

Clinical features of yellow fever cases at Vom Christian Hospital during the 1969 epidemic on the Jos Plateau, Nigeria

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Between 27 September and 27 December 1969, 103 patients diagnosed as having yellow fever were admitted to Vom Christian Hospital, near Jos, Nigeria. Headache and vomiting were the commonest presenting complaints, and 95% of the patients showed scleral icterus or bile pigments in the urine. Haemorrhage, signs of renal failure, and CNS involvement (agitation, seizures) were associated with a grave prognosis. The overall case-fatality ratio was 45.6%. The average duration of illness for fatal cases was 6.4 days and for non-fatal cases 17.8 days. Six illustrative case histories are presented.

During the latter part of 1969, an epidemic of yellow fever occurred among the rural population of the Jos Plateau and adjacent areas. Carey et al. (1972) have described the epidemiological aspects of this epidemic, including epidemic curves, morbidity, and mortality in 7 hospitals. This report described the clinical findings in respect of 103 patients who were admitted to the Sudan United Mission (S.U.M.) Vom Christian Hospital with a diagnosis of yellow fever; this group of patients represents one-third of the number of yellow-fever patients hospitalized (Carey et al., 1972).

MATERIALS AND METHODS

The patients were admitted to Vom Christian Hospital, situated near Jos at an altitude of 1 300 m. The hospital has 230 beds and serves villages up to 32 km away. The geographical and ecological aspects of the area affected by the epidemic have been described elsewhere (Lee, 1972).

A diagnosis of yellow fever was first considered during a 2-week period near the end of the extended rainy season (27 September–11 October 1969), when 6 patients died within a week of admission with symptoms of jaundice and haemorrhage and signs

of renal impairment. Laboratory confirmation was subsequently obtained. The virological, serological, and histological methods used in the diagnostic studies at the Virus Research Laboratory, Ibadan, have been described by Carey et al. (1972).

The clinical histories and physical findings presented here were drawn from records kept at the Vom Christian Hospital. One of us (E.M.M.J.) personally examined and treated most of the cases. Altogether 103 patients were admitted between 27 September and 27 December with a diagnosis of yellow fever. Most of them were peasant farmers: 84 patients were males and 19 were females.

Laboratory tests (blood counts, urinalyses, and serum bilirubin and blood urea nitrogen (BUN) determinations were performed at Vom Christian Hospital using standard methods.

RESULTS

Duration and outcome of illness

A total of 51 patients were discharged as fit to go home; 5 left against medical advice. Three patients were admitted on the day symptoms developed; two had a history of illness for 21 days prior to admission. The average number of days of illness before admission was five. The average stay in hospital for nonfatal cases was 14 days, the range being 5–42 days. The average duration of illness was 17.8 days.

Altogether 47 fatal cases were recorded. The first death thought to have been due to yellow fever

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Table 1. Age distribution of yellow fever cases

Age (years)	No. of cases by outcome		Case-fatality ratio (%)
	Nonfatal	Fatal	
0-9	0	1	} 21.4
10-19	11	2	
20-29	18	16	47.1
30-39	12	14	53.8
40-49	9	4	(30.8)
≥50	6	10	62.5
Total	56	47	45.6

occurred on 21 September, the last on 31 December. Eleven patients died on the day of admission. The average number of days in hospital prior to death was 2.5 and the average duration of illness was 6.4 days.

Table 1 shows the age distribution of fatal and nonfatal cases. Persons under 20 years of age had a lower mortality rate than older people.

Symptoms and signs

The frequencies of the recorded symptoms and signs are shown in Table 2.

The commonest presenting complaints were vomiting (67 patients) and headache (38 patients). Pains in the abdomen, lower back, chest, and joints were less frequently recorded. Diarrhoea was present in 14 patients.

Scleral icterus or bile in the urine was recorded in 98 patients. Native herbal infusions, used locally for the treatment of jaundice, had been taken by 15 patients prior to admission. Anuria developed in 15 patients and only one of these patients recovered.

The prognosis was also grave when haemorrhagic symptoms were present. Vomiting of altered blood occurred in 21 patients, of whom 4 recovered. Melaena was noted in 9 patients; 1 recovered. Bleeding from the gums was recorded in 8 patients; 3 recovered and 1 absconded. Epistaxis occurred in 8 patients; 5 recovered. Haematomata developed in the deltoid muscles of three patients who subsequently died; and three others, who also died, had bleeding from the site of intravenous infusions. Gross haematuria was present in 4 patients, 2 of whom died.

