

A Clinical and Epidemiological Study of an Epidemic of Febrile Illness with Haemorrhagic Manifestations which Occurred at Kanpur, India, in 1968*

U. C. CHATURVEDI,¹ A. K. KAPOOR,² ASHA MATHUR,³
DINKER CHANDRA,⁴ A. M. KHAN⁵ & R. M. L. MEHROTRA⁶

An epidemic of febrile illness associated with haemorrhagic manifestations and shock occurred at Kanpur, India, during 1968. The epidemic was widespread in the city, involving about one-tenth of the population; cases were more frequent in thickly populated localities with poor sanitary conditions. Those affected were mainly adolescents and adults of both sexes and multiple cases occurred in families. The disease was characterized by the sudden onset of fever, associated with severe headache and low backache. A number of patients had bradycardia, vomiting and diarrhoea and macular skin rashes associated with itching. A small percentage of the patients had haemorrhagic manifestations in the form of haematemesis, haemoptysis, melaena, haematuria and bleeding per vaginum. The mortality was very low. Dengue type 4 virus has been implicated in the epidemic.

An epidemic of febrile illness occurred at Kanpur, India, during September–October 1968, the illness being associated in a few patients with haemorrhagic manifestations and shock. Cases were noted for the first time during the first week of August 1968 and the number gradually increased, reaching peak by mid-September. The epidemic started to decline by mid-October and finally subsided rapidly during November. Our interest in investigating these cases arose from press reports in late September that a large number of cases of undiagnosed fever, so-called “mystery fever”, were occurring in Kanpur city. A team of doctors was sent from the Upgraded Department of Pathology and Bacteriology, Lucknow, to investigate and collect samples for haematological, bacteriological and virological investigations. The team visited the clinics of private medical practitioners, various hospitals in the city and houses of patients, to study the clinical presentation of the disease, to collect pathological material and, later,

to follow some of the cases. Pathological material was collected daily between 23 September and 30 October. The virological investigations implicated dengue type 4 virus in the epidemic (Chaturvedi et al., 1970). This report deals with the clinical aspects of the disease and the course and extent of the epidemic.

METHOD AND MATERIAL

Clinical features

In all, 224 unselected patients with acute febrile illness from various parts of Kanpur city formed the material for this study. The diagnosis of dengue was made clinically and was later confirmed in 56 of the patients on the basis of the virological findings. The unproved cases have also been included because of the similar clinical presentation, course and outcome of the illness.

Haematological investigations

These investigations included total and differential leucocyte counts, haemoglobin and erythrocyte sedimentation rate determinations. Peripheral blood smears were carefully examined for parasites.

Bacteriological investigations

Clot cultures from all patients in the acute phase were made on bile broth and glucose citrate broth.

* From the Upgraded Department of Pathology and Bacteriology, K. G. Medical College, Lucknow, India.

¹ Reader in Virology.

² Demonstrator in Virology.

³ Lecturer in Bacteriology.

⁴ Reader in Haematology.

⁵ Reader in Bacteriology.

⁶ Professor and Head of the Department.

Agglutination tests for enteric fever were also carried out on the patients' sera.

Epidemiological study

The number of family members falling ill, the origin of the family's water supply, the nature of the drainage system for the dwelling and the economic status of the family were recorded in all cases.

Some idea of the extent of the illness in the population of Kanpur was obtained by interviewing the general practitioners in different localities, by making a detailed study of the families of 224 patients and by examining the records of various hospitals. The fatality rate among cases studied by members of the medical team and among hospitalized cases was also noted. The mortality records of the municipal corporation of Kanpur during the period August–November 1968 were compared with the corresponding months in 1967.

RESULTS

Clinical features

The clinical findings from the 224 patients studied are summarized in Table 1.

Onset of illness. The onset of the illness was abrupt, with high fever and severe headache in all the patients. Most of the patients knew exactly at what time they were suddenly taken ill.

Fever. In a large number of patients, the body temperature rose above 104°F (40°C). The maximum rise usually occurred between 24 and 48 hours after the onset of the sickness and the temperature remained high for 4–6 days, then dropped to normal within the next 2 days. In the majority of cases the illness lasted 5–7 days, and for about 3 days in milder cases. In 4 of the virologically proved cases a

recurrence of fever and symptoms was observed after 3–5 apyrexial days, thus presenting a biphasic temperature curve.

