azar, the mortality rate was near about 90 to 95 per cent. It was in 1913, that a South American worker first reported success in the treatment of espundia, a leishmanial disease, with tartar emetic. Di Cristina and Caronia in 1915 first treated kala-azar in Italy with tartar emetic injections and obtained successful results. In the same year Rogers and Muir used this drug in Indian kala-azar.

The treatment of kala-azar with antimonyl tartrates was further developed and standardized by Knowles, Brahmachari, Muir, Napier and other workers in Bengal and Assam. The introduction of the tartrates was a great advance in the treatment of this disease, because about 70 per cent of the cases could be cured with this drug. There were however many disadvantages, *viz,* too long a course of treatment, frequent occurrence of unpleasant reactions, relapses and resistance to treatment, etc.

The next group of antimony compounds to be introduced were the pentavalent aromatic antimonials. H. Schmidt first introduced *p*-acetyl-aminophenyl-stibinate of sodium in 1915 for the treatment of kala-azar and Caronia first reported success with this compound.

Later work in India showed that this compound was not satisfactory. In 1922 U. N. Brahmachari prepared urea stibamine, a compound of urea and *p*-aminophenyl-stibinic acid. This drug was proved to be of value in the treatment of kala-azar by Brahmachari, then by Shortt and Sen, and later by Napier. It has been found by workers in all kala-azar areas of the world to be a very powerful therapeutic agent and one of the very best pentavalent antimonials. Numerous other antimony compounds, trivalent and pentavalent, were tested in India mainly by Napier. Of these compounds neostibosan, diethylamine-*p*-aminophenyl-stibinate, was found to be very satisfactory by Napier. The cure rate of Indian kala-azar with pentavalent antimonials in general was 95 per cent. Thus a disease of over 90 per cent mortality could be cured in 95 per cent cases. This was a remarkable achievement indeed.

The introduction of the aromatic diamidines in the treatment of kala-azar forms an important landmark in chemotherapy. Stilbamidine, 4 : 4′-diamidino stilbene, was synthesized by Ewins in 1939. It was used with success in the treatment of a case of Indian kala-azar by Adams and Yorke in Liverpool in the same year. During 1940 to 1941, Napier, Sen Gupta and Sen treated 101 cases of Indian kala-azar with this drug and obtained a cure rate of 98 per cent. The drug was found to be equally successful in the treatment of antimony-resistant cases of kala-azar. A neurological sequel to the administration of diamidino stilbene was first described by Napier and Sen Gupta in 1942. This finding was later confirmed by Kirk from Sudan in 1944.

Several other aromatic diamidines have been tested at the Calcutta School of Tropical Medicine, but none has been found as effective as the first compound stilbamidine.

Other important advances made were in connection with the treatment of seriously complicated cases of kala-azar. Pulmonary tuberculosis complicating kala-azar was regarded by Napier as a fatal combination, on account of the fact that the lung condition was adversely affected by the specific treatment for kala-azar. Sen Gupta (1944) showed that in such cases stilbamidine could be used for the cure of kala-azar without causing any ill effects on the tuberculous disease of the lungs. The treatment of cancrum oris, the classical and most fatal complication of kala-azar, was very unsatisfactory. The use of penicillin (Sen Gupta and Chakravarty, 1945) in the treatment of this condition during the recent years has been found to yield very satisfactory results.

Transmission of kala-azar.—Ever since the discovery of the parasite the problem of transmission of kala-azar has been of interest to all workers on this disease. It was strongly suspected that a biting insect was the transmitting agent. Rogers suspected the bed bug to be the insect vector. Patton showed that the parasite underwent some development in the intestinal tract of the bed bug, and affirmed his belief that this insect was the transmitter of kala-azar. Later work has, however, completely disproved this hypothesis.

In 1913 Mackie suggested that the sandfly ought to be studied in connection with the transmission of kala-azar. Mackie, however, was able to find only *Phlebotomus minutus* that rarely bites man and hence there was little encouragement to follow his suggestion. Acton (1919) considered that the sandfly was concerned with the transmission of kala-azar; he based his opinion on his observations on oriental sore in Iraq.

With the opening of the Calcutta School of Tropical Medicine, a fresh start of the study of the transmission problem was made by Knowles, Napier and B. M. Das Gupta.

