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Medical Considerations for Legalizing Voluntary Sterilization:

Sickle Cell Disease as a Case in Point

by F.I.D. Konotey-Ahulu, M.D.

Background Paper Presented at the
Second International Conference on
Voluntary Sterilization, Geneva
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Medical Considerations for Legalizing Voluntary Sterilization:

Sickle Cell Disease as a Case in Point

by F.I.D. Konotey-Ahulu, M.D.*

Background Paper Presented at the
Second International Conference on
Voluntary Sterilization, Geneva
February 25–March 1, 1973

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To The Members

of the

Korle Bu Teaching Hospital Sickle Cell Clinic.

FOREWORD

At the request of the Association for Voluntary Sterilization, the Law and Population Programme assisted in the preparation of the Second International Conference on Voluntary Sterilization, held on February 25–March 1, 1973, in Geneva. Along with the monograph entitled, *The World's Laws on Voluntary Sterilization for Family Planning Purposes*, by Jan Stepan and Edmund H. Kellogg (Law and Population Monograph Series No. 8), the present monograph by Dr. F.I.D. Konotey-Ahulu of Ghana was commissioned as a background paper for the Conference.

Himself an African, Dr. Konotey-Ahulu shatters the oft-held myth that the sickle-cell gene is a monopoly of Africa or Africans. He points out that such a gene is found also "in the Mediterranean countries like Greece, Turkey, Italy, Sicily etc., and it is also found in the Lebanon and South India." The enormity of the problem may be gleaned from the fact that the number of sicklers reaches 20% of West Africans and Greeks living in the region of Lake Kopais, 30% of the Irulas in South India and nearly 50% of Ugandans in one region. Would the traditional family planning method of contraception be adequate to cope with the problem of sickle-cell? This and other knotty issues are faced squarely by the author.

In the belief that a problem of such proportions should not be swept under the rug, the Law and Population Programme has decided to share Dr. Konotey-Ahulu's study with a larger readership by including it in this Monograph Series.

Luke T. Lee
Director

INTRODUCTION

It has been stated, and quite correctly, that "in those countries in West Africa in which socio-economic progress is most rapidly being achieved, sickle-cell anaemia will soon assume the proportions of a major medical problem" [1]. The disease is already a major health problem in the U.S.A., while Lehmann [2] points out that "in the Congo (Zaire), for example, more than 1,000 of every 100,000 infants born are homozygotes for the sickle-cell gene and nearly all of them will die from sickle-cell anaemia". He further states [2] that "sickle-cell anaemia causes the death of some 80,000 children in Africa every year" and he stresses not only the mortality but the morbidity that the disease causes.

I intend to deal with my topic by, 1, explaining hereditary principles in general, 2, defining sickle-cell disease, 3, delineating the size of the problem, 4, portraying sketchily the depth of the problem, 5, showing the attempts at treating the disease and 6, demonstrating the paramount place of family planning with special reference to voluntary sterilization in the management and control of the disease.

PRINCIPLES OF HEREDITY

I find myself immediately in difficulty—and it is this: How can I communicate effectively to a group of experts and laymen at the same time? I shall try to be as simple as possible, but I do apologise if I am too technical.

Heritable Characters and Chromosomes

First, I must say something about heredity and heritable characters. For every character (heritable character) you possess, be it colour of your skin or of your eyes there are a father component and mother component. These components are passed through what are known as *genes* which are found strung up on the chromosomes which in turn are localised in the sperm of the male and the ovum (or egg) of the female. Having been introduced into the female during *coitus* the sperm seeks out the ovum and fuses with it—uniting its nuclear material with that of the ovum. The paternal heritable characters (in the genes of the spermal chromosomes) are then passed on together with the maternal heritable characters (in the genes of the chromosomes of the egg) to the offspring which is the product of the male-female union. Now, in order that the offspring may have just *one* pair of genes (and not two pairs) for each heritable character the father and the mother pass on one each of their pair of genes for each particular character. This will become clearer soon when we consider the details of sickle-cell disease. But suffice it to say that the sperm contains only one half of the chromosomal constitution of the father, and the ovum one half that of the mother. The foetus then has the same quantitative chromosomal constitution as the parent.

Genes and DNA

Now a word about the observable and quantifiable heritable characters. Aberrations in structure and function of body proteins can often be traced to structural genes. Proteins contain about 20 different amino acid types and some protein chains may contain up to 500 amino acids. A structural gene is defined as "that segment of DNA (in the nuclear chromosomes) which specifies the primary structure or amino acid sequence of a particular polypeptide chain in a protein"[3]. This is done by a unique coding system called the genetic code. When there is something "wrong" with the code due to an inherited or, rarely, acquired mutation in the particular DNA (desoxyribose nucleic acid) segment specifying a particular protein the "wrong" protein is produced.

Normal and Abnormal Haemoglobins

Haemoglobin is a protein. It is the red substance present in red cells of which there are several millions found per cubic millimetre of blood. The main function of haemoglobin is to carry oxygen from the lungs to the tissues and gaseous waste products back to the lungs. Aberrations from the normal in the genetic code relating to haemoglobin production lead to the production of abnormal haemoglobins with consequent disturbances in red cell structure and function. These red cell defects can easily be detected on blood testing. So rare are acquired mutations in human beings that anyone who, on blood testing, is found to have an abnormal haemoglobin must be presumed to have inherited the gene for this from either father or mother, or where disease is caused, must have received the genes from both parents (vide infra). The commonest abnormal haemoglobin in the world is haemoglobin S which when present in the red cell has the tendency to alter the shape of the cell from round to sickle shape under a variety of conditions the chief of which is hypoxia or a deficiency of oxygen. Normal haemoglobin is called "haemoglobin A", so that the person who has inherited one gene for normal haemoglobin formation from a parent and another gene for the abnormal haemoglobin S from the other parent will not only give a positive sickling blood test but will also turn out to be "AS" on the special blood examination called haemoglobin electrophoresis[4]. The total number of abnormal haemoglobins that have hitherto been discovered[3] all of them resulting from inherited genetic coding abnormalities—is more than 150. Most of these are extremely rare having been found only once in single families, but others like haemoglobins C, D, E and KWoolwich are, like the sickle cell haemoglobin, common enough to be found in whole populations[5]. Other common genes for defective haemoglobin synthesis include the thalassaemias which occur in the greatest concentration in the Mediterranean countries. Simultaneous inheritance of the sickle-cell gene with another gene for defective haemoglobin synthesis, or of two sickle-cell genes usually produces what is known as sickle-cell disease.

DEFINITION OF SICKLE-CELL DISEASE AND SICKLE-CELL TRAIT

For genetic counseling and family planning purposes clear-cut definitions of sickle-cell disease and sickle-cell trait are absolutely essential.

I define *sickle-cell disease* as the possession of two abnormal (or if you like unusual) genes related to haemoglobin synthesis of which at least one is the sickle-cell gene. For a person to acquire the disease he must have inherited the abnormal gene from both his father and mother. The genotypes that constitute sickle-cell disease are, therefore, SS, SC, SD, SE, S-Thal etc. Note that each one of these pairs is abnormal in that it is *not* "A". The genotype comprising one *normal* gene (A) and the abnormal gene S is not included in the definition of sickle-cell disease since the criterion of *two* abnormal genes is not met.

Sickle-cell Anaemia: This is sickle-cell disease in which *both* abnormal genes are for the formation of haemoglobin S. This is also known as homozygous S disease.

