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The 1970 yellow fever epidemic in Okwoga District, Benue Plateau State, Nigeria*

2. Immunity survey to determine geographic limits and origins of the epidemic

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Serological surveys undertaken to define the geographic limits of the 1970 rural yellow fever epidemic in Okwoga District, Nigeria, indicated that surrounding areas of Benue Plateau State and East Central State were not involved. However, the surveys uncovered a separate focus of unrecognized, recent epidemic yellow fever in Mbawsi, in southern East Central State. The highest proportions of yellow-fever-immune sera outside the Okwoga and Mbawsi foci were found in zones of Guinea savannah in the Benue River basin.

Between October 1970 and January 1971 a rural yellow fever epidemic occurred in Okwoga District, Benue Plateau State, Nigeria. A companion paper (Monath et al., 1973a) showed that Aidogodo was the most severely affected village, with an attack rate of 40%; three other adjoining villages were also affected. In order to define the geographic limits and origins of the epidemic, a serological survey of yellow fever immunity was undertaken in areas both adjacent to and peripheral to the epidemic focus. The results of tests for yellow fever immunity form the basis for this report.

MATERIALS AND METHODS

Survey sites

The villages that were sampled, their locations relative to the epidemic zone, characteristic vegetation, and rainfall are presented in Table 1 and Fig. 1. All survey sites constituted rural habitats. Yellow fever cases had not previously been recognized, nor had yellow fever vaccinations been performed, in any of the areas sampled.

Sera were collected as described previously (Monath et al., 1973a). At Gboko and Wukari, blood samples were collected from persons attending outpatient clinics and from patients in hospital. At Obolo–Afor children attending 2 grammar schools were sampled. In all other villages, volunteers were asked to donate blood at specially arranged clinics.

Serological tests

Haemagglutination-inhibition (HI), complement-fixation (CF), and neutralization (N) tests were performed as described by Monath et al. (1973b).

Sera were first screened by HI at a dilution of 1 : 10 against yellow fever, West Nile, and either Wesselsbron or Zika antigens as well as an unrelated arbovirus (Ingwavuma). Sera positive by HI to one or more group B arboviruses were further tested by N test against yellow fever. Those with yellow fever N antibody were then tested by CF against yellow fever as well as West Nile, Wesselsbron, Zika, and dengue-2 in order to detect recent yellow fever infections. Selected groups of sera were further tested for N antibodies to group B arboviruses other than yellow fever, as described below.

The actual dosages of virus used in N tests were as follows: yellow fever 125–500 suckling-mouse intracerebral LD_{50} (average 245 LD_{50}); West Nile 200 LD_{50}; Wesselsbron 130 LD_{50}; Zika 20–160 LD_{50} (average 90 LD_{50}); and dengue 50 LD_{50}.

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Table 1. Locality, characteristic vegetation, and rainfall of sites in serological survey for yellow fever immunity, Nigeria, 1970–71

Site no.[a]	Locality	Distance (kms) and direction from Okwoga	Characteristic vegetation	Annual rainfall (cms)	Date of survey
1	Okwoga	—	savannah-woodland	152–203	Dec. 1970–March 1971
2	Ito	48, E		152–203	Dec. 1970
3	Gboko	148, ENE	southern Guinea savannah	152–203	March 1971
4	Wukari	438, NE		102–127	March 1971
5	Takum	185, ENE		127–152	Aug. 1970 and March 1971
6	Naka	77, NNE		127–152	March 1971
7	Abinsi	137, NE		127–152	Aug. 1970 and June 1971
8	Udei	138, NNE		127–152	June 1971
9	Gudi	212, NNE		127–152	June 1971
10	Obolo–Afor	32, WSW	savannah-woodland	152–203	March 1971
11	Issele–Uku	174, SW	Lowland rain forest	152–203	March 1971
12	Abiriba	142, S		203–254	Dec. 1970
13	Mbawsi	183, S		203–254	Jan. 1971
14	Aking	206, SE		302–406	Jan. 1971

[a] See Fig. 1.

