Bull. Org. mond. Santé
Bull. Wld Hlth Org. } 1973, 49, 235-244

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

3. Serological responses in persons with and without pre-existing heterologous Group B immunity *

T. P. MONATH,[1] D. C. WILSON,[2] & J. CASALS [3]

Serological studies of persons infected with yellow fever (YF) during the 1970 epidemic in Okwoga District, Nigeria, indicated that epidemic YF occurred despite a high prevalence of pre-existing group B arbovirus immunity, which increased with age. The viruses involved were primarily dengue, Zika, and Wesselsbron. Patterns of responses of haemagglutination-inhibiting, complement-fixing, and neutralizing antibodies in primary YF and in superinfections are defined in this paper.

In late 1970 an epidemic of yellow fever affected rural inhabitants of Okwoga District, Benue Plateau State, Nigeria (Monath et al., 1974a). Five localities within this area had been sampled during a serological survey in 1965–66 by WHO. Haemagglutination-inhibition tests on sera from these localities were performed at the Yale Arbovirus Research Unit. The results showed the area to be hyperendemic for Group B arboviruses, and the 1970 outbreak thus afforded an opportunity to study the serological and clinical responses to wild yellow fever virus in humans with and without pre-existing heterologous Group B immunity.

MATERIALS AND METHODS

1970 serological studies

The methods used to collect sera and clinical data from persons in Okwoga District are described elsewhere (Monath et al., 1974a). Paired or single sera were available for complete testing from 241 inhabitants of Okwoga and Aidogodo villages, where the epidemic occurred. All serological tests were performed at the Virus Research Laboratory, Ibadan. The virus strains that were used to prepare seed lots and antigens are shown in Table 1. Seed lots were prepared as 10% suspensions of infected suckling mouse brains in 10% normal mouse serum and were wet-frozen at −60°C. Antigens were prepared by sucrose–acetone extraction (Clarke & Casals, 1958).

HI tests on kaolin-adsorbed sera were performed according to the method of Clarke & Casals (1958) adapted for use in microtitre plates. When necessary, serum HI titres were adjusted to correspond to inhibition of 8 haemagglutinating (HA) units of antigen, as described by Evans et al. (1971). Complement-fixation (CF) tests were performed in microtitre plates according to the technique of Weinbren (1958). Titres are expressed as the dilution factor of the highest serum dilution fixing two units of complement.

Neutralization (N) tests were performed by inoculating 2–4-day-old suckling mice intracerebrally with a preincubated (37°C for 60 min) mixture of undiluted, heat-inactivated serum and virus suspension (in 0.75% bovalbumin in phosphate-buffered saline). A positive result was recorded if 6 of 6, 5 of 5, or 5 of 6 mice survived. The actual virus doses used in the

* From the Virus Research Laboratory, Faculty of Medicine, University of Ibadan, Ibadan, Nigeria, and the Yale Arbovirus Research Unit, Yale University, New Haven, Conn., USA.

[1] Present address: Vector-Borne Diseases Division, Center for Disease Control, US Department of Health, Education, and Welfare, P.O. Box 2087, Ft Collins, Col., USA.

[2] Present address: 1777 Yale Station, New Haven, Conn., USA.

[3] Yale Arbovirus Unit, Department of Epidemiology and Public Health, Yale University School of Medicine. This work was supported in part by a grant from the Rockefeller Foundation.

Table 1. Virus strains used in serological tests at Virus Research Laboratory, Ibadan, Nigeria, 1970–71

Virus		Strain designation	Year isolated	Source	No. of passages in suckling mice
yellow fever	(YF)	IB H 43913	1969	human	5
West Nile	(WN)	IB AN 4067	1965	sentinel mouse	8
Wesselsbron	(WSL)	IB AN 31956	1968	camel	6
Zika		IB H 30656	1968	human	15
dengue-1	(DEN-1)	IB H 28328	1968	human	43
dengue-2	(DEN-2)	IB H 11234	1966	human	30

N tests were: yellow fever (YF), 70–400 LD_{50}; West Nile (WN), 30–315 LD_{50}; Wesselsbron (WSL), 50–200 LD_{50}; Zika, 50–160 LD_{50}; and dengue-2 (DEN-2), 700 LD_{50}. Labile serum factor was not used in N tests.