Sickle-cell Trait: This term is used to describe a person who has inherited one normal haemoglobin gene (A) from one parent and one abnormal gene (S) from the other parent. The person, who is a sickler on blood testing as mentioned before, has the genotype AS and does *not* have a disease. When the term *heterozygote* is used to describe such a person it must be clearly stated that he is heterozygous for a normal gene (A) with an abnormal gene (S). When also the term *heterozygotes* is used to describe conditions like SC, SD, S-Thal etc. it must be clearly pointed out that the heterozygosity is between two abnormal genes lest pathological features described in an SC state be wrongly ascribed to a heterozygous sickle-cell trait (AS) state. It should be further noted that the term *trait* is reserved for the heterozygous state involving a normal gene with an abnormal gene (e.g. AS, AC, A-Thal, AD, AE, AF-highgene etc.) and should never be used to describ e a state of heterozygosity between two abnormal genes like SC, S-Thal, etc.

The above definitions, as was recently pointed out[6], agree with those of world experts constituting the "Colonial Medical Research Committee Working Party on sickle-cell trait and sickle-cell anaemia"[7] and the World Health Organisation.[8].

SIZE OF THE PROBLEM

The size of the sickle cell problem is quite staggering. For reasons which are not clear but which may have to do with resistance to *falciparum malaria* about 1 in 5 of all West Africans have inherited an abnormal haemoglobin S from at least one parent—making them AS on haemoglobin electrophoresis. One in five—a staggering 20% of the perfectly healthy population of West Africa going about their daily business and actively participating in farming, athletics etc. are sicklers, (AS). The distribution of the sickle-cell gene extends far beyond Africa. Figure 1 shows the distribution of the sickle-cell gene in the Old World from where it was transported to the New World through the Slave Trade. Note that Africa is not the only continent with sickle-cells. The gene is found in the Mediterranean countries like Greece, Turkey, Italy, Sicily etc., and is also found in the Lebanon and South India. Nearly 1 in 5 of Greeks living in the region of Lake Kopais carry the sickle-cell gene while 30% of the Irulas in South India have the gene (Table 1). It can be seen from the table that while in one region of Uganda nearly every other person is a sickler, in another part of the same country the gene is rarer than in some areas of Europe. Taking Tropical Africa as a whole however, the average

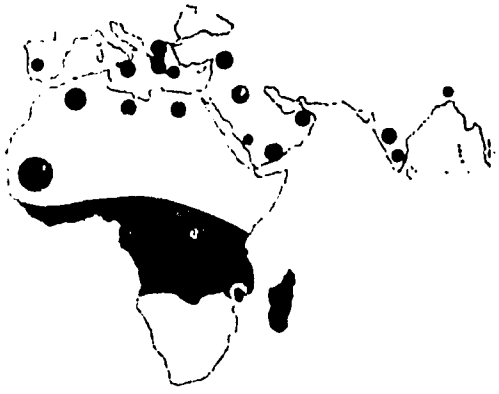
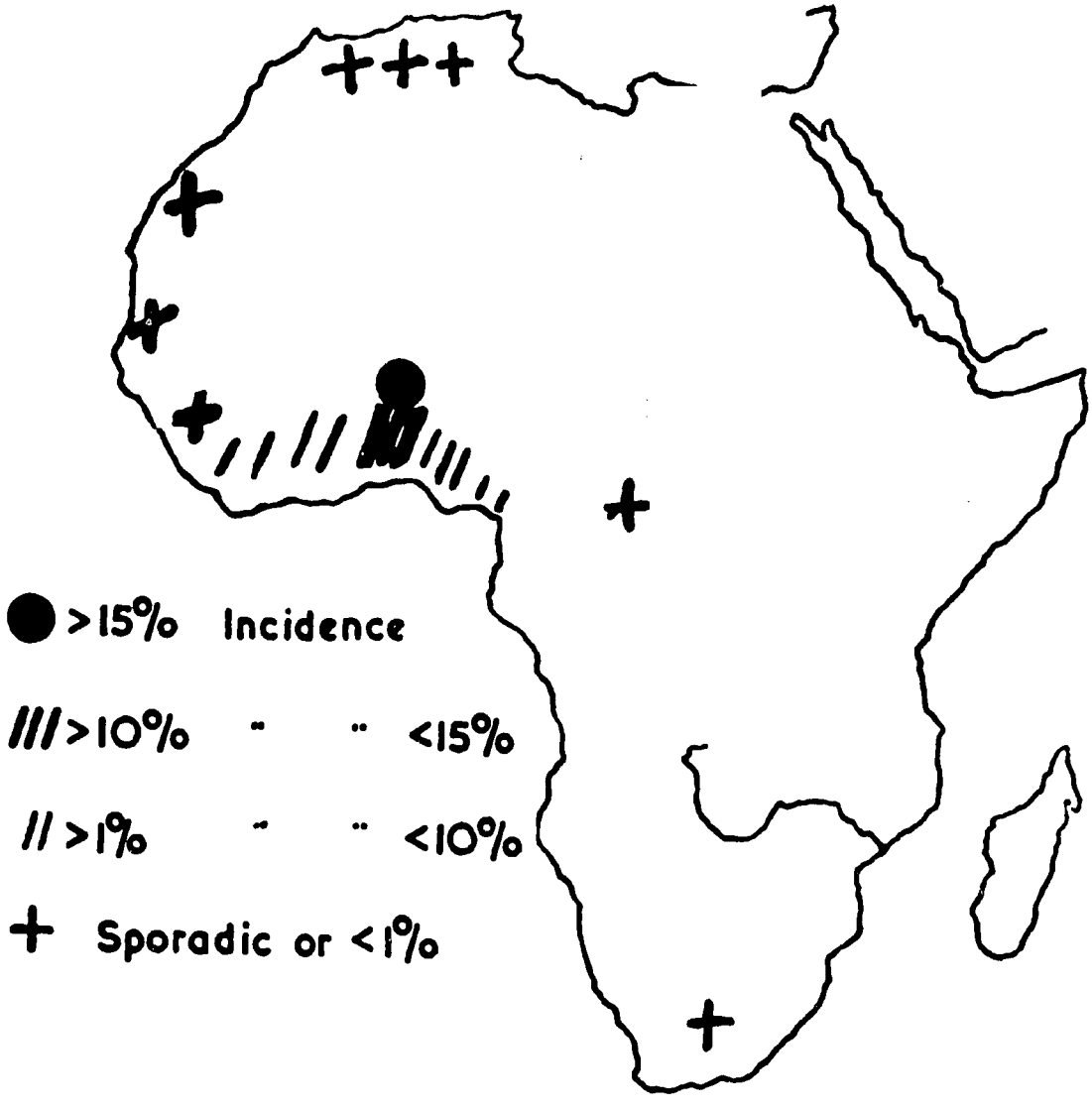


Figure 1

Distribution of the sickle cell gene in the Old World (by courtesy of Professor Lehmann[9])

Figure 2

Geographical distribution of Haemoglobin C in Africa from where it was transported to the New World. Trait incidence shown (Modified from Lehmann[9])



incidence of the sickle-cell trait is at least 1 in 5. Added to this is the fairly high concentration of the haemoglobin C trait especially in West Africa (Figure 2), the highest incidence in the world (20%) being found in Northern Ghana. The average haemoglobin C trait incidence in Southern Ghana is 10%. Taking the country as a whole, therefore, *one in three* of Ghanaians is either a sickle cell trait or haemoglobin C trait,[10-13] as illustrated as follows:

	Sickle cell Trait AS	Haemoglobin C Trait AC	Total
Southern Ghana	20%	10%	30%
Northern Ghana	10%	20%	30%

TABLE I

Incidence of the Sickle-cell Trait in Selected Regions

Regions	**% Trait**
The Baamba, Ruwenzori Mountains, Uganda	45
The Nilotic-speaking people, Uganda	21-28
The Toso, Uganda	17.8
The half-Hamitic speaking people, Uganda	0.8-3.2
Tanganyika (Part of Tanzania)	38.
Madagascar (Malagassy-Antaimoro)	20-23
Portuguese East Africa (Wide range; higher in north west)	1-40
Zambia	13-27
Southern Sudan	18
The Congo (Zaire)	24-25
Gambia	13.9
Sierra Leone	28
Liberia	12
Ivory Coast (Abidjan)	14.1
Southern Ghana	19-20
Northern Ghana	7
Western Nigeria	23
West Africa as a whole	20-23
Jamaica	10.9
U.S.A.	7.7-10
Southern Turkey (Eti-Turks)	13.3
Greece (Lake Kopais region)	17.7
South India (Todas 3.3%, Bogodras 8.4%, Irulas 30%)	3.3-30

(A complete author reference of world wide distribution of abnormal haemoglobins is found in Livingstone 1967—Reference 5.)