Hiccoughs were noted in 12 patients, of whom

Table 2. Frequency of clinical symptoms and signs in 47 fatal and 56 nonfatal yellow fever patients

Symptom (sign)	No. of patients		
	Fatal (47 patients)	Nonfatal (56 patients)	Total (103 patients)
vomiting			67
pain			
headache			38
abdominal			18
lower back			16
chest			7
joints			7
jaundice	42	56	98
anuria	14	1	15
haemorrhage	37	12	53
black vomit	17	4	21
melaena	8	1	9
haematuria	2	2	4
bleeding gums	4	5	9
epistaxis	3	5	8
other	6		10
agitation	16	2	18
diarrhoea			14
hiccoughs	10	2	12

only 2 recovered. Signs of CNS involvement were present in 26 patients. Extreme restlessness and agitation was seen in 18 patients, of whom only 2 recovered. Generalized motor seizures developed in 8 patients.

An unpleasant fishy odour of the skin was recorded in one patient admitted on the 12th day of illness one day prior to death.

Many patients were apyrexial on admission, although nearly all described fever at the onset of their illness. Several patients who died after 4-7 days of illness had temperatures over 37.8°C on the day of death. Temperature recordings in these and other patients generally did not illustrate the classically described period of remission between initial fever and the period of intoxication.

Laboratory studies

Peripheral white blood cell (WBC) counts were determined for 23 patients. No consistent picture

was found. In a few cases leucopenia was present, especially during the first few days of illness. Five patients tested on the second day of illness had counts of 1 800 (70% polymorphs); 2 400 (40% polymorphs), 5 100 (55% polymorphs), 6 700 (75% polymorphs), and 8 600 (66% polymorphs). Between the third and eleventh days counts were between 3 000 and 25 000.

Serum bilirubin was estimated in a number of patients. The highest level found was 48 mg per 100 ml of serum in a man who had been ill for 8 days and was tested 2 days prior to death.

Urine samples were routinely tested for albumin and bile as soon after admission as obtainable, and daily thereafter. Albuminuria was most marked on the third to fourth day of illness. In most cases bile pigments were absent or at low concentrations on days 3-4 and increased thereafter, whereas albuminuria decreased. Blood urea nitrogen levels of 220 mg/100 ml were recorded for three patients, all of whom died.

Special studies were performed on specimens sent to the Virus Research Laboratory, Ibadan. Yellow fever was confirmed in six cases by virus isolation from serum and in three cases by complement-fixation (CF) antibody rises in paired sera. In seven other cases a high titre of CF antibody was present in a single serum sample or stable, high titres were detected in paired sera. Of 10 liver biopsies performed, 1 was reported as "definite yellow fever", 3 as "compatible with yellow fever", and 1 as "probable yellow fever". In 4 other cases for which a histopathological diagnosis of "hepatitis" or "not yellow fever" was returned, serum specimens contained yellow fever CF antibodies.

Complications and treatment

The danger of pneumonia was realized after it had developed in several cases. Subsequently, prophylactic antibiotics were given to a number of seriously ill patients, as well as to those who complained of chest pain. Patients who were not vomiting were treated with relatively large quantities of dextrose or sugar water and vitamin supplements. The more seriously ill patients were given 5% dextrose intravenously and vitamin K intramuscularly. Hepatotoxic drugs were avoided. Where restlessness or convulsions made sedation necessary, paraldehyde was administered intramuscularly. Hospital wards and nurses' quarters were sprayed regularly against mosquitos.

Illustrative case histories

1. A man aged 24 years was admitted on 17 October from a village on the eastern edge of the Plateau, 48 km away. He gave a history of 9 days of illness, commencing with fever. Upon admission he was deeply jaundiced and complained of headache, neck pain, and substernal pain. His serum bilirubin was 36 mg/100 ml and fell to 1.6 mg/100 ml 2 days later. His WBC count was 4 700. Ward tests of urine showed 3+ bile pigments and albumin: 42 days later, his bile pigment was 1+ and his albumin nil. The patient had epistaxes on 20, 22, and 23 October and on 5 and 13 November. His main complaints after November were of pains and weakness in the legs. The patient was discharged on 19 November after 42 days of illness. Serum specimens collected on 17 and 25 October both showed a high complement fixation titre for yellow fever virus.

2. An 18-year-old man, admitted at the same time (17 October) and from the same village as Case no. 1, died of a fulminant infection on the day of admission. He was said to have become ill the previous evening. He was semiconscious and very restless. The sclera were deeply icteric and his vomit and stools were black. The liver was not palpably enlarged. Urine was not obtained for testing.