N tests were performed both on HI-positive sera (titre $\geqslant 10$) lacking evidence of recent infection (i.e., CF titre $\leqslant 8$) and on CF-positive sera with serological patterns consistent with group B arbovirus superinfection, in an attempt to define the prevalence and the etiology of prior group B exposure.

RESULTS

1965 serum survey

The results of HI tests on sera collected in 1965–66 at five localities near or within the 1970 epidemic focus (Table 2) show that this area was hyperendemic for group B arboviruses, including Zika and WSL. The criteria for defining specific (single) infections and superinfections with group B arboviruses have been described previously (Evans et al., 1971).

1970 epidemic

According to the results of HI, CF, and N tests, sera were divided into two groups. " Positive " sera (78), indicating infection during the epidemic, were those having an HI titre of $\geqslant 10$ to one or more group B viruses, a CF titre of $\geqslant 16$ to YF, and a positive YF N test. " Negative " sera (147), indicating absence of infection, were those with or without group B HI antibody that were negative by CF and N test for YF. Sera from 16 individuals had group B HI and YF N antibodies in single or paired samples but had CF titres of $\leqslant 8$. These sera were excluded from the study, since it could not be determined whether they represented persons infected during the epidemic or in the remote past.

Table 2. Results of haemagglutination-inhibition tests on sera collected in 1965 at sites near or within the 1970 yellow fever epidemic zone, Benue Plateau State, Nigeria

Age (years)	No. of sera tested	Group-B-positive sera							
		Specific					Super-infection	Indeter-minate	Total (%)
		YF	WN	WSL	Zika	other			
0–4	22	—	—	—	1	—	1	—	2 (9)
5–9	33	1	—	3	1	—	4	4	13 (39)
10–19	24	—	1	2	3	—	5	1	12 (50)
20–39	34	—	—	—	6	—	17	3	26 (76)
$\geqslant 40$	18	—	—	—	4	—	12	1	17 (94)
Total	131	1	1	5	15	0	39	9	70 (53)

Table 3. Results of serological tests on sera from individuals not infected with yellow fever, Okwoga and Aidogodo villages, Benue Plateau State, Nigeria, 1970–71

Age (years)	No. of sera tested	No. (%) positive					
		HI test	N test				
		Group B	YF	WN	WSL	Zika	DEN-2
0–9	67	9 (13)	0 (0)	1 (1)	0	3 (4)	5 (7)
10–19	32	4 (13)	0 (0)	0	0	2 (6)	3 (9)
⩾ 20	48	16 (33)	0 (0)	1 (2)	3 (6)	13 (27)	10 (21)
Total	147	29 (20)	0 (0)	2 (1)	3 (2)	18 (12)	18 (12)

In addition to the 1965 serum survey, a study of persons not infected with YF provided information on the immunological background of the Okwoga population prior to the epidemic. N antibodies to WSL, Zika, and DEN-2 viruses were found most frequently (Table 3).

Tests on positive sera distinguished individuals primarily infected with yellow fever in 1970 from those showing superinfection with YF and one or more related group B arboviruses. The criteria used to define serological responses are given in Table 4. Primary yellow fever infection was characterized by either monotypic HI and CF YF antibodies or by a mixed homotypic CF and monotypic N response. Superinfections were generally characterized by nonspecific heterologous cross-reactions in HI and CF, although for some sera a mixed homotypic HI and/or CF response (category 3) or a heterotypic HI response (category 4) was observed. All sera classed as representing superinfections had N antibodies to YF and at least one other group B arbovirus. It should be borne in mind that because 3 group B arboviruses isolated in Nigeria were not included in N tests—DEN-1, Uganda S (UGS), and Potiskum (IbAN 10069, closely related to UGS)—category 2 may, in fact, include sera from individuals infected with these agents prior to the epidemic. Specific examples of sera in each category are given in Table 5.