When one adds the other hereditary qualitative and quantitative erythrocytopathies like beta-thalassaemia and persistent fetal haemoglobin whose trait incidence is between

2 and 4 per cent the proportion of West Africans with one abnormal gene related to haemoglobin formation is perhaps not less that 35%, not to mention the 1 in 4 sex linked inherited glucose-6 phosphate dehydrogenase (G-6 P.D.) deficiency of the population. Taking the abnormal haemoglobins alone it is obvious (Figure 3) how combinations of the sickle-cell gene with itself and with other haemoglobin variant genes can produce a variety of maladies known collectively as sickle-cell disease (SS, SC etc.) Let us look at this with the eyes of a layman: If a man who has the sickle-cell trait (i.e. a normal gene A and an abnormal gene S) has a wife who also has the sickle-cell trait (AS), these are the chances of disease in the offspring: he can only give A or S—not both—and the wife also A or S to every child born. If he gives A and the wife also gives A, you have a child who is AA and who is perfectly healthy. If he gives A and the wife S (or vice versa) you have a child who is AS who also is perfectly healthy even though he or she has the sickle-cell trait. But if he gives S and the wife S you have a child who is SS who becomes a sickle cell anaemia patient.

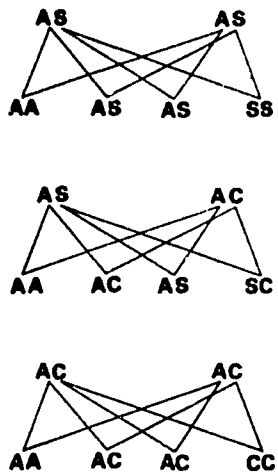


Figure 3

The probability of producing children with disease from matings between traits who are themselves normally asymptomatic. There is a 25% probability that the offspring will inherit an abonrmal gene from both parents, causing disease.

Herein lies the size of the problem:

(*a*) 1 in 3 is trait carrier

(*b*) 1 in 9, therefore, of all "marriages" brings trait carriers together

(c) 1 in 4 of all children born to such trait carriers (who are themselves perfectly healthy and therefore unaware of being carriers of abnormal genes) has two abnormal genes causing disease

(*d*) 1 in 36 (i.e. 1/9 X 1/4 of all children born in Ghana, therefore, suffers from a hereditary *disease*—SS, SC, or CC disease

(*e*) Thus, 36 births produce 1 child with disease. Therefore 1,000,000 births produce $\frac{1000,000}{36}$ sick children—28,000 approximately.

Of a million children born in Ghana nearly 30,000 *receive abnormal genes from both parents causing disease.* Of these, 20,000 have sickle-cell disease—SS and SC alone, not to mention the thousands who have sickle-cell thalassaemia, sickle-cell F–highgene and sickle-cell-'other variants'.

(*f*) To reduce it to simple, practical, terms 1% of all babies born at the Korle Bu Teaching Hospital has sickle-cell anaemia (SS) and another 1% has sickle-cell haemoglobin C disease (SC). Many of these *used* to die young. They don't easily any more, because of increasing socio-economic progress hence the statement of Professor Hendrickse mentioned earlier [1] that "sickle-cell anaemia will soon assume the proportions of a major medical problem". Having delineated the size of the problem what is the *depth* of it, judging by morbidity and mortality?

DEPTH OF THE PROBLEM

The property that the abnormal haemoglobin S confers on the red cell is to alter its shape through crystallisation of the abnormal haemoglobin under certain conditions (Figure 4). The greater the concentration of haemoglobin S in the blood the quicker is the sickling process under hypoxic and other provocative conditions *in vitro* (i.e. outside the body) and *in vivo* (within the body i.e. in the veins, arteries or tissues of the body). Now, almost all the cells in a sickle-cell disease patient are round when he feels well and has no complaints. But as soon as there is a severe change in the body's internal environment a lot of cells change from round into sickle-shape clogging up the ends of the vessels in the bones and around joints and producing a lot of pain. The patient is then said to be in a *sickle-cell crisis.* A sickle-cell disease patient who has no symptoms is said to be *in the steady state.* The commonest cause of sickle-cell crisis in my country is fever, and the most frequent causes of fever are malaria, sorethroat and coughs, and infections of the gastro-intestinal tract with diarrhoea. (Figure 5) It is physiologically and pathologically impossible for a *steady state* patient to get into crisis (i.e. to get sufficient *in vivo* sickling for symptoms) without a change in the milieu interieur [14,15] and there is usually a well known precipitating cause to produce this change [16], about 17 known precipitating causes of sickle-cell crises having been mentioned by the author [17]. The effect of such crises can be found *anywhere* in the body (Table II) producing symptoms relating to any conceivable organ. The colossal morbidity associated with the disease immediately becomes obvious.

Figure 4

Sickle-cells, produced by adding a freshly prepared solution of 2% sodium metabisulphite ($Na_2S_2O_5$) to a drop of blood with haemoglobin S. Blood with normal haemoglobin or haemoglobin C does not behave in this way.

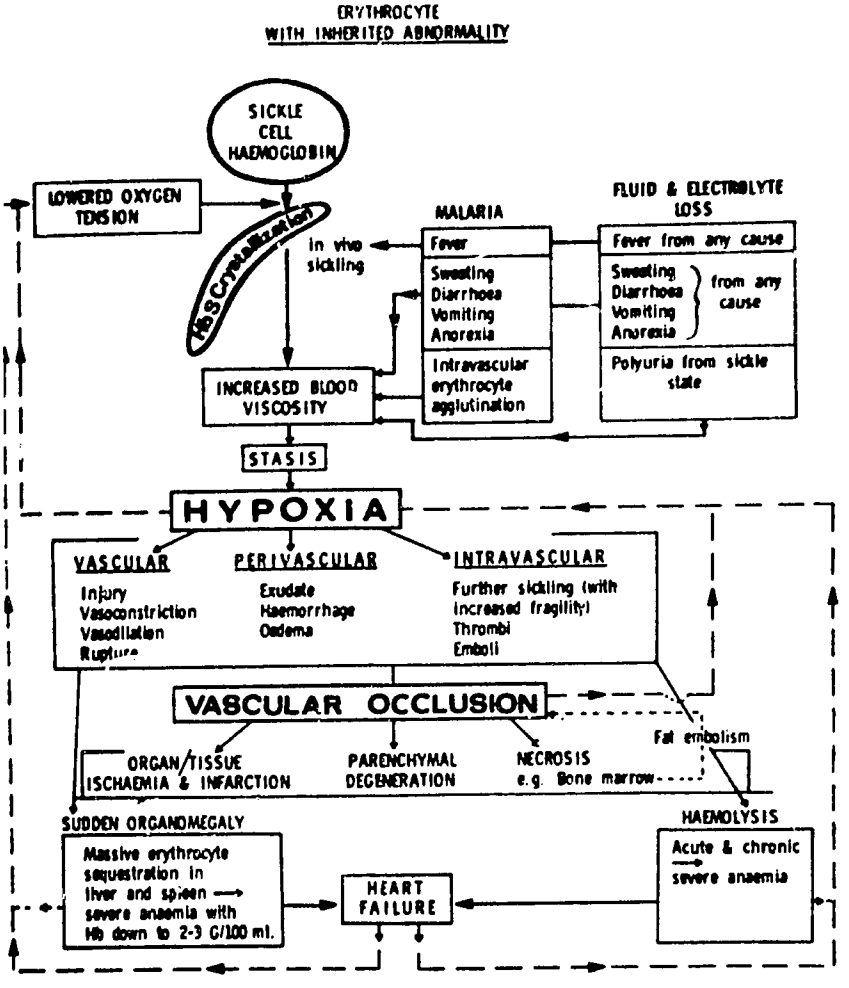


Figure 5 Pathogenesis of sickle-cell crisis in Accra (From Reference 16).