3. A man of about 50 years of age was admitted to the hospital on 23 October. He arrived from a village reporting many cases of jaundice, about 24 km from the hospital. Fever and backache had begun one week before, and he had been light-headed and dizzy for 2 days. Albuminuria had been noted at the village dispensary 2 days before admission. He was jaundiced and drowsy. A urine test showed bile pigment and albumin to be 2+. On 24 October his serum bilirubin was 12.5 mg/100 ml. The patient improved slowly, dizziness continuing to be his main complaint. On 26 November his serum bilirubin was still 5.6 mg/100 ml and he was given an 8-day course of prednisone. Serum bilirubin was 2.0 mg/100 ml on 3 December. He was discharged the next day. Paired sera demonstrated conversion for yellow fever virus. This man was seen 6 months later and appeared fit and well.

4. The son of Case no. 3, 20 years old, was admitted on 1 November. He had been ill for 5 days, complaining of pains in the back, chest, and abdomen. His urine contained 2+ bile pigment and albumin. On 2 November his temperature was 37.8°C. On the following day he vomited persistently. His liver was noted to be 2 finger-breadths enlarged on 5 November. He felt better on 6 November, but commenced hiccoughing. On 7 November, he was vomiting fluids given by mouth, his temperature was 38.2°C and there were signs of pneumonia. He developed anuria on 8 November, with a BUN level of 220 mg/100 ml. There was bleeding from the site of a venepuncture. He died that evening after 13 days of illness.

5. A man aged 24 years was admitted on 27 October after 2 days of illness. He arrived from a village 13 km

away. His sclera were slightly icteric on admission, his temperature was 36.7°C, and his pulse rate was 60. His urine contained 1+ bile pigment and 2+ albumin. Both readings increased during the following 6 days and then fell gradually. The patient started vomiting on 26 November, whereupon 5% dextrose solution was given intravenously. On 31 October, his temperature was 37.5°C, there was no further vomiting, and he was taking fluids orally. He was discharged on 12 November. Yellow fever virus was isolated from serum obtained upon admission.

6. One of very few cases from Jos town, a boy aged 15 years, was admitted on 28 October, with a one-day history of headache, backache, and vomiting. On 30 October his temperature was 37.8°C and his urine contained 1+ bile pigment and 2+ albumin. He vomited 6 times on 31 October and was given 5% dextrose intravenously. On 3 November he was bleeding from the gums and had generalized seizures. He continued to be very restless for 2 days although he was receiving 6 ml of paraldehyde, intramuscularly, every 4 hours. On 5 November he was drowsy but the bleeding had ceased. On 6 November, he was answering questions rationally and taking fluids by mouth. He continued to improve, although he has small epistaxes on 10, 11 November. He was discharged on 17 November, having had no bile pigment in the urine for 2 days.

DISCUSSION

The clinical course and symptoms recorded for patients with yellow fever at Vom Christian Hospital during the 1969 epidemic are generally consistent with clinical findings described in the literature. Clearly, most patients hospitalized at Vom had moderately severe to very severe infections, as reflected in the high case-fatality ratio (45.6%). Despite the fact that the patient population admitted to hospital was selected by severity of illness, it appears that the Jos Plateau epidemic was characterized by a relatively high incidence of clinically severe yellow fever infections. In contrast, an epidemic that occurred a year later in Nigeria (Okwoga District) resulted in many mild infections and a very low mortality (T. Monath, personal communication).

The duration of illness prior to death (6.4 days

average) was within the range reported for previous epidemics in Ethiopia (Sérié et al., 1968) and Costa Rica (Elton et al., 1951), but differed from findings in fatal cases in certain localities of Ethiopia (e.g., at Bolosso; Sérié et al., 1968) and in Nigeria (e.g., at Okwoga; T. Monath, personal communication). In the latter epidemics, fatal cases had fulminating infections with death 2-4 days after onset, usually without signs of hepatic or renal involvement.

Scleral icterus or the presence of bile pigments in the urine was noted in almost all of the cases discussed here. The rapidity and degree of jaundice has generally been found proportional to the severity of the illness and the gravity of the prognosis (Elton et al., 1951; Chambon et al., 1967), but the clinical and laboratory data available did not permit similar detailed analysis for our patients.

Haemorrhage, noted in 37 of 47 fatal cases, but in only 12 of 56 nonfatal cases, was a grave prognostic sign. The laboratory facilities were inadequate to evaluate the etiology of the bleeding diathesis. Recent experimental studies have implicated consumption of clotting factors owing to intravascular coagulation in yellow fever (Dennis et al., 1969).

Albuminuria was most marked on the third to fourth day of illness. MacNamara (1957) reported albumin in 70 of 140 urine samples, and also noted peak albuminuria on days 3-4. Signs of severe renal damage (anuria, elevated BUN) were recorded in 15 cases, all but one of which succumbed.