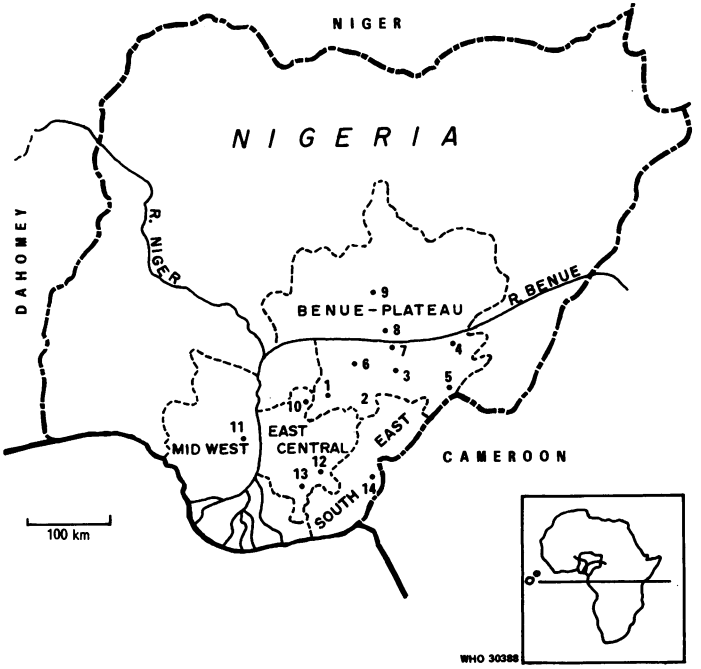

Fig. 1. Nigeria, showing serological survey sites: 1, Okwoga; 2, Ito; 3, Gboko; 4, Wukari; 5, Takum; 6, Naka; 7, Abinsi; 8, Udei; 9, Gudi; 10, Obolo–Afor; 11, Issele–Uku; 12, Abiriba; 13, Mbawsi; 14, Aking.

RESULTS

The results of HI and yellow fever N tests on single sera are presented in Table 2. At sites in the savannah-woodland and Guinea savannah zones of the Benue River basin to the east and north-east of Okwoga (Ito, Gboko, Wukari, Naka, Udei), a high prevalence of HI antibodies to one or more group B arboviruses was found. The proportion of HI-positive sera in adults approached 100% in some areas. Yellow fever N antibodies were present in the sera of 23–36% of individuals at these sites. Both group-B HI and yellow fever immunity increased with age.

Lower levels of yellow fever immunity were found at survey sites more distant from the Okwoga focus, both north and south, with one important exception: at 3 villages near Mbawsi in the south-central part of East Central State (Fig. 1, site 13), serological findings were strikingly similar to those from the epidemic focus. A high prevalence of yellow fever N antibodies was found both in children (30%) and in adults (41%), with a small discrepancy between the proportions positive by HI and N tests.

CF results

The results of CF tests performed on yellow-fever-immune sera are presented in Table 3. Positive reactions, i.e., yellow fever CF titre $\geq$ 1 : 16 (Monath et al., 1973b) were divided into specific and group reactions. Specific reactions were characterized by a titre to yellow fever at least fourfold higher than to other group B antigens; such serological patterns indicated recent primary yellow fever infection (Monath et al., 1973a). Group CF reactions were characterized by heterologous cross-reactions between yellow fever and one or more other group B antigens, with no more than a twofold difference in titre; most of these reactions represented persons with recent group B superinfections. In these cases it is not known whether yellow fever or another group B virus was the most recent infecting agent.

Although the numbers are small, it is apparent that yellow fever infections occurred in 1970 at Ito, 64 km west of Okwoga. With the exception of Mbawsi, in East Central State, all other sites had little or no serological evidence for recent epidemic yellow fever. At Mbawsi, 22 of 112 sera (20%) had yellow fever CF antibodies, including 6 sera with specific reactions.