TABLE II

Organ/Tissue involvement in sickle-cell Disease [18]

Organ/Tissue	Effect of In Vivo Sickling
1. Joints	aseptic necrosis of head of femur and humerus
2. Long Bone	infarcts with pathological fractures
3. Vertebral body	compression fracture; biconcave deformity
4. Lung	infarcts, with cor pulmonale
5. Brain	infarcts with hemiplegia and various encephalopathies
6. Kidney	acute *papilitis necroticans* with haematuria
7. Gut	ulceration and infarction
8. Skin	necrosis and ulceration
9. Liver	focal necrosis; cirrhosis sometimes
10. Spleen	infarction and atrophy commonly
11. Heart	myocardial infarction; heart failure
12. Eye	retinal infarcts with vitreous haemorrhages and *retinitis proliferans*
13. Adrenal gland	infarction with Addison's disease rarely
14. Pancreas	infarction with diaberes mellitus very rarely
15. Pituitary	infarction with hypotituitarism
16. Breast	tissue necrosis; fibro-ademopathy
17. Ovary	infarction; infertility rarely
18. Penis	priapism with occasional penile fibrosis and impotence
19. Arteries	intermittent claudication; arterial thrombosis
20. Veins	phlebothrombosis; dural sinus thrombosis
21. Nerves	infarction with asymmetrical motor and sensory peripheral neuropathy
22. Spinal cord	disseminated infarctive sclerosis rarely
23. Lymph nodes	infarction with possible disturbance of immunological status
24. Utrerus	infarction with ischaemia during pregnancy ("intermittent uterine claudication", "uterine angina")
25. Placenta	multiple infarcts; miscarriages and stilbirths
26. Bone marrow	infarcts with pulmonary embolism especially related to pregnancy; also *proliferation* leading to gnathopathy and bossing
27. Teeth	periodontal tissue infarction; caries
28. Whole blood	massive intravascular sickling with sudden death

Symptomatology in Sickle-cell Disease

Persons with two abnormal haemoglobin genes one of which is S begin to have symptoms at varying ages depending on the genotype. Sickle-cell anaemia (SS) patients usually start having symptoms young, from 6 months of age while Hb. SC persons usually begin complaining after 5 years of age or later. Table III summarises the main symtomatology among sickle-cell disease patients attending the Korle Bu Hospital Sickle-cell Clinic, Accra (Table IV). By June 1970 there were 1,697 patients in the clinic the great majority of whom consisted of SS and SC disease patients. By February, 1973 we are approaching 3,000 patients in the Paediatric and Adult Sickle-cell Clinics under the supervision of Dr. Carl A. Reindorf and the author respectively. The growth of the combined clinic, which is completely unadvertised, except through relatives of patients who have found it useful makes it the largest in the world, and as the patients are living longer underlines the great responsibility that a developing country like Ghana has towards

them. A comprehensive catalogue of the morbidity and public health aspects of the disease appears elsewhere [18] and is outside the scope of this monograph, but to give you a little idea of the morbidity burden being carried by the patients themselves, their relatives and the national health service, I shall briefly mention just 4 of the complications of the disease.

TABLE III

Symptomatology in Sickle-cell Disease

Clinical Feature	Observed Haemoglobin Genotype
1. Severe anaemia	SS mainly
2. Joint, bone and abdominal pains	SS, SC and S-Thalassaemia
3. Growth disturbance (stunted or very tall) ...	SS mainly
4. Haemolytic jaundice	SS mainly
5. Severe obstructive-type jaundice with conjugated bilirubin 10mg. per 100 ml. or more	SS mainly
6. Generalised lymphadenopathy with jaundice ...	SS mainly
7. Chronic ulcers above medial malleolus ...	SS usually
8. Sickle-cell Gnathopathy (upper jaw protrusion)	SS usually. Few S-Thalassaemia
9. 'Hair on end' or 'needle-forest' skull X-ray due to bossing	SS usually
10. Monocular Blindness	Almost always SC
11. Aseptic Necrosis of Femoral head presenting with a limp. Usually misdiagnosed as "Perthes Hip" or "Tb. Hip".	Mostly SC. Sometimes S-Thalassaemia or SS
12. Profuse unexplained haematuria—bleeding usually from left rather than right kidney ...	SC, SS
13. Epistaxis	SS and SC
14. Priapism	SS and SC
15. Clubbing of Fingers and Toes	Some SC and SS
16. Cod-fish vertebrae on X-ray	SC or SS
17. Iatrogenic Limb Girdle-Tattoo in Ghanaian patients	Adult patients with SS, SC and S-Thallassaemia
18. Sudden unexplained post-partum shock and death	SC and SS

TABLE IV

Growth of Sickle cell/Haemoglobinopathy Clinic, Accra

Date		Total Number of Patients	Quarterly Increase
1963	October 1	1	
1964	Januar 1	11	11
	April 1	30	19
	July 1	73	43
	October 1	101	28
1965	January 1	125	24
	April 1	161	36
	July 1	196	35
	October 1	231	35
1966	January 1	269	38
	April 1	310	41
	July 1	368	58
	October 1	432	64
1967	January 1	489	57
	April 1	548	59
	July 1	599	51
	October 1	689	90
1968	January 1	748	59
	April 1	812	64
	July 1	887	75
	October 1	928	41
1969	January 1	1,016	88
	April 1	1,129	113
	July 1	1,229	100
	October 1	1,335	106
1970	January 1	1,437	102
	April 1	1,555	110
	June 30	1,697	142

Anaemia

Table V shows the haemoglobin levels in the steady state of sickle-cell disease patients with 4 different genotypes—SS, SC, SF–highgene (i.e. sickle-cell gene with gene for hereditary persistence of fetal haemoglobin), and sickle-cell thalassaemia S-Thal. It can be seen that although as much as 40% of sickle-cell haemoglobin C disease patients have haemoglobin levels in the normal range i.e. 12.0G/100 ml. or more the greater proportion of sickle-cell disease patients are anaemic. This is particularly so in sickle-cell anaemia (SS) patients in whom the mean maximum (steady state) haemoglobin for 463

consecutive patients is 8.0G/100 ml. The effects of such severe anaemia result in chronic ill health punctuated by frank attacks of severe jaundice, bone and joint pains and heart failure. Where standard of living is good the degree of ill health is minimised, but most patients sleep together with others of the same family in one room, with high cross respiratory infection rates and frequent malaria attacks producing crises and greater morbidity.