Rash. A macular rash, developing between the 3rd and 5th days of the sickness, was observed in 10% of the cases. The rash was usually sparse and was seen mainly on the chest, abdomen and on the dorsal side of the upper extremity. It was commonly associated with intense itching. The rash subsided in 2–3 days but in some of the patients the itching persisted during convalescence for up to 3–4 weeks. Flushing of the skin of the face and trunk was seen occasionally.

Headache. There was nearly always a complaint of severe headache and this was usually the first symptom of the sickness.

Body pains. In most of the patients, the sickness was associated with pain of varying intensity in the back and limbs. Arthralgia was not found in any of the patients.

Alimentary system. In 4% of the cases, diarrhoea occurred during days 3–6 of the sickness. Nausea and vomiting were seen in 17% of the cases and examination of the oral cavity usually revealed a thickly coated tongue. There was no evidence of inflammation in the throat. Palpation of abdomen revealed gurgling bowel sounds. In 2 patients, the liver was enlarged and in one of them mild jaundice was present.

Respiratory system. Nothing abnormal was detected in the upper or lower respiratory tracts.

Cardiovascular system. In most of the cases bradycardia was observed; tachycardia was seen only in cases having haemorrhagic manifestations or peripheral vascular failure. In 3 of the hospital-

TABLE 1
NUMBER OF CASES PRESENTING DIFFERENT CLINICAL MANIFESTATIONS IN CONFIRMED AND UNCONFIRMED CASES

| Virus status | Acute onset | Headache | Body pains | Diarrhoea | Vomiting | Haemorrhage | Skin rash | Temperature | |
|--------------|-------------|----------|------------|-----------|----------|-------------|-----------|----------------------|------------------|
| | | | | | | | | ≤103.9°F; ≤39.7°C | >104°F; >40°C |
| Confirmed | 56 | 52 | 49 | 3 | 11 | 2 | 5 | 34 | 22 |
| Unconfirmed | 168 | 151 | 132 | 6 | 27 | 7 | 17 | 83 | 85 |
| Total | 224 | 203 | 181 | 9 | 38 | 9 | 22 | 117 | 107 |
| Percentage | 100 | 90 | 81 | 4 | 17 | 4 | 10 | 52 | 48 |

TABLE 2
LEUCOCYTE COUNTS IN CONFIRMED AND UNCONFIRMED CASES

| Virus status | Total no. of cases | Total leucocyte count per mm ³ | | | Lymphocyte counts above 45 % |
|--------------|--------------------|---|-------------|---------|------------------------------|
| | | <4000 | 4000-10 000 | >10 000 | |
| Confirmed | 37 | 9 | 26 | 2 | 8 |
| Unconfirmed | 57 | 14 | 37 | 6 | 23 |
| Total | 94 | 23 | 63 | 8 | 31 |
| Percentage | — | 24 | 67 | 8.5 | 33 |

ized patients there was clinical evidence of myocarditis.

Nervous system. Only 1 of the admitted patients showed signs of meningeal irritation.

Lymphadenopathy. Enlarged lymph nodes were seen only in 2% of cases. The glands usually affected were preauricular, inguinal or axillary or those of the posterior triangle of the neck.

Haemorrhagic manifestations. Among the cases studied by members of the medical team, 9 had haemorrhagic manifestations—namely, haematemesis (5 cases), haematuria (2) and melaena (1), in another case both haematemesis and melaena were present. The haemorrhagic manifestations occurred between the 4th and 7th days of the sickness. Two of these cases (No. 68295 and No. 68169) were later confirmed as being due to dengue virus. In none of the patients was gingivitis or bleeding from the gums observed. An analysis of the records of 220 patients admitted to the L.L.R. Hospital of the Medical College, Kanpur, during August–December 1968, revealed haemorrhagic manifestations in 8.

Shock. Shock was seen in 2 out of 224 cases studied by members of the medical team and 20 out of 220 patients in the L.L.R. Hospital presented with peripheral vascular failure; the failure usually developed between 5 and 10 days after the onset of the sickness. About 50% of these patients died in spite of the best possible care.

Convalescence. The fever left the patients extremely weak and lethargic. Convalescence was prolonged and most of the patients were not able to resume active duties for 2–3 weeks.