The numbers of yellow fever CF-positive sera showing primary and secondary serological reactions are shown by age group in Table 6. As expected, the younger age groups showed the highest proportion of primary serological responses, and the percentage of

Table 4. Criteria used to define serological responses following primary or superinfection with yellow fever virus

Tests	Serological responses			
	Primary		Superinfection	
	category 1 (22 tested)	category 2 (5 tested)	category 3 (18 tested)	category 4 (33 tested)
HI	monotypic	heterologous cross-reactions present, either nonspecific [a] or specific for YF [b]		heterologous cross-reactions present, either nonspecific [a] or heterotypic [c]
CF	monotypic	mixed homotypic (heterologous cross-reactions present but specific for YF [b])		heterologous cross-reactions between YF and 1 or more group B arboviruses (nonspecific [a])
N	not tested	YF-positive only	positive to 1 or more other Group B arboviruses	

[a] ⩽ twofold difference in titre.
[b] ⩾ fourfold higher titre to YF than to other antigens tested.
[c] titre ⩾ fourfold higher to a group B virus other than YF.

Table 5. Examples or results of serological tests for primary yellow fever infections and group B superinfections, Okwoga, Nigeria, 1970–71

Serological group	Category	Age (years)	Days after onset	HI titre [a]				CF titre [b]					N test [c]				
				YF	WN	WSL	DEN-1	YF	WN	WSL	Zika	DEN-2	YF	WN	WSL	Zika	DEN-2
Primary	1	11	9	2	0	0	0	16	0	0	0	0	—	—	—	—	—
			41	5	0	0	0	64	0	0	0	0	—	—	—	—	—
		7	31	4	0	0	0	512	0	0	0	0	—	—	—	—	—
			63	9	0	1	0	64	0	0	0	0	—	—	—	—	—
	2	25	44	6	4	5	1	64	8	8	0	8	—	—	—	—	—
			120	3	1	1	0	16	0	0	0	0	P	N	N	N	N
		12	8	1	0	0	0	0	0	0	0	0	P	N	N	N	N
			81	8	7	7	4	256	32	16	0	0	P	N	N	N	N
Superinfection	3	25	44	3	0	1	0	256	8	16	32	8	P	N	P	N	N
		30	49	4	5	5	2	1024	32	16	64	8	P	N	N	P	N
		50	38	7	7	7	5	1024	128	128	128	16	P	N	N	P	P
	4	10	× [d]	7	10	9	4	32	64	8	8	8	P	N	N	N	P
			× + 33	4	5	5	2	16	16	0	8	8	P	N	N	N	P
		6	7	5	5	7	3	256	128	128	0	0	P	N	N	N	P
			82	2	1	2	0	32	32	16	0	0	P	N	N	N	P
		8	19	7	11	15	5	64	64	64	16	8	P	N	N	N	P
			42	6	6	7	2	32	32	16	16	0	P	N	N	N	P
		45	8	8	13	16	9	256	128	128	0	0	P	P	N	P	P
			86	6	6	6	4	64	32	16	0	0	P	P	N	P	P
		10	[d]	7	7	5	4	64	128	64	32	32	P	N	N	P	P
		45	30	10	10	8	5	1024	256	512	128	32	P	P	P	P	P
		9	5	10	12	12	9	256	64	128	16	16	—	—	—	—	—
			79	6	6	6	2	32	16	16	16	8	P	N	N	N	P

[a] Wells of inhibition (0 = < 1 : 10; 1 = 1 : 10; 2 = 1 : 20; 3 = 1 : 40, etc.).
[b] 0 = CF titre < 8.
[c] P = positive (6 of 6, 5 of 6, or 5 of 5 mice survive); N = negative.
[d] Unknown no. of days.

Table 6. Age distribution of persons sustaining primary yellow fever infection or YF group B superinfection, Okwoga, Nigeria, 1970–71

Age (years)	No. of positive sera	No. (%) in category [a]					
		Primary infection			Superinfection		
		category 1	category 2	Total	category 3	category 4	Total
0–9	20	14 (70)	0 (0)	14 (70)	1 (5)	5 (25)	6 (30)
10–19	18	6 (33)	1 (6)	7 (39)	3 (17)	8 (44)	11 (61)
⩾20	40	3 (7.5)	3 (7.5)	6 (15)	14 (35)	20 (50)	34 (85)
Total	78	23 (30)	4 (5)	27 (35)	18 (23)	33 (42)	51 (65)

[a] See Table 4.

superinfections increased with age. The age-specific frequency of superinfections thus correlates well with the findings of the 1965 serum survey in which 27%, 50%, and 83% of persons 0–9, 10–19, and 20 or more years of age, respectively, showed evidence of prior group B arbovirus exposure (Table 2).

