

hepatitis B virus. Other viruses, such as hepatitis A virus, Epstein-Barr virus, or cytomegalovirus, might have been responsible for the disease in HBsAg-negative patients in this (probably) virus-induced group.

Oxyphenisatin, methylidopa, and isoniazid may induce clinical and histopathological changes resembling CAH.<sup>9-11</sup> Our findings add a few more drugs to the list of possible trigger agents. Sulphonamides, phenylbutazone, and nitrofurantoin have been associated with acute liver damage,<sup>12-14</sup> and long-standing exposure to high doses might also be associated with the development of chronic liver disease. Hydrallazine has been associated with clinical and laboratory signs of systemic lupus erythematosus<sup>15</sup> and might be a trigger factor for CAH as well.

Almost 40% of our patients already had morphological signs of CAH at the onset of clinical illness, and no trigger factor was shown. Cases of CAH within this group might have been virus- or drug-induced, and studies on cellular immunity to HBsAg<sup>16</sup> might have shown more cases of probably viral origin.

Some reports have pointed out differences in prevalence of autoantibodies between HBsAg-positive and HBsAg-negative cases of CAH.<sup>17-19</sup> Our results only partly confirm these findings. No HBsAg-positive patient had high titres of autoantibodies, which agrees with previous observations. But HBsAg-negative patients with initial histological signs of viral hepatitis also lacked high titres of autoantibodies. The high prevalence of high-titre autoantibodies in the drug-induced and cryptogenic groups could be at least partly explained by the predominance of women in these groups, as has earlier been claimed by Reed *et al.*<sup>19</sup>

An increased frequency of HL-A 1 and HL-A 8 was found in the cryptogenic group. Mackay *et al.*<sup>2</sup> reported a high prevalence of HL-A antigens 1 and 8 among 37 patients with CAH who

had not been separated according to possible trigger factors. Possibly patients with these HL-A types are more prone to develop CAH without an external precipitating factor. On the other hand, possibly these patients develop CAH because of impaired suppressor T-cell function, which might be linked to HL-A types 1 and 8.<sup>8</sup> Thus it is not excluded that some trigger factor could be involved also in cryptogenic CAH. Evidence has been presented that subclinical hepatitis B infection could be such a factor even in patients without demonstrable serum HBsAg.<sup>16</sup> But other trigger factors—so far undefined—could, of course, be involved in these genetically predisposed patients.

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# Anthrax in the Gambia: an epidemiological study

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## Summary

Epidemiological data on 448 cases of human cutaneous anthrax from the Gambia showed that this particular strain of anthrax bacillus causes widespread morbidity and some mortality with, at the same time, subclinical infection. Analysis also showed that anthrax is not an occupationally related disease in the Gambia.

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The possibility of human-to-human spread, affecting all age groups and both sexes, by means of a communal toilet article was also shown. The fact that the strain is a good toxin producer but contains a weak antigen may have accounted for the repeated clinical infection and the fact that antibody titres were generally transient. Subclinical infection in animals was also found, particularly in sheep and goats, and also, with an unusually low mortality, in cows. Insect vectors were not excluded, but were unlikely. Vultures may spread the disease from village to village. Some possible public health and immunization procedures are discussed, with a view to containing this difficult problem in this part of west Africa.

## Introduction

Anthrax is endemic in certain parts of the world and has been reported most recently from Iran.<sup>1</sup> Before 1970 anthrax was not reported in the Gambia, though sporadic cases were probably occurring. From 1970 to the end of August 1974 (four dry seasons) nearly 450 cases were seen, diagnosed, and treated in only one area of the Gambia. This paper outlines some of our epidemiological observations.

## The area

The Foni districts of the Gambia occupy some 400 square miles, to the south of the river Gambia and north of the border of the Casamance region of Senegal. About 28 500 people live in this region. The people are mainly cattle owners and farmers. Missionary nurses of the Worldwide Evangelization Crusade have been working in Sibanor village since 1967, and from 1969 there has also been a doctor (MER) visiting and working there. Until January 1970 no case of anthrax had been recognized, but before the onset of the rains that year, in mid-May, about 10 cases were seen, though the diagnosis was not suspected until the end of the rains, when more cases occurred.

