The epidemiology of infertility: a review with particular reference to sub-Saharan Africa*

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The problem of infertility, with particular reference to Africa south of the Sahara, is reviewed. In many areas, up to 40% of women are reported to have completed their reproductive years without bearing a child. The condition is widely distributed, but also often localized in pockets corresponding to geographical or tribal units. Most available demographic data provide estimates of childlessness but it is not sufficient to define the problem in terms of primary and secondary infertility, pregnancy wastage, and infant and child mortality. The major underlying cause for the high levels of infertility appears to be the sequelae of Neisseria gonorrhoeae *infection in both men and women, manifested as obstructive azoospermia and tubal occlusion. Other infections, such as those that may follow abortion or delivery, or systemic infections, may be important in some areas. The available data suggest that different patterns of infertility and pregnancy wastage, and different etiological agents and processes, contribute to the problem of infertility in the different areas. The need for a systematic, standardized research approach in several areas is clearly indicated.*

Infertility as a public health problem varies widely in different communities according to the prevalence of the condition and the importance ascribed to it by society. The most frequently quoted figure for its prevalence is 10% of couples. This figure, however, is derived either from census data that include a variable proportion of couples who are voluntarily childless or from patients in large clinical centres, rather than from total community surveys. Indeed, it is estimated that involuntary infertility affects no more than about 5% of couples (*1*); in some areas, however, prevalence rates of 30% and even 50% have been reported (*2*).

The problem would appear to be particularly acute in certain countries of sub-Saharan Africa, where attempts are being made to plan appropriate services to prevent and cure the underlying causes. In attempting to plan such services, the gaps in information have become manifest and the need for research evident. Major issues include the actual magnitude of infertility and its geographical distribution, and the need to distinguish between the different conditions that are loosely grouped under the general term of infertility.

Infertility is frequently used synonymously with childlessness both by those affected and by demographers. However, the standard definitions of infertility accepted by demographers (*3*) are not sufficiently precise for clinical–epidemiological studies into the prevalence and etiology of what physicians refer to as infertility. Infertility, sometimes referred to as infecundity, sterility, or physiological infertility, is defined by demographers as the incapacity "of a man, woman or couple to participate in reproduction (i.e. *the production of a live child*)". The inability to conceive or impregnate, and the inability to carry a conceptus to a live birth, reflect different processes and etiologies, with distinct implications for their amelioration or prevention. For the purpose of this review, it is necessary to differentiate the inability to conceive from the inability to carry a conceptus to a live birth and the failure of a live birth to survive. These three categories will henceforth be referred to as infertility, pregnancy wastage, and infant or child loss, respectively. Since infertility and pregnancy wastage are usually regarded as a single problem by couples requesting services and because some associated or causative factors may be common to both, infertility and, to a lesser extent, pregnancy wastage will be dealt with in this review.

Where the prevalence is low, infertility and preg-

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nancy wastage are caused by a variety of infectious, mechanical, immunological, hormonal, and psychological disorders that are costly to diagnose and difficult to treat successfully. Where the prevalence of infertility is high, the majority of cases seem to fall within the first two of these categories, that is, infections and the mechanical sequelae of unskilled abortion or obstetrical practices. The relative importance of these and other causes has not been well established. This review will consider mainly those conditions thought to be associated with a high prevalence of infertility and pregnancy wastage.

SOURCES OF DATA

Current estimates of the prevalence of infertility and pregnancy wastage are largely based on demographic data and on a few epidemiological and clinical studies.

In sub-Saharan Africa, demographic data have been obtained in a variety of ways and with information of varying quality. Techniques used have included the classical census with visits to each dwelling unit and collection of information on each individual, censuses performed on a sample of the population, censuses performed by assembling heads of villages or households, vital events registration, and other administrative records or surveys. The primary purpose for which the information is obtained often affects the form, character, and completeness of the information. Census or household lists used for political or tax purposes generally do not provide reliable information on infertility.

The questions asked in many surveys and the definitions used to categorize the reproductive status of individuals affect the usefulness of the information in defining the problem of infertility. Most demographic surveys include information on the number of children per woman by age and marital status. Reasons for the absence of children are not included in such data; these might include voluntary childlessness, failure of the couple to conceive, failure of the woman to carry a pregnancy to term, or failure of an infant to survive. In some surveys the number of children currently alive is recorded, in others the number born (live and stillborn), and in others the number of live births. The last has been the most frequently used. In a few census surveys, the data have been recorded in terms of number of pregnancies. Information that would indicate secondary infertility is rarely collected.

Imprecise information is a major problem of census data in many areas of Africa. Definitions of live birth and stillbirth may vary markedly in different cultural settings. Where pregnancy wastage or infant death reflect poorly on the woman, she may not be willing to admit the pregnancy or the occurrence of a live birth. In many cultures a newborn child is not considered a living person until after a certain critical period, which is at least one week and may be as much as 40 days (*80*). The naming ceremony and other rituals commonly take place after such a critical period; these often correspond to the time when the infant is no longer at risk of tetanus neonatorum, which may affect as many as 10% of newborn infants in some areas of the world. Neonatal deaths may be reported as stillbirths, or the pregnancy and death may be completely denied. A perinatal death may not be recorded owing to burial or birth registration regulations. The number of members of a household may be inaccurately reported because of either tax benefits or liabilities. Information on numbers of pregnancies may be incomplete because of memory failure or the inability to detect early abortion.

Reliable information on age is another problem in surveys or studies in many areas of Africa. Attempts have been made to determine an individual's age according to a locally derived historic events calendar, which is then related back to actual years. Another system merely classifies adult women as being in the pre-reproductive age, in the reproductive age, or having passed reproductive age, the dividing lines approximating menarche and menopause. The ages for these latter events, will, however, vary widely, depending largely on the health and nutritional status of the woman and to a lesser extent on her parity.

Demographic data can be used only as a crude index of primary infertility. In census surveys, women without liveborn children are numbered with those with primary infertility and pregnancy wastage but not with women with secondary infertility or subsequent pregnancy wastage following a live birth.

In spite of the limitations of demographic data, however, an examination of the prevalence rates of childlessness (women who have never borne a live child) in different settings and populations may be useful in developing hypotheses as to the causes of infertility and pregnancy wastage.

PREVALENCE OF CHILDLESSNESS

The following discussion is based upon data largely obtained from population samples in sub-Saharan Africa during the early and mid 1960s. These

Table 1. Indices of infertility and general fertility in Central and West Africa

Country and/or region	Population in 1000s	General fertility rate (No. births/ 1000 women aged 15-44 years	Crude live birth rate per 1000 population	Percentage of childless women aged 25-29 years	Percentage of childless women aged 50+ years
Cameroon					
West	1025	196	49.8	7.0	6.7
South-east	1185		36.4	28	23
North	1395		41.0	21	15
Central African Empire	1021	157	48	25.2	13.6
Banda	318	122	40.6		
Nzakara	30	48	20.0		
Baya	294	194	54.6		
Centre region	240	125	41.0	34.7	15.0
West region	643	187	53	19.4	10.4
River region	134	101	36	36.3	19.0
Gabon	440	116	35	34	31.9
Wolen N'tem	78	122	37		31.2
Ogoone Lolo	37	80	25		46.2
Nyanga	37	170	52		17.8
Upper Volta	4440	194	49.6	7.2	6
Niger	2600	232	50.55	12.8	5.2
Mali (Toureg)	76	209	52	26	15
Senegal	3049	178	43.3	12	5.6
Sudan	10 262		51.7		9.6
Bahr el Ghazal	991		84.6		4.2
Blue Nile	2070		45.7		8.4
Darfur	1329		41.8		7.3
Equatoria	904		54.1		21.2
Kassala	941		42.6		13.5
Khartoum	505		40.7		9.7
Kordofan	1762		50.0		9.9
Northern	873		43.0		7.8
Upper Nile	889		69.3		2.3
Zaire	21 800	171	42.7	22.1	17.6
Kwango	466	203	48.1	6.8	3.4
S. Kivu	831	211	52.3	7.1	4.6
Equateur	302	133	33.7	39.1	40.0
Tshuapa	395	113	30.5	44.1	33.0
Stanleyville	635	123	34.0	34.4	23.3
Bas-Vele	468	64	19.1	50.7	37.3
Haut-Vele	589	83	23.2	46.2	36.9
Nanie-Ma	447	129	34.3	27.9	23.5
Congo[a]		145	41.1	17	15

[a] Excludes Brazzaville and Pointe Noire.

data are subject to all the limitations of incompleteness, inaccuracy, and inadequate definitions discussed above. The crude rate of childlessness among all women of reproductive age is not a useful statistic. Even in societies where all women ultimately marry, the crude rate would be greatly influenced by the mean age of marriage, the mean age at menarche, and the numbers of women in different age groups.