N antibodies and CF patterns in sera with superinfection patterns

The N-antibody spectra in sera with patterns indicating group B superinfection are shown in Table 7. Of the viruses tested, dengue and Zika appeared to be most frequently responsible for infection prior to the YF epidemic. Of 51 individuals with prior group B immunity infected with YF, 47 (92%) had DEN-2 and 40 (78%) had Zika antibodies. Prior infections with WSL and WN viruses were less common.

Among persons with prior group B exposure who were not infected with YF during the epidemic, the frequencies of N antibodies to the various group B viruses were similar to or lower than those in YF-

Table 7. Frequency of neutralizing antibodies to group B arboviruses in persons sustaining superinfections

Serological category	No. tested	No. (%) N-test positive										
		YF and 1 other virus				YF, Zika, and DEN-2	YF and 3 or 4 other viruses	Total				
		WN	WSL	Zika	DEN-2			YF	WN	WSL	Zika	DEN-2
3	18	0	1 (6)	3 (17)	2 (11)	11 (61)	1 (6)	18 (100)	0	2 (11)	15 (83)	14 (78)
4	33	0	0	0	8 (24)	14 (42)	11 (33)	33 (100)	6 (18)	6 (18)	25 (76)	33 (100)
Total	51	0	1 (2)	3 (6)	10 (20)	25 (49)	12 (23)	51 (100)	6 (12)	8 (16)	40 (78)	47 (92)

Table 8. Comparison of frequencies of group B antibodies between persons not infected and those with YF superinfections

Group	No. of sera having group B HI antibodies	No. (%) N-test positive				
		YF	WN	WSL	Zika	DEN-2
not infected with YF [a]	29	0 (0)	2 (7)	3 (10)	18 (62)	18 (62)
superinfected [b]	51	51 (100)	6 (12)	8 (16)	40 (78)	47 (92)

[a] From Table 3.
[b] From Table 7.

superinfected persons (Table 8). This indicates that persons with prior group B immunity were not spared because of differences in the prevalence of antibodies to a specific group B virus.

Table 7 also shows differences in the N-antibody spectrum between persons with serological patterns in categories 3 and 4. Sera with N antibodies to YF and 3 or 4 other group B viruses were most likely to have heterologous CF patterns rather than mixed homotypic (specific) patterns. A broad heterologous CF response (category 4) was seen, however, in 8 persons positive by N test to YF and DEN-2 alone, whereas persons infected with YF and either WSL or Zika had specific (mixed homotypic) CF patterns.

HI and CF titres in primary infections and superinfections

Table 9 shows the distribution of HI and CF titres and geometric mean titres (GMT) in persons with primary YF infection and with superinfections.

As indicated previously, persons with primary YF infection demonstrated a high degree of serological specificity. Superinfections were characterized by broad high-titre cross-reactions in HI and CF, although the titre to YF antigen was not infrequently fourfold greater (or more) than titres to other group B antigens. In HI tests, the titre to other group B antigens was occasionally higher than to YF, especially in sera drawn early after onset. Such heterotypic responses were never observed in CF tests. The highest degree of cross-reactivity in both HI and CF tests was observed with WN and WSL antigens, in sera with or without N antibodies to either virus.

As shown in Table 5, HI titres to heterologous group B antigens tended to fall more rapidly than yellow fever titres. When paired sera were studied, heterotypic HI responses present in sera drawn early after the onset of superinfections disappeared with time.