From November 1970 accurate records were kept of all cases seen and several lesions were excised for bacteriological and histological confirmation. This occurred in April 1971, when the outbreak was investigated more closely in conjunction with the veterinary and medical departments of the Gambia and with the help of the Microbiological Research Establishment at Porton Down in England.

## Survey

Two villages on the Casamance border were visited. The yearly incidence was 4% and 11%, respectively, among the 126 and 170 people living there. Blood was taken at the end of the dry season in June 1971 from 67.5% and 60% of these populations, and 25 goats, 12 cattle, and eight sheep were bled. None of these animals had been vaccinated against anthrax. When the serological results were known a further visit was made in March 1972 to examine all who had had a positive antibody titre, particularly those who had no history of anthrax. Blood was again taken to determine antibody persistence, and further animals were bled. Because cases were congregated in certain compounds we inquired into any possible mode of transmission. It was the habit of the people to share a communal palm loafah, which was made of fibres taken from the Rhum palm (*Burassus* spp). One taken from a compound where there had been recent cases of anthrax and cultured at the microbiology department of the University of Manchester yielded a growth of *Bacillus anthracis*.

We examined and bled a young girl who had been treated for anthrax in two successive years (1971 and 1972). Her family kept no animals and the only contacts were healthy children living in a compound where cases of anthrax had occurred.

Inquiries were made by the veterinary staff of the number of animals dying over the preceding years. Compounds from all villages gave a constant history that often sheep or goats had died, but not cattle. We saw the carcass of only one cow, which had obviously been eaten by vultures, and culture of a bone yielded a heavy growth of *B. anthracis*.

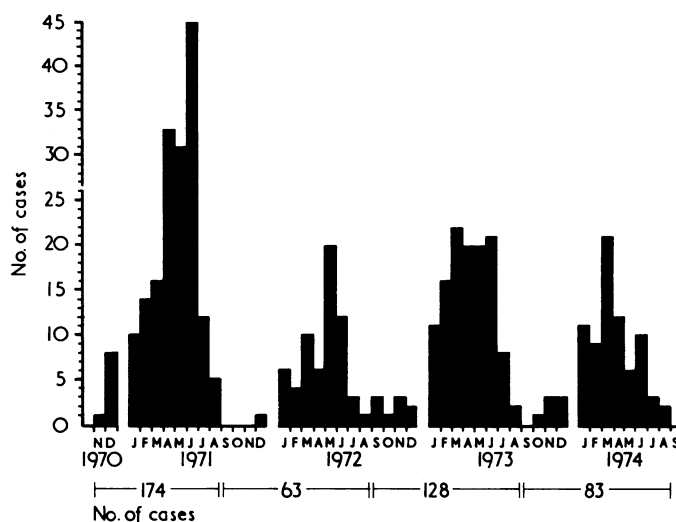
## Results

Anthrax seemed to be almost entirely related to the dry season (November to May) with some persistence into the beginning of the rainy months of June, July, and August (see fig). During the rest of the rains there were few if any cases coming for treatment. The distribution of cases together with the population figures taken from the 1973 Gambian census are summarized in table I. The two most affected districts with the greatest proportion of cases and the greatest number of villages affected each year were the Fonis of Bintang and Kansala. Though the Bintang district has its centre at Sibanor, this does not apply to Kansala. The notification of relatively few cases from Foni Bondali and the greater number from the more distant Foni Jarol can be explained by the fact that clinics are held by the mission in Foni Jarol every two weeks.