The epidemiological studies of Napier helped to narrow down the investigations to a particular area of the town. Smith was appointed as the medical entomologist to work with this enquiry. It was found that, except the ubiquitous bed bug, of the insects most constantly present in the affected area, the sandfly, *P. argentipes*, was the *persistent* human blood feeder. These workers of the Calcutta School of Tropical Medicine were impressed by the finding of this sandfly in the kala-azar area of Calcutta and in answer to an enquiry by Knowles on the subject of sandflies in the kala-azar areas, Sinton pointed out that *P. argentipes* appeared to have a distribution in India corresponding to that of kala-azar. At the time, however, this sandfly had not been reported from Assam and Madras. Knowles, Napier and Smith (1924) showed that 40 per cent of the laboratory-bred sandflies fed on cases of kala-azar developed a heavy infection with the flagellates in their midgut. In the same year the Indian Research Fund Association Kala-azar Commission with Christophers, Shortt and Barraud commenced work in Assam. Following up the observations made at the School of Tropical Medicine, they devoted considerable attention to the sandfly, and were able to confirm the Calcutta findings. They also showed that the infection in the sandfly progressed towards the mouth parts, so that if the fly took another blood meal it would in all probability contaminate the wound with flagellates. The progress of the researches was considerably helped at this stage by the discovery by Young, Smyly, and Brown in 1924 that the Chinese hamster was very susceptible to leishmania infection. The work on the transmission of the disease to the hamster by the bite of the infected sandfly was taken up enthusiastically by all the workers interested in the problem. The results of these attempts to transmit the infection by the bite of the sandfly were singularly disappointing. Though Shortt, Smith, Swaminath, and Krishnan (1931) and Napier, Smith and Krishnan (1933) and Smith *et al.* (1936) succeeded in transmitting the infection to a few hamsters out of several hundreds of animals, it

was the many failures that needed explaining, and all attempts to transmit to human volunteers were entirely unsuccessful.

The Kala-azar Commission was disbanded in 1931, and a lull in the research activities on this subject followed. In 1939, Smith was once again appointed by the Indian Research Fund Association and worked in Bihar where there was a recrudescence of the disease at the time. He was able to make a number of very important observations. He showed that survival and the progress of infection depends on whether the sandfly takes a second blood meal or subsists on fruit or plant juices. In the latter case, a large percentage of the infected flies develop a massive infection with leishmania which blocks the pharynx and the buccal cavity; when these blocked flies were fed on a susceptible animal such as the hamster or the white mouse, infection almost invariably followed. The perfection of the technique of keeping the sandflies alive for longer periods, producing 'blocked' sandflies almost at will, and transmission of the disease to a large proportion of the susceptible animals were the outstanding contributions of Smith, Halder and Ahmed (1941). Smith was unfortunately recalled on military duty in 1941, and the final experiments on human volunteers were carried out by Swaminath, Shortt and Anderson (1942) who succeeded in transmitting kala-azar to five out of six human volunteers by the bite of the blocked sandfly.

This final experiment, along with the epidemiological data and the knowledge about the bionomics of the sandfly, led to the conclusion that the usual method of transmission of kala-azar is by the agency of the sandfly *P. argentipes* in India and by other species of the sandfly elsewhere.

The solution of the kala-azar transmission problem is an achievement of medical research in India and is the outcome of years of strenuous work by the research workers of the Calcutta School of Tropical Medicine, the Kala-azar Commission, and other kala-azar research units of the Indian Research Fund Association.

On recapitulating the work done on kala-azar in India it will be noted that on almost all aspects of the disease very important contributions have been made by the different research workers in this country.

The causation of the disease, its clinical features, the morbid changes caused by it, the epidemiological factors responsible for the causation of the disease, the methods of diagnosis, synthesis of drugs that can cure 95 per cent of cases, the method of its transmission, have all been worked out by workers in India. Also the bionomics of the vector, the action of the various insecticides on it have also been worked out.

Present position of kala-azar in India.—From the above account it will be apparent that all probable methods of conquest of kala-azar are known. Also some work has been carried out in order to establish the hypothesis that the treatment of all cases in an endemic area can lead to the control if not eradication of the disease in the area. The fact that the modern insecticides such as a DDT, pyrethrum, etc., are effective against the sandfly is also known. But little has been done by the State to utilize this knowledge, and the disease is far from under control.

In Bengal, the recorded incidence of kala-azar (which is probably a fraction of the actual incidence of the disease) has been more or less steady for twenty years during 1924 to 1943. Though the disease was showing signs of regression in certain districts in West Bengal, a study of the figures relating to the incidence carried out by Sen Gupta (1944*a*) showed that the trend of incidence was towards an increase in a number of districts in East Bengal, particularly in Chittagong, Dacca and Faridpur districts. By the end of 1944 and the beginning of 1945, marked increase of incidence was noticed in those districts. From certain data available at present it appears that there has been a widespread increase of incidence in different areas of Bengal. Even in Calcutta where a well-marked focus of infection was discovered about 25 years ago, the disease is not only more prevalent in that area but it has spread to other areas of the town as well.

In Assam there has been outbreaks of kala-azar in epidemic form on several occasions. In Bihar there was an epidemic of kala-azar in 1939 to 1941. The incidence is probably fairly high in certain districts of that province. No epidemics have been reported from South India during recent years.

It may seem strange and depressing that now with all our knowledge of kala-azar, its cause, diagnosis, treatment and prevention, kala-azar should persist in such large amount in many parts of North-East India and that it should actually be increasing at the present time.

It should be remembered that some of this knowledge has only recently become available, and that the application of this knowledge on a wide scale has been handicapped by war and famine conditions which moreover have probably helped to cause the increase in kala-azar.