Chronology of HI and CF responses

The GMTs at varying intervals after onset were computed for sera from 63 infected individuals giving a history of illness compatible with YF. Figures 1 and 2 show YF GMTs for primary and anamnestic HI and CF responses. In persons with primary infections, HI antibodies were detectable at low titre in some sera during the first week after onset, and titres rose rapidly during the second and third week to a peak between 15 and 28 days. In persons with superinfections, HI antibodies were present at high titre between 0 and 7 days after onset; HI titres

Table 9. Distribution of haemagglutination-inhibition (HI) and complement-fixation (CF) titres in persons with primary YF infection and with superinfections

Serological group	Antigen	No. of sera with HI titre (Wells of inhibition)												GMT	No. of sera with CF titre									GMT
		0	1	2	3	4	5	6	7	8	9	10	11	12		<8	8	16	32	64	128	256	512	1024	2048	4096	8192	
Primary (27 persons)	YF	0	1	2	8	6	2	4	2	1	1	0	0	0	113	0	0	8	8	5	0	4	2	0	0	0	0	49.8
	WN	22	2	0	1	1	0	0	1	0	0	0	0	0	<10	19	7	0	1	0	0	0	0	0	0	0	0	<8
	WSL	18	5	1	1	0	1	0	1	0	0	0	0	0	<10	19	6	2	0	0	0	0	0	0	0	0	0	<8
	Zika[a]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	22	5	0	0	0	0	0	0	0	0	0	0	<8
	DEN-2	23	3	0	0	1	0	0	0	0	0	0	0	0	<10	26	1	0	0	0	0	0	0	0	0	0	0	<8
Super-infections (51 persons)	YF	0	0	0	3	8	6	9	10	7	2	3	1	2	472	0	0	2	3	7	9	15	5	7	2	0	1	222
	WN	2	3	0	5	4	3	6	8	4	3	4	4	5	509	10	4	7	5	10	8	2	2	2	1	0	0	28.3
	WSL	2	2	6	4	3	10	3	4	2	5	1	3	6	317	1	4	6	7	6	17	7	0	3	0	0	0	69.4
	Zika[a]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4	9	10	13	11	3	0	0	1	0	0	0	22.5
	DEN-2	3	7	5	11	11	7	2	0	1	3	0	0	1	59.0	24	10	5	7	5	0	0	0	0	0	0	0	<8

[a] Not tested for haemagglutination-inhibition.

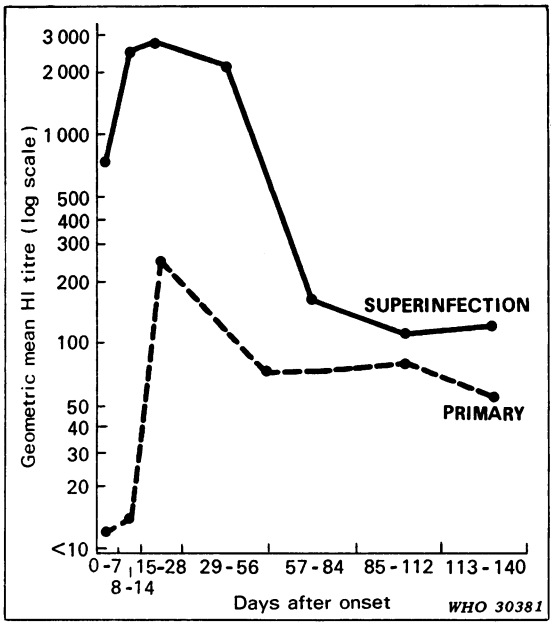

Fig. 1. Geometric mean yellow fever haemagglutination-inhibition (HI) titres by days after onset in persons with primary YF infection and superinfections, Okwoga, Nigeria, 1970–71

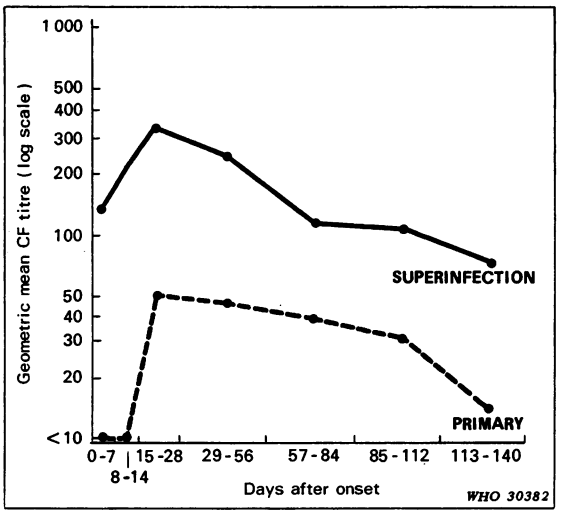

Fig. 2. Geometric mean yellow fever complement-fixation (CF) titres by days after onset in persons with primary YF infection and superinfections, Okwoga, Nigeria, 1970–71.