Measurement of prevalence rates of childlessness among women who have completed their fertility allows for reasonably reliable comparison of rates among different communities. However, an examination of the prevalence rates of childlessness in these older women does not necessarily represent the situation as it currently exists. The events leading to childlessness in such women are likely to have taken place thirty or more years earlier. To determine if the problem exists among women currently in their reproductive years, age-specific rates for childlessness for younger women are required. Selected rates for women 25–29 and 50+ years of age are presented in Table 1. The age group 25–29 has been selected to minimize differences in the age of marriage and to relate more definitively to the problem as it currently exists.

The data in Table 1 show that in many areas of Africa, a large proportion of women complete their reproductive years without giving birth to a live child. In parts of Gabon, the Sudan, Cameroon, and Zaire, prevalence rates of childlessness among women 50 years of age or older are as high as 20% to 40%.

High levels of childlessness have also been recorded in parts of East Africa and in other areas of the world. In 1960 in two regions of Zanzibar, 25.1% and 37.7% of women over 46 years of age were childless (*5*). Levels of childlessness of 13% among married women 30–34 years of age have been recorded in Jamaica (*6*).

These rates contrast with a prevalence of childlessness in women over 50 years of age of 3–6% in other areas of Cameroon, the Sudan, and Zaire and in the Niger, Senegal, and the Upper Volta (Table 1). These lower rates are comparable to rates of 3–5% in areas of India, the USA, and Canada (*1*, *7*, *8*, *9*).

REGIONAL, GEOGRAPHIC, AND ETHNIC VARIATION

Since the few detailed epidemiological or clinical studies available are limited to one area or clinical facility, comparison of data between areas and among different ethnic groups is possible only with the demographic data indices of childlessness or age-specific childlessness.

Presentation of the data on childlessness on the basis of country may mask the profundity of the problem in some regions or among particular groups where the problem may frequently be of a local character. Thus, as noted in Table 1, in Cameroon

Table 2. Variation in childlessness among different tribal groups in the Upper Volta [a]

Tribal group	Population in 1000s	General fertility rate in women aged 15–49 years	Crude birth rate	Percentage of childless women aged 25 +
Upper Volta (total)	4440	194	49.6	(25–29) 7.2 (50 +) 6
Mossi	2069	211	52.1	4.3
Bissa	204	196	52.0	3.2
Gourmantche	195	185	50.3	4.5
Bobo	289	158	44.1	17.6
Different Mandigues	298	191	48.9	6.5
Gourounsi	228	193	51.7	6.5
Senoufo	237	181	51.4	12.1
Lobi-Dagari	301	177	47.4	5.0
Peul	448	117	42.8	9.0

[a] Excludes Ouagadougou and Bobo-Dioulasso.

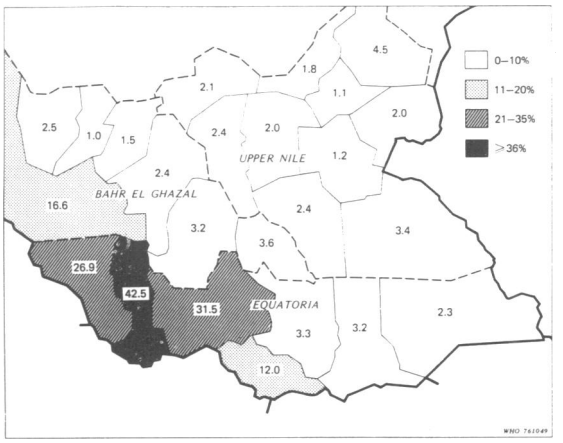


Fig. 1. Percentage childlessness among women completing reproductive age in the districts of three southern Sudan provinces.

there is a 3- to 4-fold difference in the level of childlessness between the western and south-eastern regions; even wider differences exist in Zaire and the Sudan.

The importance of collecting and analysing data according to the appropriate geographic regions and tribal groups is further illustrated by data from the Sudan (Fig. 1) and from the Upper Volta (Table 2). The provincially grouped data, as in the example from the Sudan, do not permit one to appreciate the very wide variation in and severity of the problem of childlessness. In the Upper Volta, only a few groups appear to have significantly increased levels of childlessness. Grouped data, or population samples that do not include sufficient numbers of individuals in the particular subgroup, cannot identify the problem among the affected groups.

Although the ethnic group is an important factor associated with different rates of infertility, it is likely to be merely a reflection of the habitat, social conditions, and other health problems experienced by the tribal group. In studies on two tribes in the Sudan, Henin (*10*) has examined childlessness in relation to the habitat and the social and health conditions of the nomadic and settled members of the same tribe. The prevalence of childlessness among ever-married women 20–49 years of age in the settled communities was 5% or less, whereas in the nomadic group it was between 13% and 18%. Fecundity also seems to differ in the nomadic and the settled groups: excluding childless women from the calculation, the age-adjusted mean number of births among two nomad groups was 3.13 and 3.37, compared to 5.19 and 4.45 among settled groups of the same tribe.

Among nomads the age of marriage for women was later, the interval between marriage and first pregnancy longer, and pregnancy wastage higher than in settled groups. Divorce was far more common in the nomads, barrenness being cited as the cause in 25% of cases. The low economic status of the nomads is associated with the husband and wife being separated for long periods of time, each with a part of the herd. It has been suggested that under such circumstances there may be a higher level of extramarital sexual activity. A nomadic life precludes the availability of skilled medical care, and the low economic status may adversely affect both nutrition and fecundity (*10*).

TEMPORAL VARIATIONS IN THE PREVALENCE OF INFERTILITY

A useful technique in establishing the etiology of infertility is to demonstrate that a change in the incidence or prevalence of certain factors is associated with a change in the prevalence of infertility in the same community.

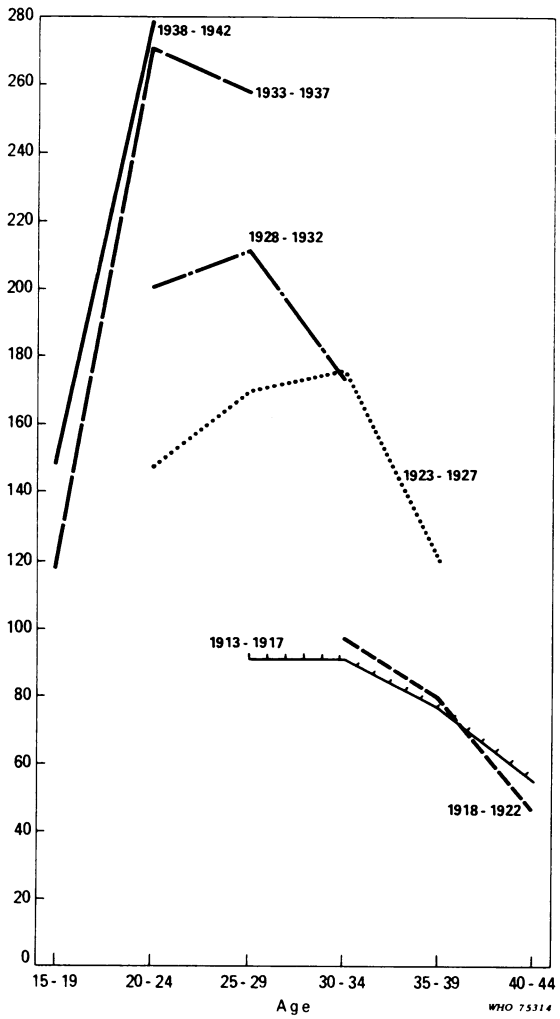
Ring & Scragg (*11*) provide age-specific fertility [a] rates collected prospectively during a 20-year period for successive 5-year birth cohorts of women in New Ireland (Fig. 2). The age-specific birth rates of the two cohorts of women born in 1913–1917 and 1918–1922 were low and nearly identical, yet that of the cohort born in 1923–1927 was nearly double. The age-specific rates of later cohorts at younger ages is even higher. Ring & Scragg attribute the rise in fertility to the effect of a mass penicillin campaign

[a] Based on data in Tables 1 and 2, the correlation of crude birth rate and childlessness in women 25–29 years of age is $r = 0.911$.

Table 3. Estimated sterility in consecutive cohorts of women born from 1914 to 1928 in Martinique [a]

Cohort	Women without children (%)	Women never married (%)	Estimated percentage of infertile women
1914–1918	16.3	6.4	9.9
1919–1923	13.2	3.7	9.5
1924–1928	7.2	3.1	4.1

[a] From Leridon, H. et al., 1970.