TABLE I—Distribution of anthrax cases by district (foni), villages, and year

District	Population	No. of Villages	% of Population Affected 1970-4	No. of Cases (No. of Villages*)				
				1970/71	1971/2	1972/3	1973/4	Total
Brefet .. .. .	5431	22	0.2	8 (2)	2 (2)	2 (2)	1 (1)	13 (6)
Bintang .. .. .	8329	52	1.8	49 (19)	22 (10)	51 (18)	27 (11)	149 (25)
Kansala .. .. .	7019	47	2.1	70 (17)	20 (12)	27 (14)	30 (10)	147 (26)
Bondai .. .. .	3500	27	0.9	5 (5)	7 (1)	13 (6)	6 (6)	31 (9)
Jarol .. .. .	4238	18	1.3	15 (2)	9 (3)	21 (5)	8 (5)	53 (8)
<b>Total</b>	<b>28 517</b>	<b>166</b>	<b>1.4</b>	<b>147 (45)</b>	<b>60 (28)</b>	<b>114 (45)</b>	<b>72 (33)</b>	<b>393 (74)</b>

\*Not always the same village each year.



Seasonal distribution of anthrax in the Gambia (448 cases).

Table II shows the relationship between cases of anthrax that occurred in one village in 1971. Serological examination showed that there was antibody present in some people who had no history or clinical evidence of anthrax. It also showed the rapid disappearance of antibodies in some who had been treated for anthrax and in some who had received no treatment. In others, treated or untreated, antibody persisted for up to 12 months. Those who had no history or signs of the disease yet whose serum contained antibody (subclinical infection) were, on the whole, living in close contact with people with anthrax. Two exceptions to this were "strange" farmers who had come from Senegal and were not in close contact with people who had anthrax, though they lived in adjoining huts in the compound. Similar results were seen to a lesser extent in other villages surveyed. The child who had had anthrax on two successive years and who was bled soon after the second attack had no detectable antibodies.

Tests carried out on the anthrax bacillus showed it to be a good toxin producer and fully virulent for laboratory mice, but it contained a weak antigen. A vaccine produced from the strain gave less protection to challenge with another laboratory strain than did a standard vaccine prepared in exactly the same way, which suggested a deficiency in the immunogenic fraction of the toxin complex.

The serological results in the animals are shown in table III. Antibodies were present in three out of four types of animals tested, but as only three dogs were bled this was not statistically significant. The sheep, goats, and cows whose serum contained antibodies seemed perfectly healthy, and none had been vaccinated against anthrax. This was most remarkable in cows. Of 12 cows bled in two villages in 1971 seven showed a positive titre. The Gambian veterinary department only vaccinated village cows if cattle had been dying, and apart from the one cow discovered this did not apply so no cows had been vaccinated.

Multiple lesions in humans, usually two or three (but sometimes eight to 10 and in one case 20), were seen in 17 cases. Analysis of the 431 human cases where full information was available and excluding eight cases in which multiple lesions occurred at different sites of the body showed that there was an equal sex distribution overall. Children of 2 years and under represented 11% of all cases, those between 3 and 15 years 42%, and those over 15 years 47%. Sex distribution was about equal in each age group. These percentages were very similar

TABLE II—Pattern of anthrax in a Gambian village 1971-2

Adults					Children					
Sex	Onset	Treated	Titre		Sex	Age	Onset	Treated	Titre	
			15/6/71	30/3/72					15/6/71	30/3/72
Compound Alkalikunda*										
F.	13/6/71	No	1/4	N.T.	{	M.	2 months	13/3/71	Yes	Nil
M.	11/6/71	Yes	Nil	Nil		M.	20 months	1/4/71	Yes	Nil
						M.	7 years	13/6/71	No	Nil
						F.	11 years	No lesion	No	1/2
F.	10/3/71	Yes	Nil	Nil	{	No affected children				
M.	—	—	Nil	Nil						
F.	13/3/71	No	Nil	Nil	{	No affected children				
M.	—	—	Nil	Nil						
M.†	No lesion	No	1/16	N.T.						
Compound Kanbaleba‡										
F.	6/5/71	Yes	1/4	1/4	{	M.	10 months	4/4/71	Yes	Nil
M.	8/5/71	Yes	N.T.	N.T.		M.	10 years	3/4/71	Yes	Nil
F.	No lesion	No	1/4	Nil		F.	5 years	3/4/71	Yes	N.T.
F.	17/5/71	Yes	1/2	1/2						
M.	—	—	Nil	Nil		No affected children				
Compound Kankodi										
F.	No lesion	No	1/4	1/2	{	M.	10 years	21/3/71	Yes	Nil
M.	—	—	Nil	Nil						
F.	—	—	Nil	Nil						
M.	23/2/71	Yes	N.T.	1/2						
M.†	No lesion	No	1/4	N.T.		No affected children				