Variable reports exist in the literature regarding WBC counts in human yellow fever cases, and Kerr (1951) has suggested that this may be the result of a lack of control observations on the populations involved. Leucopenia (neutropenia) has been consistently observed in the early course of experimental yellow fever infection of monkeys (Henderson et al., 1970). In our patients, leucopenia was noted in several patients, especially during the first days of illness, but was not a consistent finding; a normal WBC count was not diagnostically helpful.

The peculiar fishy odour noted in one case has been previously described (Manson-Bahr, 1960).

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RÉSUMÉ

ASPECTS CLINIQUES DE LA FIÈVRE JAUNE CHEZ DES MALADES HOSPITALISÉS AU CHRISTIAN HOSPITAL DE VOM PENDANT L'ÉPIDÉMIE DE 1969 SUR LE PLATEAU DE JOS (NIGÉRIA)

La présente étude porte sur 103 malades (84 de sexe masculin, 19 de sexe féminin) admis à l'hôpital de Vom avec le diagnostic de fièvre jaune. Cinquante et un d'entre eux ont quitté l'hôpital guéris, 5 sont rentrés chez eux malgré l'avis du médecin et 47 (45,6%) sont morts. Pour les malades qui ont résisté à l'infection, la durée moyenne du séjour à l'hôpital a été de 14 jours, et la durée moyenne de la maladie de 17,8 jours; pour ceux qui ont succombé, les chiffres correspondants sont de 2,5 et 6,4 jours.

Les symptômes le plus souvent observés ont été les vomissements (67 cas) et les céphalées (38 cas). On a noté, moins fréquemment, des douleurs abdominales, lombaires, thoraciques ou articulaires. Un ictère ou l'élimination de pigments biliaires dans l'urine ont été constatés chez 98 malades (95%). Le pronostic était sombre chez les patients présentant de l'anurie (15 cas, 1 seule guérison) ou des symptômes hémorragiques (53 cas, 12 guérisons). Une issue fatale a également été enregistrée chez la majorité des malades souffrant de hoquet tenace

(12 cas) ou présentant des symptômes (agitation extrême, convulsions) dénotant une atteinte du système nerveux central (26 cas).

Divers examens de laboratoire ont été pratiqués. Le nombre des leucocytes était diminué chez 2 malades sur 5 examinés le 2^e jour de la maladie, mais normal ou augmenté à partir du 3^e jour. Un taux de bilirubine sérique de 48 mg/100 ml a été décelé, 2 jours avant le décès, chez un sujet malade depuis 8 jours. L'albuminurie était surtout intense le 3^e et le 4^e jour de la maladie. Des taux d'azote uréique atteignant 220 mg par 100 ml de sang ont été trouvés chez 3 malades qui tous ont succombé.

Plusieurs patients ont été atteints de pneumonie, considérée comme la complication la plus grave. Des antibiotiques ont été administrés à titre prophylactique à un certain nombre de cas sérieux.

Les données cliniques recueillies lors de l'observation de 6 malades hospitalisés à Vom sont présentées.

REFERENCES

- Carey, D. E., Kemp, G. E., Troup, J. M., White, H. A., Smith, E. A., Addy, R. F., Fom, A. L. M. O., Jones, E. M., Bres, P., & Shope, R. E. (1972) *Bull. Wld Hlth Org.*, **46**, 645
- Chambon, L. et al. (1967) *Bull. Wld Hlth Org.*, **36**, 113-150
- Dennis, L. H., Reisberg, B. E., Gosbie, J., Crozier, D., & Conrad, M. E., (1969) *Brit. J. Heamat.*, **17**, 455-462
- Elton, N. W., Romero, A., & Trejos, A., (1955) *Amer. J. clin. Path.*, **25**, 135-146
- Henderson, B. E., Cheshire, P. P., Kirya, G. B., & Lule, M. (1970) *Amer. J. trop. Med. Hyg.*, **19**, 110-118
- Kerr, J. A. (1951) *The clinical aspects and diagnosis of yellow fever*. In: Strode, G. K. ed., *Yellow fever*, New York, McGraw-Hill
- Lee, V. H. (1972) *Bull. Wld Hlth Org.*, **46**, 641
- MacNamara, F. N. (1957) *W. Afr. med.*, **J. 6**, 137-146
- Manson-Bahr, P. (1960) *Manson's tropical diseases*, 15th ed., London, Cassell
- Sérié, C., Lindrec, A., Poirier, A., Andral, L., & Neri, P. (1968) *Bull. Wld Hlth Org.*, **38**, 835-841