(Adapted from Ring and Scragg. 1972)

Fig. 2. Age-specific birth rates by 5-year cohorts of women born between 1913 and 1942 in New Ireland.

against gonorrhoea. Thus, the two younger cohorts would have obtained the full benefit of the gonorrhoea prevention programme as they were just beginning sexual activity at the time of mass treatment; no effect is seen in the older cohorts who had already experienced 15–25 years of sexual activity at the time of the campaign. These data complement those from Martinique on the prevalence of infertility in successive cohorts, as discussed by Leridon (*12*) (Table 3).

One suggested interpretation of the data from Martinique is that the greater than 50% fall in estimated sterility in the last two adjacent five-year cohorts may be explained by the fact that the younger cohort was just entering sexual activity at the time of mass use of penicillin against yaws.

EPIDEMIOLOGICAL AND CLINICAL STUDIES DEFINING THE PREVALENCE OF INFERTILITY, PREGNANCY WASTAGE, AND INFANT AND CHILD LOSS

Little published data from Africa exists on the relative importance of the different categories contributing to the problem. Community-wide epidemiological or demographic studies dealing with infertility, pregnancy wastage, and child loss have been focused mainly on communities described as experiencing depopulation. It has been only within such studies that the relative importance of the different categories of infertility, pregnancy wastage, and infant and child loss has been examined.

The most complete epidemiological study on the prevalence of infertility, pregnancy wastage, and infant loss is that by Scragg (*13*), undertaken on the island of New Ireland in the Western Pacific. This study of several villages combined a demographic survey with clinical diagnostic studies on defined groups of women, and serves as a model for epidemiological studies of infertility. The studies by Retel-Laurentin (*14*) among the Nzakara in the Central African Republic attempt to define the prevalence and causes of infertility and pregnancy wastage using a combination of demographic and clinical techniques. These studies, although standardized in terms of a careful reproductive history by a single clinical observer, rely predominantly on subjective clinical assessment and serological examinations. Modawi (*15*) undertook an extensive clinical–epidemiological investigation of infertility in the western Equatoria region of the southern Sudan, consisting of reproductive history and clinical examination.

Infertility

In Tigah and Tabar, New Ireland, the combined primary and secondary infertility rates of 40% are clearly the main factor in depopulation (Table 4). In Solas, even when the infant mortality is 31% and the prevalence of infertility 9%, there is no resultant depopulation (*13*). In these data, approximately half the cases of infertility were primary in nature. In contrast, 75% to 80% of the cases in southern Sudan were due to primary infertility (*15*).

Table 4. Infertility, perinatal death, and infant mortality as related to population change in New Ireland [a]

Area	No. of women	Primary infertility	Secondary infertility	Stillbirths/1000 live births	Neonatal deaths/ 1000 live births	Total death rate between birth and 1 year of age	Change over generation of 28 years (%)
Lemankua	94	3.2	1.1	26	36	71	+ 154.0
Solas	133	4.5	4.5	16	131	319	+ 103.2
Tigak	196	21.9	22.7	67	80	125	— 24.8
Tabar	407	30.2	15.0	45	71	142	— 41.0

[a] From Scragg, R. F. R., 1957.

The only other data from Africa on the relative importance of primary and secondary infertility are derived from highly selected series of case reports from clinical centres. In a series of 200 cases of infertility reported by Chatfield et al. (*16*) from East Africa, nearly half were of secondary infertility. Among 482 cases of infertility reported by Moutsinga (*17*) in Gabon, 35.8% were primary.

Pregnancy wastage

Pregnancy wastage has been considered an important part of the problem of childlessness in a few areas, has been discounted in others, and has not been examined in most. In 387 ever-married women of the Nzakara tribe over 35 years of age, 33% of pregnancies ended in abortion and nearly 10% ended in stillbirth (*14*). Furthermore, according to Retel-Laurentin, infertility is often preceded by an abortion (*14*). Scragg (*13*) in New Ireland and Romaniuk (*2*) in Zaire, however, discuss the possible role of abortion in depopulation but discount its importance as a cause of childlessness.

The relative importance of induced as opposed to spontaneous abortion in pregnancy wastage is even less well known. In traditional cultures of Africa, where fertility reflects a woman's status and where infertility frequently leads to divorce, it seems unlikely that induced abortion would play a major role in childlessness except in certain situations where conception is socially unacceptable. In some traditional cultures, attempts at inducing abortion are grounds for divorce; women who have such abortions are often no longer able to marry and become prostitutes (*18*). Existing estimates of the rate of illegal abortion are limited to hospital based data in a few large urban centres (*19*).

It appears that stillbirths alone do not contribute significantly to childlessness, except possibly in a small percentage of women. Stillbirth rates in countries with limited antenatal and obstetric care are often 4–5 times greater than those in countries with well developed services. In New Ireland, the rate of stillbirths was between 16 and 67 per 1000 live births, the lower rates being found in communities with less infertility (Table 4). A rate of 66 per 1000 live births was noted by Lang (*20*) in Nigeria but no data on infertility or childlessness are available. In data collected by Retel-Laurentin (*21*), stillbirth rates (and early neonatal deaths) occur in up to 12% of pregnancies.

Infant and child mortality

In some circumstances, depopulation of a community may be the result of infant and child loss, which is regarded by couples as infertility. The association of infant and child mortality with the depopulation of several villages in Zaire is shown in Table 5 (*22*).

Infant mortality is a major factor in depopulation when it reaches rates of 45% or more in these villages. Only in one village with an infant mortality rate of 31% and an infertility rate of 6% was the population increasing. The added effect of high levels of infertility can be seen by comparing the villages of Bakuma and Mobali, both of which have infant mortality rates of about 40% but have infertility rates of 21% and 6%, respectively.

The epidemiological and clinical data on the etiology of infertility and pregnancy wastage in sub-Saharan Africa are limited. Such studies as exist are either incomplete, or are based on highly selected populations, or focus on testing the association of

Table 5. Births, infant mortality, and sterility in nine villages in Zaire [a]

Tribe	No. of women	No. of live births	Infant mortality	Infertile women (%)	Estimated population change in one generation (%)
Moughelima	189	553	57.3	2.9	−16.32
Bobwa	169	749	70.7	8	−40.4
Mambuti	100	412	80.6	7	−62.8
Popoie	260	864	60.0	5	−37.0
Babuma	175	436	43.8	21	−44.75
Mobali	354	1290	42.3	6	−1.0
Bangbwa	165	573	47.5	5	−18.5
Barumbi	100	236	52.5	12	−50.5
Bamanga	110	375	31.2	6	+10.25

[a] From Delhaise, C., 1911.

one etiological agent or mechanism with infertility or pregnancy wastage.

Retel-Laurentin (*14*) has looked at several conditions, emphasizing detailed history, clinical examination, and serological studies of specific infectious agents, but certain disorders could not be diagnosed under the field conditions of the studies. The disorders not included were tubal occlusion, tuberculous endometritis, gonorrhoea, and abnormalities in the male.

Several studies have examined different possible causes of infertility in women or couples who have presented themselves to a specific hospital or clinic for diagnosis and treatment. The populations in these studies represent highly selected groups who have access to, accept, and use the particular health facility. There are further limitations to clinical studies; for example, although it is possible to carefully document the presence of tubal occlusion in the individual patient, in clinical studies it is not usually possible to identify the underlying cause of the occlusion, such as gonorrhoea or post-partum or post-abortal infection.

Several studies have been made of the association between a specific condition and infertility and pregnancy wastage. These studies have generally focused on gonorrhoea and serological evidence of treponematosis. Association, however, is not synonymous with causation. Serological evidence of syphilis associated with infertility is likely to be an indicator of gonorrhoea.

Only in New Ireland has there been an attempt to examine the relative significance of the different causes of infertility in defined communities. Scragg's investigations included bacteriological cultures, hysterosalpingography, endometrial biopsy, semen examinations, and testicular biopsy.

THE SEQUELAE OF INFECTION WITH *NEISSERIA GONORRHOEAE*

N. gonorrhoeae infection in the woman starts as a cervicitis, usually asymptomatic, and ascends by way of the uterine mucosa to produce an endosalpingitis, which soon involves the other tubal layers. Destruction of the tubal mucosa results in either complete or partial tubal occlusion. The risks of occlusion appear greater with the chronicity of infection, which is thought to represent repeated infection.

In the male, gonorrhoea begins as a urethritis and is usually symptomatic. An ascending infection may involve the prostate gland and the seminal vesicles. The mechanisms whereby the epididymis becomes involved are not well understood, but involvement is generally thought to occur as a result of the retrograde passage of infected urine from the urethra along the lumen of the vas deferens. Both chronic seminal vesiculitis and chronic epididymitis may be associated with abnormal sperm, and the latter with an occlusive azoospermia.