It is to be hoped that in the near future a better public health and medical relief organization will come into operation and it will be possible to apply the knowledge about the prevention and cure of diseases to the whole country. Then only we may expect to control and even to eradicate the diseases of this country.

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Medical News

BRITISH CHEMICALS AND THEIR MANUFACTURERS, 1946

A COPY of the above publication has been sent to us by the Association of British Chemical Manufacturers, 166 Piccadilly, London W.1. This Directory, includes up-to-date information regarding the manufacturers of all types of chemicals, *e.g.* heavy, fine, pure, etc., and supersedes both the old Directories published by the Association. A copy will be sent gratis to any inquirer writing on business paper or giving any other genuine indication of his being likely to put the Directory to good use as a purchaser of chemicals.

The Association has opened a Branch Office for India at Janmabhoomi Chambers, Fort Street, Ballard Estate, Bombay 1. All inquiries should be addressed to the Bombay Office.

JOURNAL OF THE INDIAN ANTHROPOLOGICAL INSTITUTE. VOL. 1 (NEW SERIES), 1945

THIS issue consists of valuable articles by eminent authors namely Dessication of Asia by Sir Aurel Stein, A Survey of Ancient Gandhara by M. E. and D. H. Gordon, Archæological Miscellany by D. H. Gordon, Megalithic Monuments of Southern India by A. Aiyappan, and Gond Exogamy by M. P. Buradkar. They comprise highly interesting and extremely useful investigations recorded by actual painstaking field work on a geographical question in the light of history depicting the mutual relationship of the activity of man and nature (how the damage done by man is made good by nature), archæological contents from sites of antiquity and ancient cultures with outlined sketches of paintings and engravings, exogamy of a primitive type which may have an important bearing genetically as to the advisability or otherwise of the marriage of blood relatives (to avoid incest). The findings admirably indicate how cultures in early times were already far more differentiated than has hitherto been thought of. The journal is informative and complete with illustrations, map and bibliography. This type of journal is of interest not only to anthropologists, archæologists and prehistorians but also to the social biologists, psychologists and genecists. It is hoped that a regular publication of this exceedingly useful journal will stimulate anthropologists, present and future, to explore further for the growth of the national life of India.

J. N. B.

USE OF 'HUMAN GUINEA-PIGS' IN PRESSURE CHAMBER TESTS BY NAZIS

(Abstracted from the *Journal of American Medical Association,* 14th September, 1946, p. 84)

ARMY Air Forces Headquarters has disclosed after study of captured enemy medical reports that 'human guinea-pigs' were successfully used in German pressure chamber tests up to 30,400 feet without oxygen. The research was carried out in German laboratories in the Dachau internment camp by Nazi scientists and doctors during April 1942. Tests were made on human subjects at the direction of Heinrich Himmler, Gestapo chief. Records in the Office of the Air Surgeon reveal that tests placed human beings at a higher artificial altitude without oxygen than ever before reached. The U.S. Navy in operation 'Mount Everest' raised volunteer personnel to 29,025 feet.

DIPLOMA IN OPHTHALMIC MEDICINE AND SURGERY, CALCUTTA UNIVERSITY

THE first course of lectures as required for both parts of the Diploma in Ophthalmic Medicine and Surgery Examination of the University of Calcutta started at the Eye Infirmary, Medical College Hospitals, Calcutta, on 5th May, 1947.

The subjects include the following :—

Part I—Anatomy.	Part II—Pathology.
Physiology.	Bacteriology.
Optics.	Ophthalmic Medicine.
	Medical Ophthalmology.
	Ophthalmic Surgery.
	Operative Surgery.

The following are giving the lectures :—

Capt. E. J. Somerset, M.S. (Lond.), I.M.S., Professor of Ophthalmology, Medical College, Calcutta.

Dr. S. C. Sinha, F.R.C.S. (Edin.), Professor of Anatomy, Medical College, Calcutta.

Mr. T. Ahmed, F.R.C.S., D.O.M.S., Hony. Ophthalmic Surgeon, Medical College, Calcutta.

Capt. K. Sen, F.R.C.S., D.O.M.S., Hony. Ophthalmic Surgeon, Medical College, Calcutta.

Dr. B. K. Das Gupta, F.R.C.S., D.O.M.S., Hony. Junior Visiting Surgeon, Eye Infirmary, Medical College Hospitals, Calcutta.

Dr. P. K. Guha, M.R.C.S., L.R.C.P., D.O.M.S., Hony. Junior Visiting Surgeon, Eye Infirmary, Medical College Hospitals, Calcutta.

TRAINING OF PROBATIONER NURSES IN U.K.

THE following ladies have been selected for training as Probationer Nurses in the U.K.

Centre

Miss Aansuya Subramaniam.
Miss Nasim Farhat Ahmed.
Miss Masuda Bhatti.
Mrs. Sarla Anand.
Miss Khurshid Butt.

United Provinces

Miss Mary Clara Xavier.
Miss Beatrice Dorean Ghose.