reached a peak between 15 and 28 days, and fell rapidly between 6 and 10 weeks after onset. HI titres in both primary and superinfections showed little change between the 10th and 20th weeks.

In primary CF responses, the GMT was less than 10 during the 14 days after onset, rose rapidly between 15 and 28 days after onset, and declined gradually thereafter. In persons superinfected, high CF titres were present 0–7 days after onset; peak CF titres were reached between 15 and 28 days after onset, and the titres declined gradually thereafter.

Relationship of clinical history to serological response

Although it was not possible to classify retrospective clinical histories according to severity of illness, the frequencies of symptoms were compared in persons having primary and anamnestic serological responses.

Table 10 shows the proportion of individuals with primary infections and with superinfections who had clinical symptoms during the epidemic period. Although persons with primary serological responses, especially children 0–14 years of age, had a history of clinical illness more frequently than those with group B superinfections, the differences shown are not statistically significant. Symptoms associated with severe illness (abnormal bleeding and jaundice) were noted as frequently in the superinfected group as in those with primary infections. When the data were further analysed by specific etiology of previous group B exposure, no significant differences in frequency of symptoms were found between those with primary infections and those with superinfections.

DISCUSSION

Experimental studies in animals have shown cross-protection between group B arboviruses (Casals, 1957; Hammon & Sather, 1956; Price et al., 1967; Bond, 1969; Sather & Hammon, 1970; Price & Thind, 1971), and specifically between Wesselsbron and Zika viruses and yellow fever (MacNamara, 1953; Bearcroft, 1957; Henderson, et al., 1970). The possible role of prior infection with Zika, WSL, and dengue viruses in (1) modifying clinical YF infection and (2) interfering with the natural transmission cycle of YF virus in man or primates has been reviewed by

Table 10. Frequency of clinical symptoms in persons sustaining primary YF infection or superinfections

Serological group	Age (years)	No. of persons	No. (%) of persons with symptom			Total no. (%) ill	No. (%) with no illness
			Fever, headache only	Abnormal bleeding	Jaundice		
primary	0–14	21	19 (90)	1 (5)	5 (24)	19 (90)	2 (10)
	⩾15	6	4 (67)	0 (0)	3 (50)	5 (83)	1 (17)
	Total	27	23 (85)	1 (4)	8 (30)	24 (89)	3 (11)
super-	0–14	14	4 (29)	2 (14)	3 (21)	9 (64)	5 (36)
infection	⩾15	37	12 (32)	1 (3)	17 (46)	30 (81)	7 (19)
	Total	51	16 (31)	3 (6)	20 (39)	39 (76)	12 (24)

Henderson et al. (1970). It has been suggested that immunologic cross-protection might explain the absence of YF from certain geographic regions (Asia, coastal Kenya, Zika forest).

Studies conducted during the 1970–71 Okwoga outbreak in Nigeria, however, have shown that epidemic interhuman transmission of yellow fever virus occurred in a population with a high prevalence of prior immunity to several group B arboviruses. N tests on sera both from those not infected with YF (Table 3) and from those infected with YF (Table 7) showed that the viruses mainly responsible for pre-existing group B immunity were dengue and Zika.

It must be recognized that the presence of N antibodies in undiluted serum may be the result of infection with two or more heterologous related viruses (Wisseman et al., 1962; Tignor & Price, 1971). Theiler & Casals (1958) showed that persons with probable prior exposure to Ilheus who were secondarily infected with YF developed protective antibodies to dengue 1 and 2 viruses. It is possible that a similar mechanism may explain some of the dengue N antibody observed in our study, especially the higher prevalence of dengue immunity in YF superinfected persons than in those with prior group B exposure but not YF infected (Table 8).