Table 6. Fertility and the prevalence of gonorrhoea in men and women in a random sample of the population from two districts of Uganda

District	Total population in 1000s	General fertility rate 16–45 years	Male examinations		Female examinations	
			No. examined	Isolation of *N. gonorrhoeae*	No. examined	Isolation of *N. gonorrhoeae*
Ankole (high fertility)	859	241	166	7 (4.2%)	168	4 (2.4%)
Teso (low fertility)	565	115	270	24 (8.9%)	295	54 (18.3%)

Pelvic inflammatory disease and tubal occlusion associated with gonorrhoea

Pelvic inflammatory disease resulting from contagious spread of *N. gonorrhoeae* is the most common complication of primary genital tract infection, affecting an estimated 1–10% of women with primary infection (*23*, *24*, *25*). Most commonly, salpingitis arises at the end of menstruation from a carrier state (*25*); the infection transiently affects the uterus and endometrium and then produces acute inflammation of the tubal mucosa (*26*). Destruction of the mucosa and subsequent scarring frequently leads to a partial or complete tubal obstruction. Even with antibiotic treatment, bilateral tubal occlusion was diagnosed as a sequela to acute salpingitis in 20% of the cases in one series (*27*). In another series of patients in whom long-term follow-up was possible in Sweden, infertility due to tubal occlusion was noted in 5.5% of women treated for gonococcal salpingitis (*28*); the rate for non-gonococcal salpingitis was even higher.

The effect of multiple episodes of gonorrhoea is unknown, although in Westrom's series in which causes of non-gonococcal and gonococcal repeated pelvic inflammatory disease are combined, a single episode of salpingitis resulted in tubal obstruction in 12.8% of the women, two infections resulted in 35.5%, and three infections resulted in 75% tubal obstruction (*28*). The association of gonococcal infection with tubal occlusion in individual cases is often difficult to establish (*29*); the longer the duration of the salpingitis, the less likely it is that *N. gonorrhoeae* will be identified in the individual (*30*). Scragg (*13*) has concluded that in New Ireland there is a correlation between high levels of gonorrhoea and high levels of tubal occlusion. However, other possible causes of tubal occlusion could not be excluded.

In one series of 86 consecutive patients in Uganda hospitalized for acute pelvic inflammatory disease, one third were positive for *N. gonorrhoeae*; 25% of the patients were infertile compared to 15% in a matched hospital control group (*31*). Pregnancy wastage, at 28.6% of all pregnancies, was also noted to be high. Causes of the pelvic inflammatory disease other than *N. gonorrhoeae* are likely in view of the fact that nearly 20% of cases were post-abortal or puerperal infections.

Gonorrhoea and the sequelae of sterility in the male

The relative importance of gonorrhoea sequelae in men in relation to the prevalence of infertility has not been well documented. The natural history of the disease in men is quite different from that in women. The probability of a man acquiring *N. gonorrhoeae* infection following a single known exposure is 22% (*32*). It is estimated that fully 90% of newly infected men become symptomatic (*26*); however, gonorrhoeal prevalence rates among men of 1.8% to 8.9% have been reported from Uganda, with only half of the men being symptomatic (*33*) [a] (Table 6).

In the era before effective chemotherapy, epididymitis was reported as occurring in 17–30% of males with gonorrhoea (*34*). Pelouze (*35*) describes epididymitis in 20% of his cases seen after the fifth day of disease. Pelouze cites other studies that indicate childlessness followed in 10.5% of men who had gonorrhoea without epididymitis, 23.4% of those who had unilateral epididymitis, and 41.7% of those who had bilateral involvement. In areas with developed and widely available health services and com-

[a] ARYA, O. P. & TABER, S. R. Correlates of venereal diseases and fertility in rural Uganda. Unpublished documents WHO/VDT/75.400, WHO/VDT/RES/75.339, WHO/VDT/RES/GON/75.96 (1975).

Table 7. Fertility, infertility, pregnancy wastage, and evidence of venereal disease in three villages in the Upper Volta [a]

Village	No. women examined	Crude birth rate	Percentage childless (no live births)		Abortions/ 100 pregnancies		Mean No. live births	Percentage with moderate to strong positive serological test for syphilis		Percentage of men with urethral blenorrhoea	
			25–34	45–49	15–44	45 +	45 +	15–34	35–49	clinical examination	by history
Moko	133	49.5	6.3	7.1	22.2	22.1	4.62	3.0	11.4	9.4	20.6
Kerba [b]	208	31.8	13.2	28.6	23.7	23.6	3.22	1.2	26.3	29.5	39.2
Dedougou [b]	239	28.5	15.6	26.1	26.2	38.2	2.06	8.9	36.3	23.1	37.4

[a] From Retel-Laurentin, A., 1973.
[b] Penicillin campaign carried out 15 years earlier.

pulsory antibiotic treatment of gonorrhoea, a complication rate for epididymitis of 0.7% has been noted (*24*). In studies based on government, mission hospital, and dispensary reports, Griffith (*36*) has shown an inverse correlation between the general fertility rate for 15 districts in Uganda and both gonorrhoea rates and the frequency of urethral strictures. Although ascertainment of cases of both conditions is not likely to be complete, the consistency of the relationship and its confirmation in other communities confirms the existence of the association. Retel-Laurentin (*37*), in three villages in the Upper Volta, has shown a similar correlation of low crude birth rate, completed family size, and frequency of childlessness with increasing levels of urethral blenorrhoea in the male (Table 7).

The association between gonorrhoea and infertility in general

In the absence of valid and reliable serological or other tests for gonorrhoea that are applicable several years after the original infection, the establishment of an association must depend on the simultaneous comparison of the prevalence rates of both infertility and gonorrhoea in different communities. Some supporting evidence can be obtained by cohort analysis of the prevalence of infertility or age-specific birth rates in communities where mass penicillin

Table 8. Childlessness, crude birth rate, infant mortality, and rate of reported cases of gonorrhoea—Sudan 1955/56

Region	Childlessness among women past reproductive age (%)	Crude birth rate	Infant mortality rate	Reported cases of gonorrhoea/ 1000 population [a]
Bahr-el-Ghazal	4.2	84.6	111.8	7.9
Blue Nile	8.4	45.7	72.2	3.5
Darfur	7.3	41.8	75.6	13.6
Equatoria	21.2	54.1	132.9	14.2
Kassala	13.5	42.2	82.0	6.3
Khartoum	9.7	40.7	71.4	47.6
Kordofan	9.9	50.0	76.0	10.2
Northern	7.8	43.0	66.7	0.75
Upper Nile	2.3	69.3	143.9	7.3

[a] Report of the Medical Services, Ministry of Health, Democratic Republic of the Sudan, for the year 1964–65.

treatment for yaws or even gonorrhoea has taken place, as in Martinique and New Ireland (*11*, *12*). An association of gonorrhoea with infertility has been inferred in several communities by comparing, on a community basis, such indices as prevalence rates of *N. gonorrhoeae* in surveys, rates of reported gonorrhoea, and urethritis and urethral stricture rates with such indicators of infertility as the percentage of childless women, general fertility rates, and total fertility (*36*). Arya [a] has shown a high correlation of infertility and gonorrhoea prevalence in two communities, one of a high and the other of a low level of infertility (Table 6). In contrast, no such correlation between reported cases of gonorrhoea and childlessness is evident from the health statistics of the Sudan (Table 8).

PELVIC INFLAMMATORY DISEASE AND TUBAL OCCLUSION ASSOCIATED WITH NON-GONOCCOCAL INFECTIONS

Non-gonococcal infections are being increasingly identified as causing acute pelvic inflammatory disease and tubal occlusion. Reports from the USA and Sweden indicate that, despite extensive diagnostic studies, *N. gonorrhoeae* is shown to be the cause of salpingitis in less than half of the patients with pelvic inflammatory disease (*28*, *38*, *39*). A previous delivery, abortion, or curettage has been associated with about 20% of such cases.

Bacteroides fragilis and possibly cytomegalovirus, chlamydia, and other organisms have recently been associated with non-gonococcal salpingitis (*39*). Furthermore, non-gonococcal salpingitis, despite early and prolonged therapy, has been associated with an even higher rate of tubal occlusion (16.6%), than that following gonococcal infection (5.5%) (*28*), presumably owing to the greater resistance of a mixed group of organisms to antibiotics more specific to *N. gonorrhoeae*. Similar differences in the sequelae of gonococcal and non-gonococcal salpingitis have been noted by Falk (*38*).