\*Another 31 people were bled and no antibodies found.

†Casamance farmer.

‡Another 14 people were bled and no antibodies found.

§Another 15 people were bled and no antibodies found.

N.T. = Not tested.

to the overall age distribution in four similar villages in this area obtained from the 1973 census. Therefore, no sex or age group was more significantly affected by anthrax than any other.

Most lesions in adults were on the head and neck (63%), few on the trunk (21%), and least on the extremities (16%). This also held in young children and in older children, in whom the percentage distributions were 52%, 28%, and 20% and 70%, 16%, and 14% respectively. The ages and sexes, therefore, were combined and the distribution of anthrax lesions is shown in table IV.

Only two children had gastrointestinal anthrax and both died. The brother of one of these had died in the village with similar symptoms two days earlier. A further 10 patients died, but this was probably a low estimate of the overall mortality because we obtained a history of some people (with anthrax lesions) having died in the village, and several patients were taken home in extremis. There was no relation between death and the age of the patient or the site or number of the lesions (table IV).

TABLE III—Serological results in animals. Results are numbers of animals

Antibody Titre	Cattle	Goats	Sheep	Dogs
Nil	24	26	13	3
1/2	7	1	3	
1/4	2		1	
1/8	5		1	
Total	38	27	18	3

TABLE IV—Percentage of anthrax lesions at each site and number of deaths (all ages and sexes combined)

Site	% of Lesions		%	No. of Deaths
Head	60	Cheek	19	2
		Eye	14	1
		Forehead	11	1
		Chin	7	1
		Scalp	4	1
		Nose	2	1
		Lip	2	
		Ear	1	
Neck	5			1
Trunk	20	Shoulder	6	
		Chest	6	
		Abdomen	4	
		Back	4	1
Arm	8			
Hand	2			
Leg	5			1

## Discussion

Anthrax is a disease primarily of animals and only secondarily of man, in whom infectivity is thought to be low.<sup>2</sup> The incidence, probably underestimated, in the Foni regions of the Gambia was 1.4%, with at least 45% of the villages of this region being affected over the past four years. Unlike most other diseases in the Gambia<sup>3</sup> anthrax occurs almost entirely in the dry season. The anthrax bacillus germinates at 20-44°C in a humidity of over 80%.<sup>4</sup> These conditions are found in the wet season in the Gambia. The number of anthrax spores in the ground possibly falls at this time because germination occurs and the anthrax bacillus is destroyed by soil bacteria. There may be other factors in the dry season, such as winds distributing the spores and close cropping of the grass by animals. In some villages there were several cases in each year, in others many cases in one year were followed by few the next, and in some only one or two patients came for treatment in the four years. There is little movement of cattle, sheep, or goats between villages, but it is quite possible that vultures spread the disease. The people do not eat a dying animal, which may account for the few cases of gastrointestinal anthrax. This contrasts with anthrax in Kenya,<sup>5</sup> but is similar to that in other parts of the world, where cutaneous anthrax is the most common form.<sup>6</sup> The distribution of the cases in the Gambia by age, sex, and site of lesion was not similar to the pattern in Iran.<sup>6</sup> Our results suggest that in the Gambia the disease is not related to occupation.

Though arthropods can transmit the disease, at least experimentally,<sup>7</sup> arthropod transmission was unlikely since most arthropods are much more common in the wet season, and the few which are active throughout the year, such as *Stomoxys* spp, tend to bite the lower leg, so the site distribution would have been different.