Haematological findings. The majority of cases had a normal leucocyte count. Leucopenia was found in 23 out of 94 cases examined and the total

leucocyte count was found to be as low as 1700/mm³ in some of the cases. The differential leucocyte count revealed neutropenia with relative lymphocytosis; lymphocytosis above 45% was seen in 31 out of 94 cases. Numbers of monocytes were increased in some cases, in 1 case by as much as 17%. The details of these findings are shown in Table 2.

Bacteriological findings. Blood-clot cultures were sterile after 7 days incubation and agglutination tests were also negative for salmonella infection.

Epidemiological findings

Period. As already stated, the epidemic started in the month of August reaching a peak by mid-September; it began to decline from mid-October and subsided rapidly by November. The data collected from the out-patient department of the Employee State Insurance Hospital, Kanpur, show that the number of patients suffering from the illness revealed a similar trend (Table 3). These cases were typical and they could be distinguished without difficulty from other diseases.

Table 3 shows details of the patients suffering from the illness admitted to the L.L.R. Hospital. The admission rate of such patients was highest during the month of September. The haemorrhagic manifestations were also more apparent during September and October. The total number of cases of this illness treated in the out-patient department of the L.L.R. Hospital during August to December was 1200.

Age incidence. The distribution of cases by age-group shown in Table 4 demonstrates that, of the patients studied by the medical team, 58 were in the 11–20-years age-group and 89 were aged between 21 and 30 years. The youngest patient was aged

TABLE 3
 DETAILS OF PATIENTS ADMITTED TO THE L.L.R. HOSPITAL, KANPUR,
 AND NUMBERS OF PATIENTS TREATED IN THE OUT-PATIENTS DEPARTMENT
 OF THE EMPLOYEE STATE INSURANCE (ESI) HOSPITAL, KANPUR

| Month | No. of patients at admitted to L.L.R. Hospital | | | | No. of patients treated at ESI Hospital |
|-----------|--|-------|------|--------------|---|
| | Total | Cured | Died | Haemorrhages | |
| August | 3 | 3 | — | — | 33 |
| September | 102 | 97 | 5 | 4 | 232 |
| October | 80 | 75 | 5 | 3 | 105 |
| November | 27 | 26 | 1 | 1 | 84 |
| December | 8 | 8 | — | — | — |

TABLE 4
 AGE-INCIDENCE OF ILLNESS

| Virus status | Total | Age-group (years) | | | | | | | |
|--------------|-------|-------------------|------|-------|-------|-------|-------|-------|------|
| | | 1-5 | 6-10 | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | ≥61 |
| Confirmed | 56 | 2 | 3 | 17 | 23 | 7 | 2 | 2 | — |
| Unconfirmed | 151 | 7 | 7 | 41 | 66 | 20 | 5 | 3 | 2 |
| Total | 207 | 9 | 10 | 58 | 89 | 27 | 7 | 5 | 2 |
| Percentage | | 4.3 | 4.8 | 28.2 | 43.0 | 13.0 | 3.4 | 2.4 | 0.97 |

2 years and the eldest 65 years. Though the disease affected all age-groups, most cases were found among adolescents and young adults.

Morbidity. On the basis of opinions expressed by the physicians of Kanpur city at a meeting of the local branch of the Indian Medical Association, and from the views of health officers and estimates from press reports, the total population affected by the epidemic was estimated to be roughly 200 000, which means about one-tenth of the population of Kanpur city. This is probably a very crude estimate but in the absence of a detailed door-to-door survey it is not possible to state more accurately the extent of the epidemic.