Nevertheless, the following observations support the hypothesis of a widespread prevalence of prior dengue infection in Okwoga: (1) a large number of sera were positive by N test for dengue only or for YF and dengue only; (2) since a large virus dose was used in dengue N tests (700 LD_{50}), positive sera had a log neutralization index of at least 2.5; (3) in experimental studies, monkeys infected with Zika and challenged with YF failed to develop dengue antibodies (Tignor & Price, 1971).

The high prevalence of dengue immunity in Okwoga district is unusual and has been noted elsewhere (Monath et al., 1974b). In rural areas of Benue Plateau State, *Aedes aegypti*, the vector generally thought to be important in dengue transmission in Nigeria, is probably present only during the rainy season, since it breeds in tree holes rather than in domestic oviposition sites. Studies are needed to determine (1) whether dengue transmission occurs throughout the year (dry and rainy seasons) in rural areas of Benue Plateau State, (2) what vector–host relationships are involved, and (3) what role a similar mechanism might have in maintaining endemic yellow fever transmission.

No statistically significant difference could be shown between the overall frequency of illness, abnormal bleeding, or jaundice between persons with primary infections and those with superinfections during the Okwoga epidemic. However, our studies did not disprove an effect of prior group B exposure upon either clinical severity or the incidence of interhuman YF transmission. In YF epidemics allowed to run their course, without changes in mosquito vector density, infection rates have been 90% or more (Taylor, 1951), considerably higher than in Okwoga. Moreover, the Okwoga epidemic was apparently mild, with a low case-fatality rate (Monath et al., 1974a). Since the number of YF-infected

individuals tested was small, the reliability of retrospective clinical histories less than optimum, and the prevalence of illness not due to YF considerable (Monath et al., 1974a), an effect of prior group B immunity on the clinical course of YF could easily have been missed.

The serological patterns observed in persons with primary YF infections and those with YF superinfections are generally consistent with the findings of other authors (Theiler & Casals, 1958; Fabiyi, 1961). Primary infections were characterized by a longer interval between infection and appearance of HI and CF antibodies, lower peak HI and CF titres, and a higher degree of specificity than superinfections. Our findings differed, however, in three respects from those of Theiler & Casals (1958). First, the HI and CF tests alone could not distinguish all primary infections from superinfections (e.g., category 2 from category 3, Table 4); N-test results were required. Secondly, whereas Theiler & Casals noted the development of broad HI cross-reactions 3–6 weeks after primary YF infection, nearly all persons in Okwoga with primary infections had monotypic HI patterns as late as 15 weeks after onset. Finally, in contrast to Okwoga, individuals with secondary infections in Trinidad did not develop YF-specific CF reactions and frequently had heterotypic reactions. These contradictory observations are not explained by differences in the time intervals between infection and drawing of sera; they may relate to differences in the nature or sequence of viruses or virus strains involved.

RÉSUMÉ

L'ÉPIDÉMIE DE FIÈVRE JAUNE DE 1970 DANS LE DISTRICT D'OKWOGA, ÉTAT DU PLATEAU DE BENUE, NIGÉRIA: 3. RÉACTIONS SÉROLOGIQUES CHEZ DES PERSONNES PRÉSENTANT OU NON UNE IMMUNITÉ HÉTÉROLOGUE PRÉEXISTANTE ENVERS DES ARBOVIRUS DU GROUPE B

On a étudié les réactions sérologiques chez des personnes infectées par le virus de la fièvre jaune (FJ) lors de l'épidémie de 1970 dans le district d'Okwoga, Nigéria. En dépit d'un degré élevé d'immunité hétérologue préexistante à l'égard d'arbovirus du group B, l'épidémie a entraîné une forte morbidité de l'ordre de 47%.