N tests using Group B arboviruses other than yellow fever

The question of the specificity of the yellow fever N test was raised by the finding of high proportions of yellow-fever-immune sera among children and adults in areas not affected by yellow fever in 1969 or 1970. Consequently, yellow-fever-immune sera from Gboko, Wukari, Naka, Udei, and Gudi were screened by N test against West Nile, Wesselsbron, Zika, and dengue-2 viruses. Results are presented in Table 4.

Of 40 yellow-fever-immune sera tested, 8 (20%) were positive to yellow fever alone. Specific yellow fever immunity was found at all localities except Udei. As expected, specific immunity was more common in children than adults. Only 5 of 34 yellow-fever-immune adults had specific (monotypic) yellow fever antibodies, whereas 16 adults were positive to yellow fever and 3 or more other group B viruses. The presence of N antibodies to dengue-2 virus was most commonly associated with yellow fever immunity (32 of 40 sera positive to both viruses), followed by Zika (20 of 40 positive), Wesselsbron (19 of 40), and West Nile (6 of 40).

DISCUSSION

On the basis of CF tests on sera from Ito, yellow fever cases probably occurred during 1970 in this savannah-woodland region immediately to the west of Okwoga. The infection rate (less than 14%) was lower than in the epidemic focus (Monath et al., 1973a). Other, more peripheral, regions of Benue Plateau State and northern East Central State were apparently spared.

The finding of high proportions of yellow fever N-positive and CF-positive sera at Mbawsi in southern East Central State indicated a separate focus of recent yellow fever activity. One case of yellow fever was confirmed by serological tests in a young woman hospitalized with jaundice at Umuahia (16 km north of Mbawsi) in January 1971 (Monath et al., 1972). Moreover, CF titres in sera collected at Mbawsi were consistent with very recent infection. The geometric mean yellow fever CF titre (GMT) for positive sera from Mbawsi (117.0) was similar to the GMT for sera collected shortly after the epidemic at Okwoga (114.0).

The epidemiological significance of Mbawsi in Nigeria remains a matter for speculation. Although the original vegetation was lowland rain forest, Mbawsi, like most of East Central State, is characterized by relatively open secondary growth, predominantly oil palm bush. Nonhuman primate hosts are very thinly distributed in this deforested area of eastern Nigeria. Galagos are present, but intensive collecting near Aba

Table 2. Results of HI and N tests on single sera tested for yellow fever antibodies in Nigeria, 1970–71

Site no. [a]	Locality	Age [b] (years)	No. tested	No. HI-positive (%)		No. N-positive (%)	
1	Okwoga Okpudu Aidogodo	0–14	107	49	(46)	40	(38)
		⩾15	161	89	(55)	67	(42)
		T	268	138	(52)	107	(40)
2	Ito	0–14	13	4	(31)	1	(8)
		⩾15	31	26	(84)	9	(29)
		T	44	30	(68)	10	(23)
3	Gboko	0–14	—	—		—	
		⩾15	29	29	(100)	9	(31)
		T	29	29	(100)	9	(31)
4	Wukari	0–14	8	8	(100)	0	(0)
		⩾15	22	22	(100)	10	(46)
		T	30	30	(100)	10	(33)
5	Takum	0–14	23	15	(65)	3	(13)
		⩾15	—	—		—	
		T	23	15	(65)	3	(13)
6	Naka	0–14	21	4	(19)	2	(10)
		⩾15	25	16	(64)	10	(40)
		T	46	20	(44)	12	(26)
7	Abinsi	0–14	17	4	(24)	0	(0)
		⩾15	—	—		—	
		T	17	4	(24)	0	(0)
8	Udei	0–14	12	3	(25)	3	(25)
		⩾15	16	8	(50)	7	(44)
		T	28	11	(39)	10	(36)
9	Gudi	0–14	10	2	(20)	1	(10)
		⩾15	28	6	(21)	1	(4)
		T	38	8	(21)	2	(5)
10	Obolo–Afor	0–14	18	3	(17)	1	(6)
		⩾15	8	3	(38)	0	(0)
		T	26	6	(33)	1	(4)
11	Issele–Uku	0–14	—	—		—	
		⩾15	42	36	(86)	2	(5)
		T	42	36	(86)	2	(5)
12	Abiriba	0–14	25	0	(0)	0	(0)
		⩾15	33	11	(33)	7	(21)
		T	68	11	(16)	7	(10)
13	Mbawsi area (3 villages)	0–14	27	12	(44)	8	(30)
		⩾15	85	55	(65)	35	(41)
		T	112	67	(60)	43	(38)
14	Aking	0–14	34	2	(6)	1	(3)
		⩾15	54	16	(30)	4	(7)
		T	88	18	(20)	5	(6)