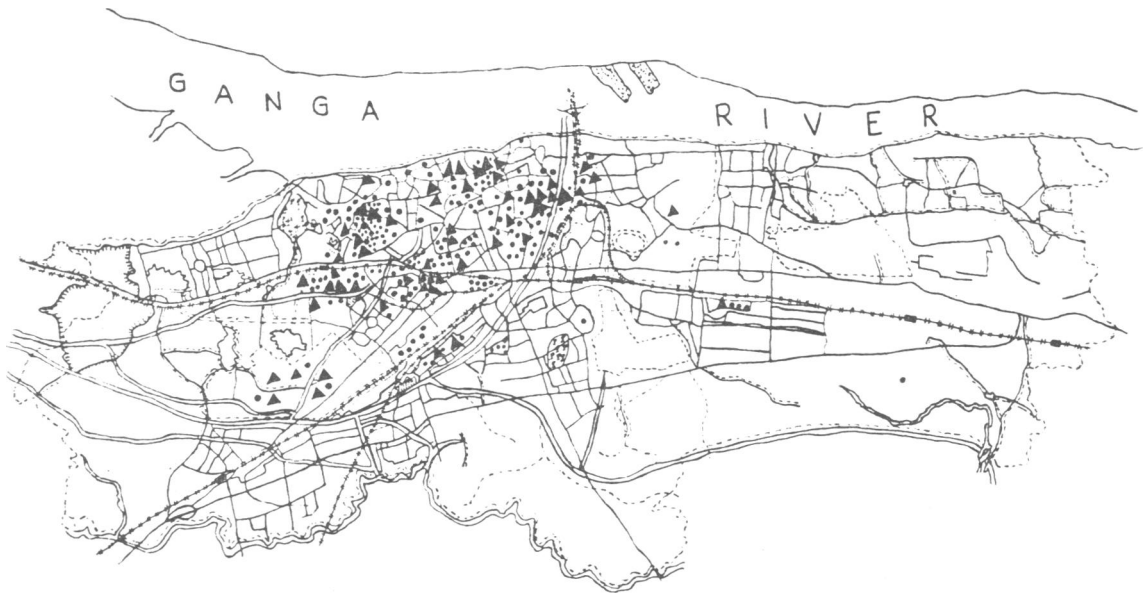
Although the epidemic was widespread in the city, cases were more frequent in certain areas, e.g., Gumti Number 5, Juhi, Lajpatnagar, Shastrinagar, Parade and adjoining areas; the numbers of cases were comparatively small in other localities. Fig. 1 shows the distribution of 224 cases, of which 56 were virologically confirmed, studied by the medical team in Kanpur city. It was also noted that various

members of a patient's family were affected one after another and, ultimately, almost the whole family was involved. The morbidity rate in heavily affected areas was about 75%.

Socio-economic strata. A study of the socio-economic strata of cases studied by the medical team revealed that 71% of patients belonged to the lower-income group (200 rupees or less per month);¹ 29% of the patients had an income of above 200 rupees per month and only a few had incomes above 500 rupees per month. A study of the locality and the houses where these patients lived revealed that they were living in the most thickly populated area of the city with poor sanitary arrangements. Altogether, 83% were using filtered water from the city water supply while 17% were using well-water; 41% of the patients had no water-closet system. In Gumti Number 5, Juhi, Lajpatnagar, Shastrinagar and Govind Nagar, etc., there were many open drains providing suitable sites in which mosquitos could

¹ 100 rupees = approximately US\$13.3.

FIG. 1
DISTRIBUTION OF VIROLOGICALLY CONFIRMED AND UNCONFIRMED CASES PERSONALLY STUDIED BY MEMBERS OF THE MEDICAL TEAM AT KANPUR CITY



Scale: 1 cm = 1.28 km.

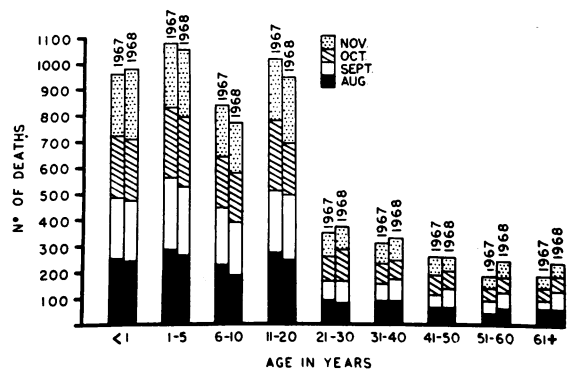
breed. In the neighbourhood of these areas were colonies of slum-dwellers.

Deaths. Among the 224 cases studied by the medical team, 1 patient died from haemorrhages and peripheral vascular failure. The fatality rate was higher among cases admitted to the L.L.R. Hospital, the number of deaths being 11 out of 220 patients. Details of these cases are presented in Table 5. To study the fatality rate in the population of Kanpur, data about the total deaths in different age-groups during August–November in the years 1967 and 1968 were collected from the municipal corporation. Fig. 2 demonstrates that there was not much difference in total deaths in the population during the years 1967 and 1968. These data indicate that although the morbidity rate during the epidemic was high, mortality was very low.