TABLE.—*Haemoglobin Levels in Sickle Cell Disease Patients in the Steady State.*†

Haemoglobin (S/100 ml)	SS	SC	SFh	STh
16·5		• •	•	
15·75		•		
15·00		• . . . . • 16		
14·25		• . . . . • 14	• •	
13·50	•	• . . . . • 36	•	• •
12·75	• • •	• . . . . • 37	•	• • •
12·00	• . . . . • 11	• . . . . • 49		• • • • •
11·25	• • • • • • •	• . . . . • 25	•	
10·50	• . . . . • 18	• . . . . • 57	•	• • • • •
9·75	• . . . . • 25	• . . . . • 41		• • •
9·00	• . . . . • 55	• . . . . • 37	• • •	•
8·25	• . . . . • 53	• . . . . • 23	• • • •	• • • •
7·50	• . . . . •110	• . . . . • 28	•	• • • •
6·75	• . . . . • 76	• • • •		• •
6·00	• . . . . • 69	• • • • • • • •		
5·25	• . . . . • 26	•		
4·50	• • • • • • •			
3·75	• •			
Mean	7·998	11·202	11·137	10·317
SD	1·645	2·210	2·767	2·113
Total	463	377	16	30

†BMD Biomedical Computer Programs 07D output. Each star represents a patient. Where the total number of patients for the same range of haemoglobin level exceeds 10 the exact number is shown after the row of stars. Note that 154 (41%) of 377 Hb SC patients had haemoglobin levels of 12·0 g/100 ml or more. Inter-genotype differences in Hb levels are highly significant ($P < 0{\cdot}001$).

Table V

Sickle-cell ulcers

These are commonly found in the actively growing sickle-cell anaemia patients (Figure 6). The incidence of skin ulcers is nil in young children but rises sharply to nearly 20% in the teenage Hb. SS patients and sometimes higher in the older age groups. Healing of the ulcer is slow, taking 4 months or more in some cases (Figure 7) with a high incidence of wound breakdown. Four months in hospital at a modest $30 a day (which is what it costs the Ghana Government to look after 1 patient at Korle Bu Teaching Hospital per day) is nearly $4,000. The annual bill to the country (for medical treatment in Ghana is virtually free to the patient) for ulcers alone is very huge. Sometimes the ulcer produces effects on the underlying bone (Figure 8) with occasional direct involvement resulting in osteomyelitis (Figure 9).

Figure 6

Chronic ulcer in 19 year old sickle-cell anaemia (SS) lady (27th February, 1968).

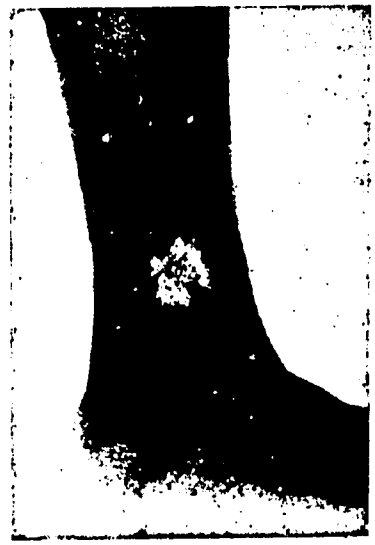


Figure 7

Healed ulcer in same Hb. SS lady (27th June, 1968).

Chronic Osteomyelitis

Sickle-cell disease patients are prone to infection of their bones known as osteomyelitis. This is because *in vivo* sickling occurring in the bones, causes destruction (or infarction) of the bone matrix and allows bacteria, especially of the typhoid group, to grow in the bone. One of the author's patients, the lady whose X-ray appears in Figure 9 spent nearly 12 months in hospital with multiple discharging sinuses from chronic osteomyelitis. This can go on for years so that morbidity, *not* mortality, becomes what is often most dreaded in the disease. I probably have the patient with the most prolonged active sickle cell disease osteomyelitis on record. [18] This lady, whose right leg is shown in Figure 10 is still alive. Born in 1896 this Hb. SC woman was educated by the Basel Missionaries and had had cold season rheumatism since childhood. In her own words "As soon as it rains I get the trouble", but tendency to severe rheumatic pains disappeared as she grew older. Her main problem has been discharging sinuses on right foot and leg, left arm and upper back which began in 1915. The leg sinuses continued unabated in spite of curettive surgery until the whole foot became reduced to a dimunitive stump underneath a grostesquely disfigured leg. This woman must have passed through a lot of social, psychological and emotional trauma during her younger days, in addtion to the pain she has had for 58 years from this leg.

Figure 8

X-ray of R. leg of a 20 year old Hb SS lady. Note ulcer above medial malleolus with underlying periosteal reaction in tibia.

Figure 9

X-ray of R. leg of 24 year old Hb. SS woman. Note large ulcer above medial malleolus and gross changes in tibia due to osteomyelitis.

Although I show you such a severe case of osteomyelitis as part of the *depth of the problem* in order to leave no one in doubt about the necessity for *family planning* in sickle-cell disease, I hasten to add that only 65 (4.8%) of 1,348 consecutive patients with sickle cell disease had osteomyelitis in the Sickle-cell Clinic. [18]

Hip Trouble

Aseptic necrosis of the femoral head is not a rare complication of sickle-cell disease, occurring in 40 (6.6%) of 603 consecutive Hb. SC patients [18] and nearly (2.8%) of 600 sickle-cell anaemia patients. The hip involvement may be gross, destroying the head of the femur (Figure II) and causing much pain. The limb is usually shortened causing serious defects in gait. Hospitalisation for orthopoedic correction will become more frequent as more and more sickle-cell disease patients live to adulthood. The author sees a peculiar augenic significance attached to hip necrosis in sickle-cell disease: "Some of my sickle-cell-disease male patients with hip involvement find coitus impossible because body movement of any sort produces agonising pain, while some women with bilateral disease have no sex life at all, due to inability to part the legs (the hips being fixed). It seems to me this is one further means Nature has devised to limit dissemination of the sickle-cell gene". [20]

The other methods devised by Nature to limit the spread of the gene would seem to be

(*a*) decreased longevity (though the 77 year old SC lady would seem to belie this)

(*b*) diminished physical activity generally leading to diminished ability to compete with others for spouse.

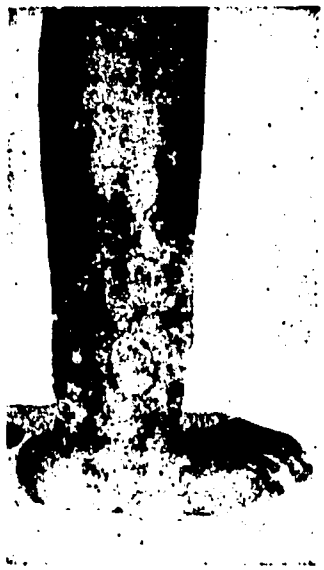


Figure 10

Leg deformity in 77 year old Hb SC woman with 58 year old history of osteomyelitis.

Figure 11

Aseptic necrosis in R head of femur in 46 year old sickle-cell hereditary persistent fetal haemoglobin man. Pain in this man was so bad he avoided coitus—see text.

(*c*) Raised maternal mortality rate in sickle-cell disease patients.

(*d*) Impotence as sequela of priapism in the male patients.

(*e*) Placental infarcts and increased stillbirth rate in sickle-cell disease patients.

(*f*) Vitreous haemorrhages, especially in Hb. SC patients, leading to blindness and reduced ability to compete for spouse.

(*g*) tendency to delayed puberty in both male and female.

If *Nature* is doing her best to reduce procreation in sickle-cell disease should we hestitate to provide family planning here?

TREATMENT OF SICKLE-CELL DISEASE

Although the disease is incurable because it is hereditary it is possible to treat it in such a way that patients can lead a satisfactory life with ability to succeed in University and in various professions. The Ghanaian approach to the treatment of sickle-cell disease summarised in Table VI emphasises not so much the disease treatment as the Patient management and the need to raise living standards. The modern approaches to treatment like *urea*, and *cyanate*, coming mainly from the U.S.A. miss, in my opinion, the most important point about sickle-cell disease viz: if poverty and squalor are removed the triggers of sickle-cell crises e.g. infections are almost abolished and even SS patients do well without blood transfusion. But the most important aspect of management of the disease taking a long term view both in the interests of the patient and of the nation's health is genetic counseling and family planning.