[a] See Fig. 1.
[b] T = total, all ages.

Table 3. Results of CF tests on yellow-fever-immune sera, Nigeria, 1970–71

Site no. [a]	Locality	No. of N-positive sera tested/ total in sample [b]	Negative or inconclusive [c]	Positive		
				Specific reactions [d]	Group reactions [e]	Total
1	Okwoga	107/268	16	51	40	91
2	Ito	10/44	4	2	4	6
3	Gboko	7/29	7	0	0	0
4	Wukari	8/30	6	0	2	2
6	Naka	12/46	11	1	0	1
8	Udei	10/28	9	0	1	1
9	Gudi	2/38	2	0	0	0
10	Obolo–Afor	1/26	1	0	0	0
11	Issele–Uku	2/42	2	0	0	0
12	Abiriba	4/68	4	0	0	0
13	Mbawsi	42/112	20	6	16	22
14	Aking	4/88	1	1	2	3

[a] See Fig. 1.
[b] Not all N-positive sera were tested by CF.
[c] Yellow fever CF titre $\leqslant 1:8$
[d] Yellow fever CF titre $\geqslant 1:16$ and at least fourfold higher than to other Group B antigens.
[e] Yellow fever CF titre $\geqslant 1:16$ with heterologous cross-reactions with other Group B antigens.

in June (Kemp, G. E., unpublished data) yielded only *G. demidovii*, a species thought to be refractory to yellow fever infection (Haddow & Ellice, 1964). Primary forest, said to harbour large populations of monkeys, is present along the Cross and Imo Rivers, which border East Central State. These areas require further investigation.

Very scanty information is available regarding potential mosquito vectors in East Central State. Preliminary entomological surveys have indicated that wild-breeding *Stegomyia* mosquitos (in particular *Aedes africanus* breeding in bamboo stumps) are the most prevalent potential vectors, and that domestic-breeding *A. aegypti* are virtually absent.

Table 4. Results of neutralization (N) tests using other group B arboviruses on yellow-fever-immune sera

Locality	Age (years)	Total no. of N-positive sera tested	YF-positive only	Positive to YF and:				Positive to YF and:			Not tested
				West Nile	Wessels-bron	Zika	dengue 2	1 other virus [a]	2 viruses	3 or more viruses	
Gboko	$\geqslant 15$	9	2	0	3	4	6	2	1	3	1
Wukari	$\geqslant 15$	10	3	2	4	6	7	1	2	4	0
Naka	0–14	2	2	0	0	0	0	0	0	0	0
	$\geqslant 15$	10	0	2	4	4	8	3	1	4	2
Udei	0–14	3	0	0	3	0	3	1	2	0	0
	$\geqslant 15$	7	0	1	3	5	7	2	1	4	0
Gudi	0–14	1	1	0	0	0	0	0	0	0	0
	$\geqslant 15$	1	0	1	1	1	1	0	0	1	0
Total, all localities	0–14	6	3	0	3	0	3	1	2	0	0
	$\geqslant 15$	37	5	6	15	20	29	8	5	16	3
	total	43	8	6	18	20	32	9	7	16	3

[a] In each case this other virus was dengue type 2.

Except at Mbawsi, relatively lower proportions of yellow-fever-immune sera were found in eastern Nigeria than in the Guinea savannah zone of the Benue River basin. Although unrecognized epidemic yellow fever occurred at Mbawsi in 1970, it appears unlikely that this area represents an important focus of endemic or enzootic virus activity.