DISCUSSION

An epidemic of febrile illness associated with haemorrhagic manifestations occurred at Calcutta in 1963–64 and was found to be due to both dengue and chikungunya viruses (Pavri et al., 1964; Sarkar

FIG. 2
TOTAL DEATHS AT KANPUR DURING AUGUST–NOVEMBER IN VARIOUS AGE-GROUPS IN 1967 AND 1968



et al., 1964). Similar epidemics occurred at Madras, Vellore and Pondicherry due to infection by chikungunya virus (Myers et al., 1965; Rao, 1966). The epidemic at Visakhapatnam during 1964 was due to dengue virus (Paul et al., 1965). In northern India, for the first time, a severe epidemic of febrile illness

TABLE 5
 DETAILS OF PATIENTS WHO DIED IN THE L.L.R. HOSPITAL, KANPUR,
 AND AMONG PATIENTS STUDIED BY MEMBERS OF THE MEDICAL TEAM ^a

| Patient | Age (years) | Sex | Date of death | Duration of illness (days) | Haemorrhages |
|------------------------|-------------|-----|---------------|----------------------------|-----------------------------|
| 1. S. R. (Miss) | 18 | F | 12.9.68 | 7 | Bleeding per vaginam |
| 2. M. R. (Mrs.) | 68 | F | 20.9.68 | 9 | Absent |
| 3. T. P. | 21 | M | 23.9.68 | 6 | Absent |
| 4. S. (Miss) | 14 | F | 26.9.68 | 8 | Haemoptysis |
| 5. O. P. N. | 35 | M | 26.9.68 | 7 | Haematemesis |
| 6. R. A. | 25 | M | 4.10.68 | 8 | Haematemesis and melaena |
| 7. J. | 25 | M | 5.10.68 | 6 | Melaena |
| 8. U. P. (Miss) | 16 | F | 6.10.68 | 7 | Haematemesis |
| 9. M. L. | 20 | M | 11.10.68 | 5 | Haematuria and haematemesis |
| 10. C. B. | 30 | M | 29.10.68 | 6 | Haematemesis |
| 11. T. D. (Mrs.) | 35 | F | 6.11.68 | 6 | Absent |
| 12. S. S. ^b | 32 | M | 30.9.68 | 8 | Haematemesis |

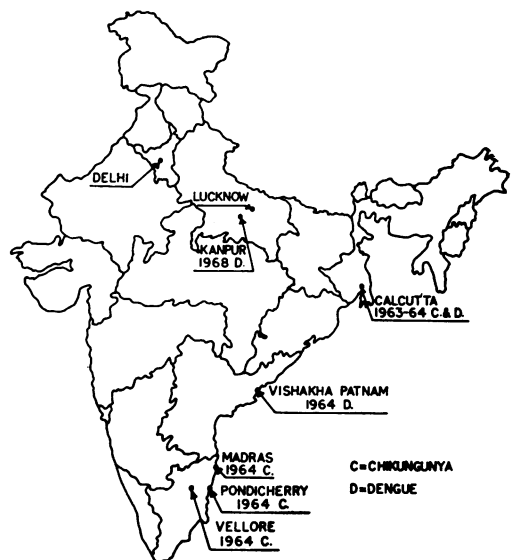
^a The cause of death in all cases was peripheral vascular failure.

^b Virus isolated and diagnosed as dengue type 4 (68295).

associated with haemorrhagic manifestations occurred in 1968 at Kanpur after the rains, a period which is known to be associated with dense mosquito breeding. The epidemic therefore happened during the period when mosquitos are most prevalent in this area.

The main question, but the most difficult to answer, is whether the illness at Kanpur was a new disease. The findings of high incidence of group B haemagglutination-inhibiting (HI) antibodies in persons who escaped the present sickness (Chaturvedi et al., 1970) and a similar HI finding in the neighbouring town of Lucknow, and also the isolation of dengue type 2 viruses from cases of pyrexia at Lucknow (U. C. Chaturvedi, unpublished data) in 1966-67, indicate a long-standing activity of group B virus in the area. In the experience of clinicians at Kanpur, however, a sickness of such a magnitude and severity, associated with haemorrhagic manifestations, had not occurred in the past. Kanpur, centrally situated in the Gangetic plain, is connected to Calcutta by both rail and air and there is heavy traffic between the two cities. It appears possible that a new strain of dengue virus

FIG. 3
 LOCATIONS OF EPIDEMICS OF FEBRILE ILLNESS
 ASSOCIATED WITH HAEMORRHAGIC
 MANIFESTATIONS IN INDIA



entered Kanpur city some time during 1968. There are indications that dengue and chikungunya viruses have been spreading from Calcutta along the coastal region to new areas (Fig. 3) and the virus responsible for this outbreak therefore might have travelled

northwards, invading Kanpur. Why the disease had not spread to Kanpur sooner after the 1963-64 epidemic in Calcutta, and why the spread occurred only during 1968, are questions which are yet unanswered.