OTHER VENEREAL DISEASES

Syphilis

Syphilis produces pregnancy wastage, not infertility. The characteristic outcome of pregnancy in a women infected with *Treponema pallidum* will be spontaneous abortion, a macerated fetus, stillbirth, a congenitally infected infant who has a decreased chance of survival, or a healthy infant who has passively acquired syphilis-related antibodies. The more chronic the infection, the more likely that the child will be healthy (*46*) (Table 9). Syphilis, therefore, is a self-limiting factor in pregnancy wastage.

Studies of syphilis in relation to pregnancy wastage or infertility have generally depended on sero-

[a] ARYA, O. P. & TABER, S. R. Correlates of venereal diseases and fertility in rural Uganda. Unpublished documents WHO/VDT/75.400, WHO/VDT/RES/75.339, WHO/VDT/RES/GON/75.96 (1975).

Table 9. Effect of syphilis on the outcome of pregnancy compared with the results of non-syphilitic pregnancies [a]

	Non-syphilitic		Untreated early syphilis		Untreated late syphilis		Syphilis treated during pregnancy	
	No.	%	No.	%	No.	%	No.	%
Normal full term living infant	8897	86.3	40	18.2	61	74.4	435	94
Living syphilitic infant	—	—	90	40.9	2	2.4	5	1.1
Premature,[b] non-syphilitic	930	9.0	5	2.3	2	2.4	2	0.4
Neonatal death:								
full-term infant	49	0.5	4	1.8	1	1.2	1	0.2
premature [b] infant	177	1.7	26	11.8	6	7.4	4	0.9
Stillborn:								
at full term	57	0.5	40	18.2	10	12.2	11	2.3
premature	213	2.1	15	6.8	0	0	5	1.1
Total	10 323		220		82		463	

[a] From Ingraham, N. R., 1951.
[b] Defined as $\leq$ 2.27 kg at birth.

logical evidence of treponemal infection. However, such serological studies have been confounded by cross-reactions of *T. pallidum* to *T. pertenue* (yaws) and *T. carateum* (pinta), which have not been associated with pregnancy wastage. Of the few epidemiological studies examining the association of syphilis with infertility and pregnancy wastage, that of Retel-Laurentin (*37*) presents data supporting such an association in the Upper Volta (Table 7). In three communities representing different levels of fertility, childlessness and abortion were higher and the mean number of live births was lower in villages with a higher percentage of serological reactors to syphilis. Although she concludes that syphilis is an important factor in low fertility, the lack of effect on the abortion ratio in Kerba and the lack of a difference in the abortion ratio between Kerba and Moko suggests that syphilis is not the major determinant. Its prevalence may well have reflected the presence of gonorrhoea or other infection. Only in Dedougou, where the abortion ratio was highest, does there seem to be a decrease in abortion rate corresponding to the time of the penicillin programme.

No cases of syphilis had been diagnosed in the region in Scragg's studies (*13*), although granuloma venereum was common. No serological data on syphilis were presented.

Baker (*40*) has positively correlated the prevalence of infertility and the incidence of syphilis in five villages in Zaire. Again, it is likely that the incidence of syphilis paralleled that of gonorrhoea, which was not studied in these investigations.

A few studies have used the approach of correlating the prevalence of positive treponemal serology in groups of women who have complained of infertility or pregnancy wastage. A study undertaken among 163 women in hospitals or clinics in the Upper Volta, where cross-reactions between yaws and syphilis could not be differentiated, concluded that there is a higher association of serological reactions in cases of habitual abortion. However, treponema infection accounted for only a small portion of the cases of pregnancy wastage, and was of even less significance in infertility (*41*). Retel-Laurentin (*14*) has concluded that abortion is a significant part of the problem of childlessness among the Nzakara in the Central African Empire, and that treponema infections do play a major role in pregnancy wastage.

The available clinical and epidemiological data following yaws eradication programmes suggest, but do not establish, venereal syphilis, which was once uncommon but is now becoming more common as a cause of positive serological reactions. Low levels of positive serological reactions to syphilis of 0.5–2.89% among young adults have been noted in Nigeria (*42*, *43*). Higher levels of seropositive reactions to syphilis (or yaws) have been described of 9.4% among soldiers (*33*) and 30% among bar girls in Uganda (*33*, *44*). In a general hospital and dermatology clinic population, only five of 362 patients with venereological complaints were diagnosed as having syphilis (*45*). In a community health centre in Uganda, the incidence of primary syphilis was 1.6 per 10 000 outpatient attendances and for secondary syphilis 8.2 per 10 000 outpatient attendances. The rate for gonorrhoea was 54 per 10 000 (*44*). No attempts have been made to correlate such data with the occurrence of pregnancy wastage or infertility.

From the available data and our knowledge of the natural history of syphilis, there is no evidence that syphilis plays a part in the etiology of infertility. In small, fairly promiscuous communities, the recent introduction of syphilis may result in lowered fertility rates owing to increased levels of pregnancy wastage, but in individual women the process should be self-limiting. More important, if syphilis is common in a community, it is likely that gonorrhoea is also common.

Lymphopathia venereum, granuloma inguinale, and chancroid

There exist no data or studies that have shown an association of any of these conditions with either infertility or pregnancy wastage. In Scragg's study (*13*), although lymphopathia venereum (granuloma venereum) was a frequent reason for admission to the New Ireland hospitals, none of the infertile women in the survey had evidence of this condition. Granuloma inguinale has not been diagnosed in the region.

Although no references to the association of granuloma inguinale and infertility have been noted, the histological appearance of the endometrium may resemble tuberculous involvement of the genital tract. It should probably be considered in individual cases of infertility, but its epidemiological significance is questionable.

OTHER DISEASES

Tuberculosis

Tuberculosis of the genitals is generally considered to be secondary to other foci, usually the lungs, but it is not uncommon for the primary focus to be

healed or undetected. The tubes constitute the initial site of genital tuberculosis, which on gross appearance may be similar to other forms of chronic salpingitis. Endometrial involvement is secondary to tubal involvement, and is estimated to occur in 50% of cases of tuberculosis salpingitis. Histological evidence of a chronic endometritis suggests a possible tuberculous etiology. Involvement of the cervix, vagina, and vulva are rare and are also thought to be secondary to infection higher in the genital tract.

In contrast to the common finding of a closed, bulbous, inverted and obliterated fimbriated end of the tube characteristic of chronic gonorrhoeal salpingitis, in tuberculous salpingitis the fimbriae remain everted and the orifice open, despite gross enlargement of the tubes.

Pelvic and tubal tuberculosis are frequently painless, although the periodic expulsion of exudate from the tubal orifice may result in pain and a raised temperature. Although it was once considered that infertility secondary to tubal tuberculosis was generally not reversible the effectiveness of long-term chemotherapy on subsequent fertility has not been fully evaluated.

Infertility is the most common complaint of women with genital tuberculosis. In one series from Ibadan of 82 women with genital tuberculosis, 69% complained of infertility (*47*). The frequency with which genital tuberculosis is found among infertile women has ranged from 2% to 6% in other African studies (*16*, *48*). If a 2 : 1 ratio of salpingitis to endometrial involvement is accurate, this observed frequency should be doubled. The 82 cases in Ibadan represented 0.74% of all gynaecological admissions over a 12-year period. During an earlier period in the USA, a rate of genital tuberculosis of 0.22% of hospitalized gynaecological patients was reported (*49*). Since infertility has been reported as the major reason for gynaecological consultation in several African centres, despite the selective nature of the hospital populations, it is unlikely that tuberculosis plays a major role in the epidemiology of infertility.

Leprosy

Although leprosy is common in many of the areas of the world where high levels of infertility are encountered, there is no evidence that infection with *Mycobacterium leprae* contributes significantly to the problem of infertility among women, but there is evidence of its possible effect in men.

Although the testis is unaffected by tuberculoid leprosy, it is frequently involved in lepromatous leprosy, in which the infection is both intertubular and intratubular. In a study of 179 adult men with leprosy, 28% were found to have testicular atrophy and 19% had gynaecomastia (*50*). Autopsy examination or surgical biopsy of testicular tissue in 20 men with lepromatous leprosy all showed lepromatosis orchitis ranging from infiltration of vessel walls and adjacent tissue to atrophy of seminiferous tubules progressing to complete fibrosis (*50*).

With increasing fibrosis there comes a point where decreased blood supply leads to atrophy. Involvement is usually bilateral and when extensive is associated with azoospermia and infertility. The effect of therapy on the reversibility of the infertility has not been evaluated.

Involvement of the ovaries, endometrium, uterine wall, or cervix is rare, there being only a few isolated case reports in the medical literature. However, in a series of patients from an Indian leprosy outpatient clinic, 7 of 66 married women were infertile. Premenstrual endometrial biopsy revealed the secretory phase in 9 of 50 women (*51*).