The highest prevalence of neutralizing antibodies to yellow fever was found in localities in the Benue River basin. With the exception of the epidemic focus (Okwoga) and an immediately adjacent area (Ito), these localities were not affected by recent epidemics. Yellow fever immunity increased with age, and monotypic yellow fever N antibodies were found at most localities, especially in children. Interpretation of the presence of yellow-fever-immune sera in these widely scattered areas is not possible at present. If yellow fever virus circulates at a low level of transmission between epidemics in localized, stable, or wandering foci, the vector–host relationships of the endemic or enzootic mechanism remain conjectural. Recent studies by the Virus Research Laboratory suggest that localized pockets of riverine forest along the Niger and Benue rivers may provide large numbers of nonhuman primates and potential vectors throughout the year.

On the basis of the serological results, hyperendemic circulation of other group B viruses, such as Zika, Wesselsbron, and dengue, unquestionably exists in the savannah zones despite extensive drying between November and March or April. Domestic-breeding *A. aegypti* are rarely found in the predominantly rural areas of the Benue basin (V. H. Lee, unpublished information). Elucidation of the vector–host relationships of endemic circulation of these other group B arboviruses in this region may well provide answers to questions about yellow fever virus transmission. In particular, study of the epidemiology of dengue may provide fruitful information, since dengue and yellow fever N antibodies were associated in a high proportion of individuals both in the present and in previous surveys (MacNamara et al., 1959). If dengue virus is maintained year-round in a human–human cycle by mosquito vectors (other than domestic *A. aegypti*) surviving the long dry season, a similar cycle may operate for yellow fever.

RÉSUMÉ

L'ÉPIDÉMIE DE FIÈVRE JAUNE DE 1970 DANS LE DISTRICT D'OKWOGA, ÉTAT DU PLATEAU DE BENUE, NIGÉRIA: 2. ENQUÊTE IMMUNOLOGIQUE EN VUE DE DÉTERMINER LES LIMITES GÉOGRAPHIQUES ET LES ORIGINES DE L'ÉPIDÉMIE

On a mené une enquête sérologique dans les régions orientales et septentrionales du Nigéria afin de déterminer l'extension géographique et les origines de l'épidémie de fièvre jaune (FJ) observée dans le district d'Okwoga en 1970.

Les sérums ont d'abord été examinés en inhibition de l'hémagglutination (IH), puis les échantillons positifs en IH ont été soumis à l'épreuve de neutralisation (N). Les sérums renfermant des anticorps N contre la fièvre jaune ont alors subi une épreuve de fixation du complément (FC). On a aussi recherché la positivité en épreuve N de sérums sélectionnés à l'égard d'arbovirus du groupe B autres que le virus FJ.

On a décelé des anticorps N antiamarils dans le sérum de 23-36% des personnes vivant dans les zones de savane guinéenne du bassin du fleuve Benue, et dans le sérum de 4-10% seulement des habitants des régions forestières du Nigéria oriental. Une exception a été relevée à Mbawsi près d'Umuahia, dans l'Etat central oriental, où 38% des prélèvements étaient positifs.

On a constaté une forte prévalence des anticorps FC antiamarils, témoignant d'une épidémie récente, dans deux endroits: Ito et Mbawsi. Ito, à 45 km d'Okwoga, est situé à la périphérie de la zone épidémique. En revanche, Mbawsi représente un foyer séparé d'activité amarile épidémique non reconnue en 1970-71.

Ces résultats sérologiques montrent que les arbovirus FJ, ainsi que d'autres virus du group B, circulent à l'état hyperendémique dans la zone méridionale de savane guinéenne du Nigéria et qu'ils persistent pendant la longue saison sèche. Les relations vecteur-hôte n'ont pas été élucidées, mais il semble que des moustiques domestiques de l'espèce *Aedes aegypti* ne soient pas en cause.

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