TABLE VI

Management of Sickle-cell disease Patients in Ghana [21]

1. *In the steady state:*

   (*a*) Efficient and early immunisation programme for children;

   (*b*) maintenance of good nutritional state;

   (*c*) regular antimalarial drugs with prompt treatment of infections;

   (*d*) daily folic-acid supplements; and

   (*e*) regular check-ups in sickle-cell clinic

2. *In crisis:*

   (*a*) Prompt unmasking and treatment of precipitating cause;

   (*b*) intravenous fluid and electrolyte theraphy to correct any discernible change in the milieu interieur;

   (*c*) mild analgesics and hypnotics, with early ambulation; and

   (*d*) blood when needed, but not routinely.

3. *Complications:*

   Look for them, and refer patient to appropriate specialist. Beware of hazards such as general anaesthesia.

4. *Prevention:*

   (*a*) Avoid known precipitating causes of crisis if possible;
   (*b*) educate patient to tell doctor he is SC or SS; and
   (*c*) genetic counseling, pimarily of patients, with family planning.

GENETIC COUNSELING, FAMILY PLANNING AND VOLUNTARY STERILIZATION

The size and depth of the patient problem is at once so vast and deep that genetic counseling and family planning must needs start with the patient i.e. those with 2 abnormal genes. We have seen already that if a trait carrier marries another trait carrier there is a 1 in 4 chance producing disease (Figure 3). If, however, a trait marries one with disease then the chances of having a child with the disease are 1 in 2 (Figure 12). Where there is a large sickle-cell disease and homozygous haemoglobin C population like Ghana it is extremely important to identify these patients before marriage since they have a 1 in 3 chance of encountering a trait partner. Those *already* married have an even greater problem because 1 in 3 of their husbands or wives (as the case may be) *is* a carrier of an abnormal haemoglobin gene whether he knows it or not. It is important to identify the married women with the disease quickly and curtail further procreation. Table VII shows number of times 184 sickle-cell disease women in the Clinic had become pregnant by June, 1970. The number has increased considerably since but it still must be a very tiny fraction of what is happening in the whole country. One in three of the husbands of these women has an abnormal haemoglobin gene. Already, many of them attend the sickle-cell clinic with their children who also have the disease. Limitation of family size is immediately urged upon them pointing out the hazards of pregnancy *per se*.

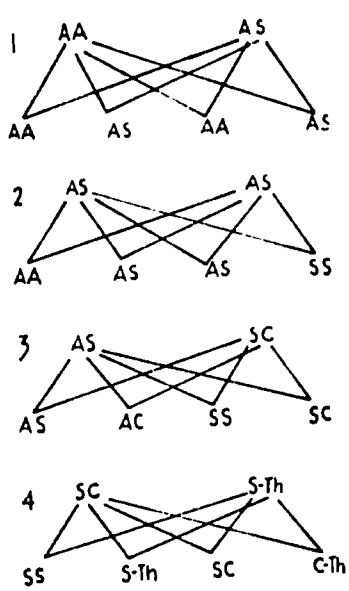


Figure 12

The probability of disease in the offspring of parents of different genotypes in Ghana. 1. 50% trait children of matings between normal homozygotes and traits. No disease in family. 2. 50% traits, 25% sickle cell anaemia individuals among children of trait matings. Disease occurs in 25% of offspring if law of probability obeyed. 3. 50% trait and 50% diseased children of matings between traits and patients. 4. All children have the disease when matings occur between patients. All the mating combinations mentioned above and many others have actually occurred in Ghana.[18]

Genetic counseling is not difficult since the disease has been known and called by tribal vernacular names for centuries [22] before Herrick first described it in Chicago. [23] To the illiterate simple terms are used to explain the genetic inheritance as follows:-

A A = Good/Good = no chweechweechwe*
A S = Good/Ache = no chwechweechwe
S S = Ache/Ache = chwechweechwe present

*Chwechweechwe is the name of sickle-cell disease in Ga.
Note onomatopoiea, reflecting the relentless and repetitive gnawing pains in the bones characteristic of the disease.*

TABLE VII

Number of Times 184 Sickle Cell Disease Patients Became Pregnant

No of times Pregnant	No. of Patients Pregnant				Total No of Patients
	SS	SC	SF	STh	
1	13 (44.8)	32 (23.5%)	2 (16.7%)	3 (42.9%	50
2	5 (17.2%)	16 (11.8%)	4 (33.3%)	1 (14.3%)	26
3	5 (17.2%)	22 (16.2%)	4 (33.3%)	2 (28.6%)	33
4	6 (20.7%)	20 (14.7%)	1 (8.3%)	0	27
5	0	15 (11.0%)	1 (8.3%)	0	16
6	0	13 (9.6%)	0	0	13
7	0	9 (5.1%)	0	0	9
8	0	7 (5.1%)	0	0	7
9	0	1 (0.7%)	0	0	1
10	0	0	0	0	0
11	0	1 (0.7%)	0	0	1
12	0	0	0	1 (14.3%)	1
13	0	0	0	0	0
Total	29 (15.8%) (100%)	136 (73.9%) (100%)	12 (6.5%) (100%)	7 (3.8%) (100%)	184 (100%)

Knowing the seriousness of the malady patients are the most co-operative of the Ghanaian population to adhere to genetic counseling and family planning advice not only for their own sakes but for the sake of their children.

Family Planning Methods for Patients

(*a*) *Intra-uterine Device:* This is not well tolerated on both subjective and objective assessment. Patients complain frequently of "not liking it", perhaps due to excessive menstrual loss. Objectively, haemoglobin levels fall and this is a serious handicap in a situation where deterioration of anaemic state must be avoided at all costs.

(b) *Diaphragm, foam and other mechanical devices:* Patients are adverse to these methods since their use require some degree of sophistication not to mention unqualified co-operation from the husband.

(c) *Abortion:* This can hardly be called a family planning method for patients and yet some of my patients having suddenly found themselves pregnant took it upon themselves to get rid of the pregnancy with the tragic physical and public health consequences that have been shown[24] usually to accompany induced abortion. The recent development of amniocentesis with intrauterine diagnosis and selective abortion may be hailed as a "break-through" for disease-trait partners or trait-carrier couples who can then get married without the hidden fear of knowingly being responsible for a sickle-cell disease child. The public health and long-term genetic implications of intrauterine diagnosis and selective abortion have recently been competently discussed by Motulsky and his colleagues[25], but this method as a family planning tool is unlikely to succeed in the sickle-cell environment for the following reasons:-

i. Abortion is unlikely to be universally accepted as a family planning method for obvious reasons some of which are ethical, religious, and social.

ii. Intra-uterine diagnosis through amniocentesis is in its infancy and the degree of sophistication required for its usage, not to mention the cost, makes it extremely unlikely that it will ever be used on the scale required to make any impact on the incidence of the disease as we have just surveyed it.

iii. The hazards of general anaesthesia, if even selective abortion was possible, would have to be carefully considered especially in sickle-cell disease patients unless the abortion was carried out without general anaesthesia.

iv. The ignorance even among *experts* as to what constitutes sickle-cell disease and what does not is appalling and has been mentioned recently.[6,18,19] The ignorance is to the extent that some athletes who have represented their country at the Olympic Games in Mexico (at a height of more than 7,000 ft. where sicklers are supposed to flake out) and beat the world, went back to their country to be found to be sicklers on mass screening compaigns and were promptly labelled sick. Some Insurance Companies in the U.S.A. have been known, quite unjustifiably, but probably on the advice of some genetic "expert", to load the life insurance bill of sickle-cell traits (AS) by 50%. The havoc such experts might cause in an amniocentesis-selective-abortion team would be incalculable. Why? Because they would be aborting anything, anything that had the sickle-cell gene in it. And at the rate certain states are rushing in with bills for obligatory genetic screening in the U.S.A.[18,26] bills for amniocentesis and selective abortion in certain categories of people may not be too far off. It would then be a tragedy as in indeed it appears at the moment, if the perfectly healthy *sickle cell trait* (AS) was confused with *sickle-cell disease*. And in any case with improved standard of living and new approaches to treatment it would take some persuading for mothers to agree willingly to get rid of a sickle-cell disease foetus.