There is no evidence, in women suffering from leprosy, of any increased risk of an adverse effect on the outcome of pregnancy. Rather, there has been repeated documentation of an aggravation of active lepromatous leprosy in association with pregnancy (*51*, *52*). There is no published material available on the possible association of leprosy with either male or female infertility in sub-Saharan Africa.

Mumps

Lambert (*53*), in summarizing the earlier clinical and epidemiological literature and in obtaining data from Swedish army recruits, concludes that mumps orchitis is rare before puberty, occurs in 20% of adult men with mumps, and is bilateral in 10–20% of such men, that is 2–4% of the total. The subsequent marriage and fertility patterns of 98 army recruits who had documented bilateral mumps orchitis and of an equal number of control subjects were then investigated (Table 10). On the basis of Lambert's data, it can be concluded that bilateral orchitis is associated with a 25–33% reduction in fertility. Azoospermia and testicular atrophy were frequently encountered. In another series of 49 patients with orchitis, 39 had some degree of testicular atrophy but only one had azoospermia (*54*).

Although sperm counts in those with a history of mumps orchitis differ significantly from normal controls, it cannot be assumed that this difference indicates a difference in fertility. Even where azoo-

Table 10. Marriage rate and fertility in orchitis and control patients[a]

	Men with bilateral orchitis		Control cases	
	No.	%	No.	%
Total number	98	100	98	100
Married men	68	69.4	85	86.7
Fertile men	47	48	81	82.7
Fertile married men	46	67.6	80	94.1
Conceptions:				
total	112		205	
per man	1.1		2.1	
per married man	1.6		2.4	
per married fertile man	2.4		2.5	
Average duration of marriage (years)	12.5		13.6	

[a] From Lambert, B., 1951.

spermia following mumps has been diagnosed, it may sometimes be reversible (*55*). There are no data that examine the risks of mumps orchitis and of subsequent infertility in men whose health and nutritional status is less than optimum. Although the data from developed countries suggest that mumps plays at the most a small role in the overall problem of infertility, such a conclusion many not apply to sub-Saharan Africa.

There is no available evidence suggesting that mumps oophoritis, a far rarer complication than orchitis, has any significant role as a cause of infertility.

Toxoplasmosis

Infection with the protozoan *Toxoplasma gondii* is associated with a variety of clinical patterns in man and animals throughout the world. The organism is an obligate intracellular parasite inhabiting nucleated cells of all types but particularly those of the reticuloendothelium, muscle, and the central nervous system. It exhibits a proliferative and a cystic stage. The forms of infection seen in man include: congenital infection of a fetus during asymptomatic or mild primary infection of the mother; a benign illness with lymphadenopathy; uveitis; and, rarely, a severe systematic disease with pneumonia, myocarditis, and meningo-encephalitis. The association of toxoplasmosis with spontaneous abortion has not been well documented (*56*).

The generally held view is that *T. gondii* represents a one-time risk from a primary infection of a pregnant woman. The result of such an infection is either a stillbirth, a congenitally infected, often premature infant, or a normal infant. This generally held view is questioned by Langer (*57*), who suggests that *T. gondii* may encyst in a number of tissues, including the endometrium, and hypothesizes a local release of *T. gondii* from cysts on stimulation of the process of placentation, leading to a low-grade endometritis. This local infection fails to stimulate antibody production, but causes rejection or infection of the fetus. He describes a high incidence of a positive titre to toxoplasmosis in women with repeated pregnancy wastage. He also isolated *T. gondii* from several tissues in 23 of 70 women with repeated pregnancy wastage. In one woman, the organism was isolated from brain tissue of two successive stillborn babies. Serological evidence of latent rather than primary infection was obtained from 19 of the 23 women (*57*).

Data from Zaire suggest an important though not a major role for toxoplasmosis in pregnancy wastage. Wery-Paskoff et al. (*58*) indicated that a significantly higher percentage of women with a stillborn child had a high antibody titre to toxoplasmosis than those whose child was born alive. From their data, 98.6 out of 1000 stillbirths may be attributable to toxoplasmosis. In examining three communities, one of which had significantly higher perinatal mortality rates, Robertson (*59*) in England demonstrated the probable role of toxoplasmosis in raising the percentage of stillbirths.

Schistosomiasis

Although both *Schistosoma mansoni* and *S. haematobium* may be found in the genitals, the importance of schistosomiasis in infertility and pregnancy wastage is unknown. In areas of the Caribbean, where the incidence of *S. mansoni* in autopsy material is 14.6%, Arean (*60*) examined 78 238 surgically removed specimens of genital organs over a period of 30 years; he found involvement with *S. mansoni* in 18 specimens only, 10 involving the tubes or ovaries. In another series of 64 consecutive autopsies in Southern Rhodesia (*62*), the female pelvic organs were examined for schistosomiasis by histological and digestive techniques; evidence of schistosomiasis, mainly *S. haematobium*, was noted in 37 women. Schistosomal inflammation and granuloma forma-

tion were common in the bladder and rectum of these patients but were not evident in the fallopian tubes or the ovaries, despite the presence of schistosome ova in these tissues. The investigators concluded that the female genital tract is more likely to be affected by *S. haematobium* than by *S. mansoni*.

A number of individual case reports have described lesions attributable to schistosomiasis in association with acute and chronic salpingitis and tubular obstruction (*62*, *63*). The epidemiological significance of schistosomiasis in the etiology of infertility is unknown.

Malaria

There is no evidence to suggest a relationship between malaria and infertility, but there may be an effect on pregnancy wastage and neonatal mortality. A mean decrease of 100–300 g in birth weight has been widely reported as being associated with malarial infection (usually *Plasmodium falciparum*) involving the placenta (*64*). More recently the implementation of a malaria eradication programme has been associated with a rise in mean birth weight, and a significant decrease in infants of low birth weight, particularly in primigravid mothers (*65*). In these latter studies, primigravid births below 2500 g fell from 40% to 20% after the eradication programme.

At present there is no evidence to indicate whether malaria involving the placenta increases the risk of spontaneous abortion or stillbirth. On the assumption that low birth weight is a leading factor in neonatal mortality and since early neonatal death is often regarded as pregnancy wastage, then malaria can be thought to contribute to the problem of childlessness, possibly through pregnancy wastage and definitely as a result of infant and child mortality.

Filariasis

Infection with *Wuchereria bancrofti* has, in many regions of the world, a particular predisposition to the lymphatic system of the genital organs of both men and women (*66–69*). Early filarial infection in men is associated with funiculitis and epididymo-orchitis, originating with involvement of the lymphatics of the tunica vaginalis and of the spermatic cord. Hydrocele and lymphovaricoceles or chyloceles are common sequelae of filarial infection in men, and are often used as clinical–epidemiological indicators of filarial infection (*68*, *69*). Modawi (*15*) noted that among 166 men from infertile unions 11.9% had hydroceles, 4.4% lymphovaricoceles, 6.6% epididymo-orchitis, and 7% testicular atrophy. The rate of these among fertile males was not noted.

Similar patterns of lymphangitis and lymphatic obstruction have been observed to involve the lymphatics of the broad ligament and the fallopian tube in women (*66*). Clinical symptoms of acute, subacute, and chronic salpingitis have been attributed to filarial infection (*63*). Secondary bacterial infection of filarial genital lesions in both men and women have been described, but the frequency and significance of such infections has not been established.

According to Modawi (*15*), the areas of high levels of infertility in the Sudan correspond to the endemic regions for filariasis. Modawi describes the only pocket of infertility outside the endemic zone of filariasis in Equatoria Province of the Sudan as being inhabited by a tribe that had previously resided within the endemic zone. Tubal occlusion among the women and hydrocele, lymphovaricocele, and testicular atrophy were common and it was considered likely that these were sequelae of filariasis.

Mycoplasmas

Reports suggesting that mycoplasmas might be associated with infertility have not been confirmed in more recent studies (*70*, *71*).

Other infections

Other micro-organisms reported to be associated with pregnancy wastage include the spirochete of relapsing fever, *Brucella melitensis*, and rickettsiae (*14*, *72*, *73*). The role of these infections in sub-Saharan Africa has not been well established.

Many infectious agents are known to result in infertility or fetal wastage in domestic animals (see the *Annex*, pp. 340-341). However, the significance of such agents in human infertility and pregnancy wastage is unknown.