Pour préciser les antécédents immunologiques de la population d'Okwoga, on a utilisé *a*) des sérums recueillis par l'OMS en 1965 à l'intérieur ou près de la zone épidémique; *b*) des sérums prélevés chez des sujets non atteints par le virus amaril pendant l'épidémie; et *c*) des sérums donnant des réactions anamnestiques indiquant une exposition à des antigènes du groupe B antérieure à la surinfection par le virus FJ. Les épreuves d'inhibition de l'hémagglutination (IH) effectuées sur les sérums prélevés en 1965 ont montré que 27%, 50% et 83% des sujets infectés par le virus FJ, dans les groupes d'âge 0 à 9 ans, 10 à 19 ans et 20 ans et plus respectivement, étaient porteurs d'anticorps témoignant de surinfections par des virus du groupe B. D'après des épreuves de neutralisation (N), les virus responsables de cette immunité préexistante étaient par ordre de fréquence décroissante les virus de la dengue, Zika et Wesselsbron. Chez les sujets atteints d'une infection amarile primaire, les anticorps IH et de fixation du complément (FC) ont été décelés plus tardivement et à des titres moins élevés que chez les sujets présentant une surinfection. La grande majorité d'entre eux étaient porteurs d'anticorps antiamarils IH et FC monotypiques. Avec les sérums des sujets surinfectés, on notait de multiples réactions croisées en épreuves IH. Les épreuves FC donnaient des réactions spécifiques pour le virus FJ chez 35% des sujets surinfectés, mais dans la plupart des cas la distinction entre infections primaires et surinfections a été fondée sur les résultats des épreuves N. On n'a jamais observé de réponses hétérotypiques lors des épreuves FC. Les titres d'anticorps IH dirigés contre un virus hétérologue du groupe B ont été parfois plus élevés que les titres d'anticorps antiamarils, notamment dans les premiers temps suivant la surinfection. On n'a pas noté de différence appréciable entre les sujets atteints d'une infection primaire et les sujets surinfectés sous le rapport de la fréquence des symptômes cliniques.

Ces observations montrent qu'une épidémie de fièvre jaune peut survenir dans une région où la circulation de virus de la dengue, Zika et Wesselsbron est intense. Elles ne confirment ni n'infirment l'hypothèse suivant laquelle une immunité hétérologue préexistante atténue la gravité de la fièvre jaune, diminue la létalité ou limite la transmission du virus.

REFERENCES

Bearcroft, W. G. C. (1957) *J. Path. Bact.*, **74**, 295–303

Bond, J. O. (1969) *Bull. Wld Hlth Org.*, **40**, 160–163

Casals, J. (1957) *Trans. N.Y. Acad. Sci.*, **19**, 219–235

Clarke, D. H. & Casals, J. (1958) *Amer. J. trop. Med. Hyg.*, **7**, 561–673

Evans, A. S. et al. (1971). *Amer. J. Epidem.*, **93**, 111–121

Fabiyi, A. (1961) *Ann. trop. Med. Parasit.*, **55**, 235–241

Hammon, W. McD., & Sather, G. E. (1956) *Proc. Soc. exp. Biol. (N.Y.)*, **91**, 521–524

Henderson, B. E. et al. (1970) *Amer. J. trop. Med. Hyg.*, **19**, 110–118

MacNamara, F. N. (1953) *Brit. J. exp. Path.*, **34**, 392–399

Monath, T. P. et al. (1974a) *Bull. Wld Hlth Org.*,

Monath, T. P. et al. (1974b) *Bull. Wld Hlth Org.*,

Price, W. H. & Thind, I. S. (1971) *Amer. J. Epidem.*, **94**, 596–607

Price, W. H. et al. (1967) *Amer. J. Epidem.*, **86**, 11–27

Sather, G. E. & Hammon, W. McD. (1970) *Proc. Soc. exp. Biol. (N.Y.)*, **135**, 573–578

Taylor, R. M. (1951) *Epidemiology*. In: Strode, G. K., ed., *Yellow Fever*, New York, McGraw-Hill, p. 427

Theiler, M. & Casals, J. (1958) *Amer. J. trop. Med. Hyg.*, **7**, 585–594

Tignor, G. H. & Price, W. H. (1971) *Amer. J. Epidem.*, **94**, 386–396

Weinbren, M. P. (1958) *East African Virus Research Institute Report*, **8**, 38–39

Wisseman, C. L., Jr. et al. (1962) *Amer. J. trop. Med. Hyg.* **11**, 550–556