(*d*) *Oral Contraceptives:* The pill is what sickle-cell disease patients of child-bearing age and sickle-cell trait women most readily ask for. And yet this is denied them on what I personally consider to be scanty evidence. Dunn and Haynes[27] and Haynes and Dunn[28] published isolated cases of thrombosis in sickle-cell haemoglobinopathy patients on oral contraceptives and suggested that oral contraceptives are not good for sicklers. To my mind the case is quite unproven and requires extensive study with careful statistical analysis. This is urgent and requires to be done immediately and for this reason: it is quite possible that oral contraceptives have no more thrombotic effect on sicklers than on non-sicklers. As has been stated recently by the author: "Before attributing symptomatology in the sickle-cell trait person to haemoglobin S some more information about the individual should be obtained otherwise *incidental sickling* may be considered to be *pathological sickling*, or on the other hand what is in fact sickle-cell disease may be described as sickle-cell trait. It comes as a surprise to the unwary when told that 20% of all diabetics, and hypertensives, and 'strokes', and 'n-grown toe nails in Accra have the sickle-cell trait until he realises that 20% also of all healthy people in Accra are sickle-cell traits"[6]. Similarly not less than 10% of all thrombotic episodes occurring in American blacks must be in people who have the sickle-cell trait, because 10% of normal, healthy American blacks are sickle-cell traits. To find thrombosis in one such, who happens to be on the pill, and to state categorically that the pathology is due to the sickling is to do gross injustice to the thousands of sickle-cell traits who probably could take the pill without mishap. With hundreds of *sickle-cell-disease* women in Accra producing children at an alarming rate and with a country-wide population of literally a million *sickle-cell trait* women we in Ghana are uniquely placed to test whether the sickler is, in fact, more at risk than a non-sickler on the pill. We have the personnel at all levels of investigative sophistication to be able to do this. All we need are funds to buy expensive equipment not only for serial blood viscosity studies usingt he method of Dintenfass[29], but for detailed haemoglobin electelectrophoretic and other studies. I hope this challenge, aimed obviously at the oral-contraceptive drug manufacturers and the population research funders, will be duly taken up to allow us to give you conclusive results within the next 5 years. For, surely, to have a population-expansion restriction programme which excludes at least 1 in 5 of the women is quite unrealistic. This is what will happen if and when it is conclusively proven that the pill is significantly more harmful to sicklers than non-sicklers with p at least 0.05. Such a situation would then immediately throw us upon *voluntary sterilization.*

VOLUNTARY STERILIZATION IN SICKLE-CELL DISEASE

This has already begun in the Korle Bu Hospital sickle-cell clinic, but in only isolated patients. The most easily persuadable sickle-cell disease women who are likely to consider the suggestion of voluntary sterilization are those seen in the Clinic in their nth pregnancy where n is greater than 6. Our aim at the moment is to try through education,

persuasion and all the tact we can muster to reduce n to 5 and then to 4 and then perhaps to 3 or 2. But it is proving a difficult task. Recently I saw in the Clinic a sickle-cell haemoglobin C woman who had just had her 5th baby. After gentle persuasion she whole-heartedly agreed to family planning and voluntary sterilization. I asked her to bring her husband the following week so that the obstetrictian could be approached and the date of operation finalised. The husband came, and after listening to my story said: "I entirely agree, but allow us just one more; we have 5 boys and I want a girl very badly". Usually it is the other way round—husbands insisting on more children in order to have a good sprinkling of males. A voluntary sterilization advice needs to be carefully preceded by education regarding the hazards of pregnancy in sickle-cell disease. These hazards are well known[30,31] Patients whose relations have died in childbirth are more likely to listen fo family planning advice than those who have no family experience of this. The Memphis (Tenessee) experience where 10 percent of sickle-cell disease women died in childbirth[32] is certainly not ours in Ghana nor that of Perkins in New York[33]. Because of a high standard of midwifery and of hospital obstetric care in Accra multiple pregnancy in sickle-cell disease is common. A remarkable example of this from Ghana was the sickle-cell beta thalassaemia woman (with a sickle-cell haemoglobin C disease husband) who had 13 children from 12 pregnancies,[13,34]. All the children were, of course, haemoglobinopathic (Figure 13); the 43 year old mother has only now agreed to voluntary sterilization. But the number of children that the sickle-cell trait women can produce is sometimes fantastic. The greatest number I have seen is the case of a Ga woman (Figure 14) who in 12 pregnancies produced 18 children all but 3 of whom are living. A good half of the 12 pregnancies resulted in twin births. Fortunately she is already well past her menopause, but she alone contributed no less than 9 sickle-cell genes to her offspring generation, while the sickle-cell disease parents shown in Figure 13 between them contributed 18 abnormal genes related to haemoglobin formation to the next generation through their 9 surviving children the eldest of whom has already been pregnant twice. But in the African *milieu* "the contribution made by female hyperfertility to the trait frequenty is much less than that made by a polygamous man"[35].

Voluntary Sterilization in Relation to Polygamy

It has been a source of constant amazement to me why family planning projects in Africa seem to be aimed only at the women when the men are quite often responsible for extraordinary gene proliferation. The effects of polygamy on the frequency and distribution of genes have been discussed recently,[36] with the author urging "the need for fresh thinking in modern Population Genetics" which is so Western-oriented as to miss the whole point of the colossal impact of polygamy on the spread of abnormal genes and, with them, hereditary disease. The factors which the author thought were involved in enhancing the sickle-cell rate were enumerated as follows:-

Factors Enhancing Sickle-cell Rate [36]:

1. Balanced Polymorphism which hypothesizes that sickle-cell traits have a preferential survival advantage over either homozygote (normal and abnormal)-recent review.[37]

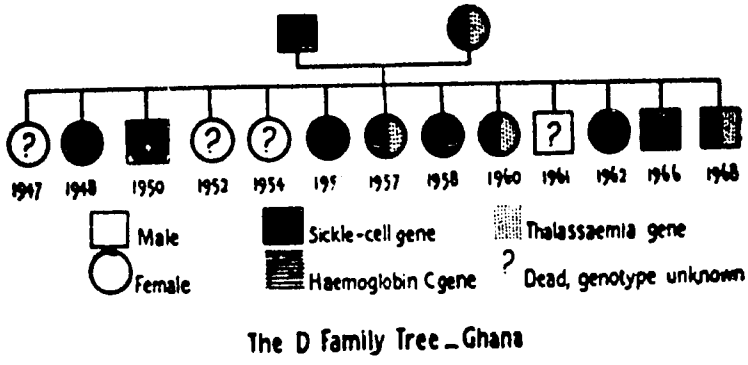


Figure 13

Marriage between sickle-cell thalassaemia woman and sickle-cell haemoglobin C disease man resulting in completely haemoglobinopathic family with sickle-cell anaemia (SS), sickle-cell haemoglobin C disease (SC), sickle-cell beta-thalassaemia (S-Th al) and haemoglobin C thalassaemia (References 13 and 34).

Figure 14

A 56 year old sickle-cell trait Ga woman who had 12 pregnancies (half of them twin) resulting in 18 children, 15 of them alive and well. Sequence and outcome of pregnancies: (1). One (2). One (3). One (4). Twins (5) One (6) Twins (7) One (8) Twins (9) Twins (10) One (11) Twins (12) Twins. All born alive, eldest 40, youngest 15 years old.