SEQUELAE OF ABORTION AND OBSTETRICAL AND OTHER PRACTICES IN RELATION TO SUBSEQUENT FERTILITY

Tubal occlusion

Tubal occlusion may be a consequence of a pyogenic non-gonococcal salpingitis following abortion or delivery. Infection with a variety of organisms often originates in the cervix or uterus, and extends by way of the lymphatics and blood vessels

of the parametrium and broad ligaments. The lumen and mucosa of the tube are rarely involved, but rather there is extensive interstitial involvement of the tube with thickening and oedema. The lack of mucosal involvement is associated with less risk of occlusion than is present following gonorrhoeal salpingitis. However, in two series, as noted previously, non-gonorrhoeal salpingitis is associated with a higher rate of tubal occlusion than is gonorrhoea (*28*, *38*).

There are no reports from sub-Saharan Africa on the frequency of post-partum or post-abortal salpingitis or the risk of subsequent infertility. The rate of secondary infertility, particularly if primary infertility is low, can be used as a crude indicator of the possible importance of post-abortal and post-partum infection. For example, high levels of secondary infertility have been described in the Western State of Nigeria where 15% of women married for 11–15 years have either never borne a child or have borne only one; 40% have borne no more than two children (*74*).

In all studies that have included an examination for tubal occlusion, this condition has been shown to be the most important mechanism accounting for infertility in sub-Saharan Africa and other areas where a high prevalence of infertility exists (see discussion of gonorrhoea). Bilateral tubal blockage was established by hysterosalpingography in 56 (70%) of 79 infertile women in Scragg's studies (*13*). In Ghana, a clinic-based study of 398 women from infertile marriages showed 40% to have tubal occlusion (*75*). Other hospital-based studies in Africa have shown 50–70% of the infertile women to have tubal obstruction (*29*, *76*, *77*). In developed countries, tubal occlusion accounts for no more than 20% of cases of infertility.

Mati et al. (*78*) in Kenya demonstrated by laparoscopy bilateral tubal occlusion in 76 (73%) of 104 women diagnosed as having primary infertility. In an earlier study from Kenya, tubal occlusion was demonstrated by insufflation in 61% of women with primary infertility (*16*). Regardless of the comparabilty of the laparoscopy and insufflation techniques, in this urban East African setting the majority of cases of infertility are related to tubal obstruction. In Gabon, bilateral tubal occlusion diagnosed by hysterosalpingography was reported in 54.8% of women with primary infertility and in 38.4% with secondary infertility (*17*). These differences are significant and suggest different causes for primary and secondary infertility.

Obstetrical and other trauma to the genital tract

The condition of cervical incompetence is suspected as being a cause of repeated second-trimester abortion. Damage to the cervical canal due to laceration, infection, and scarring from previous injury with subsequent relaxation is thought to result in increased uterine contractility causing expulsion of the products of conception, usually in the second trimester. The condition is usually described in one in every 900 to 1000 deliveries in most developed countries. No data have been published on the prevalence of cervical incompetence in Africa. One report deals with the surgical management of 41 cases (*79*).

Aside from the obvious effects of unskilled obstetric practices on the risk of puerperal sepsis, certain delivery and birth rituals may add to the risk of infection or injury. The practice of the Hausa of pouring nearly boiling water into the genital tract following delivery may decrease the risk of some infections but may also increase the risk of burns and possible scar formation (*80*). The possible association of different birth practices with the risk of infertility has not been systematically studied.

Certain rituals involving the genital organs may produce infection or injury that interferes with conception or increases the risk of pregnancy wastage. Such practices as female circumcision or infibulation are found throughout the world. Clitoridectomy performed under septic conditions may result in ascending infection in the genital tract. Infibulation, a far more radical procedure with very high immediate risk of haemorrhage and infection, may frequently result in severe scarring and nearly complete obliteration of the vaginal introitus. Coitus is difficult, painful, and frequently associated with perineal trauma and risk of infection. Unassisted delivery in the case of infibulation is nearly impossible, perineal damage the rule, and potential injury to the infant not uncommon. Although the so-called Pharonic form was banned in the Sudan in 1946, it is not known to what extent it is still practised both there and in areas where it was not banned. Mustafa (*81*) claims that 20–25% of the cases of infertility in the Sudan are due to infibulation. Difficulties in delivery including prolonged labour, uterine inertia, and severe perinatal damage may increase the risk of perinatal mortality. In Meuwissen's study in Ghana (*75*) marked vaginal changes were noted in 41 (10.3%) of 398 infertile women. These changes consisted mainly of sclerous

stenosis resulting from ritual circumcision and native treatments.

Clitoridectomy is widely practised in areas of Africa. Hanry (*82*) noted that 84% of Muslim girls in the upper classes of a Guinean school had had clitoral excision between the ages of 8 and 11 years, and 3 out of 10 Christian girls had had a clitoridectomy.

OTHER CAUSES OF FEMALE INFERTILITY AND PREGNANCY WASTAGE

Sickle cell disease

Although it has been stated that the woman homozygous for sickle cell haemoglobin (either SS or SC) rarely survives to reproductive age, among those that do there are frequent reports of high levels of infertility, pregnancy wastage (including spontaneous abortion and stillbirth), and premature delivery (*83–85*). The heterozygous state has not been noted to increase the risk of pregnancy wastage (*85, 86*). Sickle cell–haemoglobin-C disease carries a high risk of maternal mortality (*83*).

Despite the high levels of haemoglobinopathies in areas where infertility may exist, it is unlikely that these conditions play a significant role in the epidemiology of infertility and pregnancy wastage, unless the heterozygous state can be shown to be deleterious to fecundity or pregnancy. Even in areas where the sickle cell trait reaches levels of 20–40%, the level of disease in the community would be only 1–4%, and this would be further reduced since only 20% of women with sickle cell disease survive to reproductive age in the area of Africa under review (*87*).

Hormonal disorders

In all clinical series of patients who have undergone a range of diagnostic tests and studies, a small percentage have been assumed to have a hormonal imbalance accounting for their infertility. This conclusion is usually based on the diagnosis of a proliferative endometrium at the time of premenstrual biopsy. In the series reported from Africa (*16, 75, 77*), 6–15% of the patients were so diagnosed.

Thyroid disease and goitre

Despite frequent references to the role of thyroid disease in infertility, there has been no recent documentation of such an association. Although there are well-defined pockets of endemic goitre in Africa as well as in other areas of the world, there are no available data on fertility, childlessness, or pregnancy wastage for such areas.

Nutrition

The association of nutrition or dietary deficiencies with hormonal changes has not been explored, and evidence that infertility is associated with altered nutrition is indirect. Irregular menstruation has been noted in marginally undernourished women, and amenorrhoea has been noted during severe undernutrition (*88, 89*). Gopalan & Nadamuni Naidu (*90*) suggest that pregnancy wastage increases among malnourished women. Differences in nutrition have been suggested as part of the differences in the fertility rate between nomads and non-nomads of the same tribe (*10*). In this tribe, a difference of 1.5 years in the age of first maternity in women married at 14 years of age or earlier has been suggested as possible evidence of delayed puberty due to malnutrition.

OTHER CAUSES OF MALE INFERTILITY

The male factor in infertility has been examined in a few studies in Africa and has been discussed in part under the section on gonorrhoea. Other than complete azoospermia, it is difficult to interpret variations in sperm count, morphology, and motility in terms of altered fertility, particularly as the studies rarely include more than one semen sample per patient. Techniques and care in the collection and processing of specimens vary markedly. Furthermore, evidence exists that some men with oligospermia and morphological abnormalities of the sperm are capable of successful insemination. Under such circumstances, only data relevant to azoospermia will be presented.

Azoospermia was found in 20 (8.9%) of 224 men of infertile marriages in Ghana (*75*) and in 26 (9.2%) of 280 men from infertile marriages in Nigeria (*91*). The relative importance of gonorrhoea or other infectious diseases in relation to azoospermia has not been established. In European clinics, azoospermia is found in no more than 5% of men of infertile marriages.

In a study involving 8000 infertile patients in India, a significant association of obstructive azoo-

spermia and a history of smallpox were noted (*92*). Azoospermia was noted in 42.6% of 895 men with a history of smallpox and infertility and in 17.9% of a control group without a history of smallpox but with infertility. Testicular biopsy in 358 patients showed a significant difference in the frequency of obstructive azoospermia; this observation has not been confirmed in any other studies.

PSYCHOLOGICAL CAUSES OF INFERTILITY

Psychological causes of infertility without particular reference to their pathophysiological mechanism are often referred to anecdotally in infertility clinics. Psychological mechanisms often follow the well-known pattern found in European and North American infertility clinics, by which conception takes place during the course of diagnostic studies but before any biomedical therapy has been initiated. In the published reports on the causes of infertility in Africa, no reference has been made to the frequency of this pattern. Individual case reports from Africa of psychological factors in impotence and infertility have been published, but no systematic studies have been undertaken.