ACKNOWLEDGEMENTS

We are very grateful to Dr B. B. Singh, Mr H. O. Tondon, Mr L. M. Bahuguna, Mr K. G. Shrivastva and Mr Zhamman for their valuable assistance during the course of the study. We are indebted to Professor Ram

Singh, Kanpur Medical College, for permitting us to study his cases and collect data from the L.L.R. Hospital. The financial assistance of the Indian Council of Medical Research is also gratefully acknowledged.

RÉSUMÉ

ÉTUDE CLINIQUE ET ÉPIDÉMIOLOGIQUE D'UNE ÉPIDÉMIE D'UNE AFFECTION FÉBRILE ACCOMPAGNÉE DE MANIFESTATIONS HÉMORRAGIQUES À KANPUR (INDE), EN 1968

Une importante épidémie d'une affection fébrile s'est déclarée à Kanpur en août 1968. Elle a pris des proportions alarmantes en septembre et en octobre puis s'est éteinte spontanément en novembre.

Le début de la maladie était brutal et marqué par une hausse subite de la température, de fortes céphalées et des douleurs lombaires. Dans 10% des cas, une éruption maculeuse accompagnée d'un prurit intense est apparue; 4% des malades présentaient de la diarrhée, et 17% des nausées et des vomissements. La bradycardie était très fréquente. On a observé des adénopathies chez 2% des malades et des manifestations hémorragiques (hématémèse, hématurie, méléna) dans 4% des cas. Un état de choc est survenu chez 22 malades dont la moitié environ sont morts par collapsus vasculaire. L'examen hématologique a montré de la leucopénie ou de la leucocytose dans respectivement 24% et 8,5% des cas et une forte lymphocytose chez 33% des patients. La convalescence, marquée par de l'asthénie et de la somnolence, a été longue.

L'enquête épidémiologique a révélé que l'acmé de l'épidémie avait été atteint en septembre. Les deux sexes et tous les groupes d'âge ont été touchés, la morbidité et la mortalité étant toutefois plus élevées chez les adolescents et les jeunes adultes. D'après une estimation grossière, l'affection aurait atteint un dixième de la population de Kanpur. Les cas ont été surtout fréquents dans les quartiers populeux de la ville où se trouvaient réunis divers facteurs favorisants: densité de population, niveau socio-économique bas, mauvaises conditions d'hygiène et proximité de taudis propices à la pullulation des moustiques.

L'évolution de la maladie a été en général bénigne et la guérison est survenue après 2-3 semaines. On a dénombré 11 décès sur 220 malades hospitalisés. De l'ensemble des données relatives à la ville de Kanpur, il ressort qu'en dépit de la morbidité élevée, la mortalité est restée à un niveau très bas.

REFERENCES

- Chaturvedi, U. C., Mathur, A., Kapoor, A. K., Mehrotra, N. K. & Mehrotra, R. M. L. (1970) *Bull. Wld Hlth Org.*, **43**, 289-293
- Myers, R. M., Carey, D. E., Ruben, R., Jasudass, E. S., Renitz, G. D. & Jadhav, M. (1965) *Indian J. med. Res.*, **53**, 694-701
- Paul, S. D., Dandawate, C. N., Banerjee, K. & Krishnamurthy, K. (1965) *Indian J. med. Res.*, **53**, 777-789
- Pavri, K. M., Banerjee, G., Anderson, C. R., Aikat B. K. (1964) *Indian J. med. Res.*, **52**, 692-697
- Rao, T. R. (1966) *Bull. Wld Hlth Org.*, **35**, 87
- Sarkar, J. K., Pavri, K. M., Chatterjee, S. N., Chakravarty, S. K. & Anderson, C. R. (1964) *Indian J. med. Res.*, **52**, 684-691