It is said that human-to-human transmission occurs only rarely,<sup>8</sup> but it seems to be common in the Gambia for antibodies were found in people living in close contact with patients and *B anthracis* was isolated from communal loofahs. The mode of transmission may be similar to that which occurred as a result of infected shaving brushes in Great Britain and Russia<sup>8</sup> and of the use of "Sepidab" in Iran.<sup>1</sup> The difference in the Gambia lies in the fact that these loofahs are shared within a family and so may facilitate human-to-human spread.

Antibody levels have not often been studied in large outbreaks of anthrax. Our results show a wide variation of response, with persistence for up to a year in some cases, even after



treatment, and rapid disappearance in others. Antibodies were discovered in some people who had no history or evidence of anthrax. This pattern has been reported previously: 11 out of 72 otherwise healthy workers in a goat hair mill were found to have antibodies.<sup>9</sup> Recovery from anthrax is said to be followed by prolonged immunity and recurrences are said to be extremely rare,<sup>8</sup> but we have not confirmed this in the Gambia. Serological examination showed that though antibodies may persist for 12 months (possibly as a result of repeated subinfective doses or subclinical attacks) there was at least one authenticated recurrence within 12 months of primary infection, which corresponded with the laboratory findings that this strain contains a weak antigen.

Unlike the mortality in Iran,<sup>1</sup> in the Gambia mortality was not related to any particular site, to the multiplicity of lesions, or to the extent of local inflammatory response. We did not confirm either that mortality and morbidity were related to the nutritional state of the people; on the contrary, their nutritional state was at its best at the time of maximum attack.

How can this disease be eradicated? It is not limited to the Gambia, being present in the adjoining area of Senegal. It is firmly established in animals, particularly sheep and goats, and it would be impossible to immunize these effectively. Humans could be immunized,<sup>10</sup> but three or four injections are needed to give even temporary immunity. An international organization would have to carry out an immunization programme and organize the necessary annual booster doses. Nevertheless, even temporary immunity may break the cycle by allowing a natural reduction of spore counts in the soil. Public health measures to ensure the correct disposal of animal carcasses and the control of vultures may also help. An attempt could be made to change the habit of using the palm-fibre loofah, to limit its use to one per person, and to advise disposal of the loofah before it became contaminated with anthrax spores.

There is no evidence to suggest that the disease is declining

in severity or prevalence, and from what is known of the antigenicity of this organism it is most unlikely that natural or "herd immunity" will protect the population even when they are repeatedly exposed to the disease. The converse may be true unless active steps are taken to check or eradicate the disease before it becomes endemic and spreads to other villages and areas of the country.

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# Effect of breast-feeding on pituitary-ovarian function after childbirth

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## Summary

**Pituitary and ovarian function at the end of pregnancy and during the first six weeks after delivery was investigated serially in women who fully breast-fed their infants and in women who did not. In the women who did not breast-feed the plasma prolactin level decreased rapidly and from the third day after delivery was significantly lower than in the breast-feeding mothers, reaching**

**the normal range of the menstrual cycle by the third week of the puerperium. In the breast-feeding mothers the plasma prolactin was still raised six weeks after delivery. The levels of FSH in both groups were identical and increased over the third week of the puerperium. Plasma oestrogen fell steeply in both groups during the first two weeks after delivery. In the breast-feeding mothers plasma oestrogen remained depressed but increased in the non-lactating women, reflecting follicular development in the ovary in response to FSH; the plasma oestrogen levels were significantly higher in the non-lactating women from the 17th day of the puerperium onwards. These findings support the concept that in breast-feeding women prolactin delays the return of ovulation by inhibiting the ovarian response to FSH stimulation.**

## Introduction

Breast-feeding postpones the return of ovulation and menstruation after childbirth, and postpartum amenorrhoea is related to the duration of breast-feeding.<sup>1-4</sup> Studies on the influence of lactation on ovulation have shown that breast-feeding women

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