SOCIAL AND HEALTH SERVICE IMPLICATIONS OF INFERTILITY AND PREGNANCY WASTAGE

Social implications

Most traditional cultures place a high social value on fertility, particularly as a demonstration of the consummation of the marriage and as one expression of the couple's social role. Complex sets of family and social relationships, beliefs, and agreements are incorporated into the marriage system and procreation.

Infertility has been viewed as punishment for some social transgression. In one tribe in Uganda, if the bride payment is not divided properly between the relatives of her parents then it is believed that the marital union will be punished by barrenness of the woman (*93*). Bride price, dowry, and other forms of marriage payment are common, and are often modified in the case of barrenness or divorce. The importance of offspring is seen in the formal systems of attachment to, and control by, the paternal or maternal family; for example, the marriage payment frequently gives control of a child to the husband's family (*93*).

Failure to bear children is an accepted basis for divorce in many cultures (*17, 76, 94*) and regardless of whether it represents a cause or effect, childlessness is significantly higher among divorced women in some cultures (*10, 13*). Barrenness has been viewed as a personal tragedy and humiliation (*95*). The failure of a pregnancy to terminate in a live birth is considered to reflect on the adequacy of a woman, or in extreme examples, as evidence of sexual misconduct. In some cultures, impotence of the male also may be grounds for a woman obtaining a divorce. Among the Jie in Uganda, a marriage is not considered consummated until the birth of children *and their survival through infancy* (*96*). In the southern Sudan, the dearth of children among the Murle tribe has resulted in raids on neighbouring tribes to obtain women and children (*15*).

Although the primary cause of inability to conceive may be an infectious agent, such as *N. gonorrhoeae* or a variety of other organisms in cases of post-abortal or puerperal sepsis, the underlying or contributing factors may reflect social disorganization. Population shifts from rural to urban areas and extensive migration of contract labour may both contribute to an increase in prostitution, which has been widely associated with increased risks of gonorrhoea (*44, 45, 97*), and illegal abortion (*98*).

Health service implications

In the infertile woman, the prospect of successful treatment of the major causes of infertility, such as tubal occlusion, would be poor even if sufficient technical and financial resources existed. Once tubal occlusion has been demonstrated, successful surgical therapy requires highly skilled staff and specialized facilities.

In one series of patients, although tubal patency had been demonstrated in 50% of patients following surgery, pregnancy occurred in only 14.8% and half of these pregnancies ended in spontaneous abortion or ectopic pregnancy so that the final success rate was only 7.4% (*99*). Disappointing results have also been obtained elsewhere (*78*). Results in developed countries are similar; only highly specialized clinics with the top surgeons have more than 20% success.

Beyond the question of infertility and pregnancy wastage for the individual couple, the public health implications are even greater when one considers

that these conditions represent the consequence of a series of other events or disease problems, each of which may have additional risks to personal health for both adults and the unborn child and place additional burdens on the health service. Infertility and pregnancy wastage represent only a small proportion of the health problems related to human reproduction. They may be a consequence of infection following unskilled obstetrical practices or septic illegal abortion, other consequences of which may include incompetence of the cervix, vesiculovaginal fistula, birth trauma with injury to the infant, etc. Tubal occlusion is but one consequence of gonorrhoea; others include partial occlusion with resultant ectopic pregnancy, ophthalmia neonatorum, and arthritis. Repeated gonorrhoeal infection in the male may lead to urethral stricture, chronic obstructive changes in the ureter, or chronic renal disease. A high level of fetal wastage due to syphilis would serve as an indicator of other major long-term health problems related to syphilis.

Infertility becomes a problem of major social concern when great demands for treatment are placed on the health services. In areas of Africa, as many as 10% of consultations by women are for infertility (*76*) and as much as ¼–½ of the gynaecological service consultations are for infertility (*16*, *100*). In addition, infertility leading to depopulation of some areas limits the social and economic development of a region.

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RÉSUMÉ

ÉPIDÉMIOLOGIE DE L'INFÉCONDITÉ: REVUE DU PROBLÈME EN CE QUI CONCERNE PARTICULIÈREMENT LES PAYS D'AFRIQUE AU SUD DU SAHARA

Il ne semble pas qu'il existe dans la littérature d'études portant sur des pays africains situés au sud du Sahara ou sur d'autres pays en développement, dans lesquelles aient été examinées toutes les causes potentielles d'infécondité et de grossesses improductives. On a l'impression, mais cela n'est pas confirmé, que la situation varie quelque peu d'une région à l'autre. Néanmoins, il apparaît que partout où il y a degré élevé d'infécondité, l'obstruction tubaire joue un rôle majeur et que la principale cause étiologique de cette dernière est probablement la gonococcie. On ne possède que des données insuffisantes sur le rôle relatif d'autres causes d'infécondité et sur l'importance des grossesses improductives et leur origine.

Si l'on se fonde sur les données épidémiologiques et cliniques peu nombreuses, qui ont été publiées, on voit que les affections auxquelles on attribue l'infécondité comprennent d'autres causes d'obstruction tubaire telles que la salpingite purulente, les troubles nutritionnels et hormonaux, la tuberculose génitale, la blennorragie chez l'homme, la filariose, la schistosomiase ainsi que les séquelles de variole et d'oreillons chez l'homme.

D'après la présente étude, les causes de grossesses improductives semblent être notamment la syphilis, la toxoplasmose, la béance du col utérin, les infections rickettsiennes, les hémoglobinopathies ainsi que les séquelles de traumatismes de l'appareil génital chez la femme.

Il semble donc que de très multiples causes peuvent toutes contribuer à des fréquences élevées d'infécondité et de grossesses improductives. Il est probable que le tableau de la prévalence et de la distribution soit principalement influencé par la gonococcie qui semble la cause majeure de l'infécondité. Cependant, des différences relatives aux autres causes peuvent aussi entraîner des variations dans l'allure de la distribution.

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Annex

PRINCIPAL INFECTIVE AGENTS INVOLVED IN INFERTILITY AND FETAL MORTALITY IN DOMESTICATED ANIMALS

AGENTS MAINLY ASSOCIATED WITH LESIONS IN GENITAL GLANDS AND PASSAGES

1. Picornaviruses, including foot-and-mouth disease virus involved in degeneration of testicular parenchyma in cattle.
2. Uncharacterized virus causing interstitial orchitis in bulls and purulent inflammation of the genital tract in cows.
3. Infectious pustular vulvovaginitis virus of cows, possibly closely allied to or identical with bovine rhinotracheitis virus. A similar herpesvirus is found in swine.
4. Epivag (epididymitis and vaginitis) agent, probably a picornavirus.
5. *Mycoplasma* spp. causing reversible azoospermia in bulls and *M. hyorhinitis* causing peritubular inflammatory infiltration in swine testes.
6. *Brucella ovis* causing ram epididymitis; other *Brucella* spp. causing epididymitis and orchitis (see also item 11).
7. *Trypanosoma equiperdum* causing orchitis in stallions and vaginal lesions mares.

AGENTS MAINLY INVOLVED IN FETAL AND PERINATAL MORTALITY BUT GENERALLY ASSOCIATED WITH LESIONS OF GENITAL ORGANS

8. Equine rhinopneumonitis virus causing abortion in mares.
9. *Miyagawanella* [a] species causing abortion in cattle and sheep.
10. *Brucella abortus*, *B. melitensis*, and *B. suis* [a] in various farm animals, particularly ruminants.
11. *Leptospira interrogans*,[a] various serotypes.
12. *Salmonella dublin*, *S. abortus ovis*, *S. typhimurium*, and other serotypes.[a]
13. *Listeria monocytogenes* [a] in sheep and cattle.
14. *Vibrio fetus* [a] in cattle and sheep; also *Trichomonas foetus* in cattle.
15. *Aspergillus fumigatus*, *Absidia ramosa*, and other fungi [a] causing abortion in cattle and pigs.
16. *Toxoplasma gondii* [a] in various animal species, but particularly in swine, sheep, rabbits, and cats.
17. Other micro-organisms more commonly associated with post-natal mortality but sometimes involved in fetal mortality: coliform organisms, streptococci, staphylococci, and corynebacteria.

AGENTS CAUSING FETAL DEATH OR EXPULSION AS PART OF A SYNDROME OF GENERALIZED INFECTION

18. Rinderpest virus.
19. Foot-and-mouth disease virus.
20. Swine fever virus.
21. *Pasteurella multocida* [a] and other species.
22. *Mycobacteria*.[a]
23. Piroplasma.
24. Trypanosomes.[a]
25. Other acute infections.

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[a] Known or strongly suspected to be zoonotic agents, i.e., transmissible in nature between man and vertebrate animals.