2. Enhanced fertility of sickle-cell traits (male and female). [13,18,34]

3. Sickle-cell disease patients (SC, S-Thal and SS) living long enough to produce children [38-42]

4. Inbreeding.[18]

5. Polygamy by traits and diseased. [18,35,36,43]

6. Combinations of above.

Polygamy/polygyny may for eugenic considerations be defined as the possession of (and production of children by) more than one "wife" irrespective of whether the "wives" are acquired simultaneously or sequentially. Defining biological "fitness" as "the number of genes one contributes to the offspring generation"[44] the male in Africa, unlike the male in some "Western countries" has a greater fitness than the female.

SOME FACTS ENCOURAGING POLYGAMY ARE

1. Absence of law forbidding it, or/and religiously encouraged

2. Early death of children to the first wife (or wives).

3. Social status e.g.

   (*a*) Paramount chief, or king

   (*b*) Wealthy estate

   (*c*) Prestige index

4. First wife (or wives) begetting not enough male children

5. Economic helpmeet.

As a sickle-cell trait (AS) man has a

1 in 3 chance of 1st wife being a trait carrier
1 in 9 chance of 1st two wives being trait carriers
1 in 27 chance of 1st three wives being trait carriers

the potential genetic effects of polygamy soon come out through his differential procreative superiority over the female. This differential procreative superiority of the male sex in Africa comes out clearly in the following few (but perhaps extreme) examples:-

i. A 68 year old Ghanaian ex-paramount chief personally known to the author has 75 living children. He is sickle-cell trait (AS). Several of his children have sickle-cell disease.

ii. Figure 15 shows a newspaper report of a man with 23 wives and more than 90 children. There was a 1 in 3 chance of this man being an abnormal haemoglobin trait carrier and a 1 in 100 chance of being SC disease. Eight of the wives would be AS or AC with predictable genetic consequences in the offspring.

THE MIRROR

Gmp. SATURDAY, JUNE 19, 1971 No. 932

● OKOMFO KLUTSE PICTURED WITH SOME OF HIS WIVES.

MAN WITH 23 WIVES

FROM KOFI SAPANTH, SUNYANI

WITHIN 20 years of married life a 68-year-old fetish priest-cum-farmer has had 94 children from his 23 wives. Eighty-three of the children are still alive.

The man, Kofi Klutse, who lives at Bechem in the Brong-Ahafo Region, told the "Mirror" as if in mockery of the red triangle, official emblem of the National Family Planning, that five of his wives were due shortly to have new babies.

The five were reported additions would swell his household to 116. He lost one of his wives about two years ago.

The fantastic size of his family does not seem extraordinary to him at all and he laughs heartily at jokes poked at the number of his children.

● OKOMFO KLUTSE

...And 94 children

Every month MORE PEOPLE SAVE WITH THE EAGLE!

GHANA COMMERCIAL BANK

Little boy

—Big thief

Figure 15 Polygamous man in the news.

FATHER OF 140 CHILDREN

A GHANAIAN herbalist and fetish priest, Bosomfo Yaw Mensah, has 26 wives and 140 children. He lives in a village 13 miles off Mankrong Junction near Sweedru in Central Ghana.

There are 62 of his children in various educational institutions, half of them in secondary schools. His eldest child, aged 34, is a driver. Originally he had 35 wives and 150 children, he claims, but some of them have passed away. Each of the wives has a room to herself.

Bosomfo Mensah spends roughly £500 per term in fees on his school-going children. He spends about £20 a day on food for his entire family including 49 grandchildren.

The lowest amount he spends on occasions such as Christmas on gifts to his family is about £1,000.

Figure 16

Another polygamous man in the news. In African Challenge, (Jos, Nigeria) No. 243 July, 1972, page 5.

iii. Figure 16 shows the report of a Ghanaian herbalist with 140 children. Why have the Family Planning Projects left such people alone? If each of the 26 wives had been successfully persuaded to have *only* 2 children this man alone would still have had 52 children. Surely there is a case for population adult education drive aiming at preparing people for a *voluntary sterilisation law* not only for women but also for the men.

As the author has stated before: "In countries where polygamy is legalised because of religious, cultural or other reasons, if sickle-cell trait men could be carefully persuaded to abstain from polygamy, and if they did in fact abstain from polygamy, the sickling rate in the population would be gradually reduced. And if polygamy was abolished for everybody (sicklers and non-sicklers alike) the absolute number of sicklers and hence sickle-cell disease patients in the population would still be less than if polygamy was allowed.[35] The author further stated[35]: "This 'polygamy' role is not limited to the S gene. Other haemoglobinopathic genes C,D,E,F-highgene, thalassaemia might be proliferated in the same way especially in Islamic countries where upward tof our wives could be allowed." It was since discovered that Dabbous and Firzli[45] found in Lebanon that there was a preponderance of sickle-cell trait (and sickle-cell anaemia) among Mohammedans than in other groups. They explain it by: "Moslems inhabited low lying malarious plains and valleys."[45] But could the difference not be due to polygamy by Moslems? Other heritable chatacters (good and bad) apart from hereditary erythrocytopathies could be spread by polygamy. As the author has already pointed out[35]: "Nor is the process limited to this generation. It does not bear calculating the effect that one abnormal gene possessed by King Solomon could have had an posterity, for 'King Solomon loved many strange women . . . he had 700 wives, princesses, and 300 concubines'. (I Kings Chapter 11 vs 1 & 3)".

CONCLUSION

The sickle-cell disease problem has been faced squarely and the approaches to management discussed. The dimensions of the problem are such as to make a mass education programme succeeded by a national family planning exercise a dire necessity. The United Nations has declared that family planning, and the right to determine responsibly the number and spacing of children, is a human right.[45] And yet the exercise of this right is far from becoming a reality in most developing countries where the adverse effects of large family size or close spacing of births are most markedly seen on the welfare and development of children.[47] The safety of oral contraceptives has been questioned especially in a population where 1 in 5 is a sickler. This has been done on scanty evidence in my opinion and there is need for controlled studies to prove conclusively the effect of the pill on sicklers. But even if oral contraceptives were shown to be as safe in sicklers as in non-sicklers there would still remain the involvement of the male population in the family planning programme in Africa, and voluntary sterilization would seem to be

the best approach to the problem since "male and female sterilization techniques, which, are surprisingly safe, quick, and relatively inexpensive and acceptable to many people since they do not interfere with normal sexual activity, have been developed with surprising rapidity."[45] In formulating a Voluntary Sterilization Law in Africa it should be remembered that it would be very difficult for voluntary sterilization for family planning purposes to be considered "entirely separately (as suggested by Stephan and Kellogg [46]) and not under a statute designed to deal with eugenic or therapeutic sterilization." Where 1 in 3 of the population is a carrier of an abnormal gene the difference between *eugenic* and *non-eugenic* in these matters must be blurred. In such an environment "the man who refuses to take a younger wife when his wife arrives at the menopause is doing the country (Ghana) a great service not only by reducing the population explosion, but, if he is a 'sickler', by deliberately limiting his contribution of genes to the community"[43]. Voluntary sterilization would be ideal for such men and a suitable law preceded by mass education is what is needed to bring this about.

Finally, a word to those who have got the message. The zeal of those who sincerely believe that genetic counseling and family planning are what are urgently needed for the African situation must be tinged with commonsense and directed by caution. It is being suggested in certain quarters in the U.S.A. that some kind of legal pressure be put on trait carriers to stop them from marrying. The answer to this kind of approach is in the true story I often told on my American lecture tour sponsored by the National Foundation last year: "My father is haemoglobin C trait (AC) and my mother is sickle-cell trait (AS). Eleven of us were born. The three with SC disease have died and the remaining eight of us share, as you would expect, AA, AC and AS. I took Papaa's A and Mamma's A making me AA. If any of these over-zealous modern genetic counselors were around my home town Odumase Krobo when my parents were engaged, and had they the means to determine that Papaa was AC and Mamma AS they would have persuaded them against each other, or sterilised them or something, with the result that I wouldn't have been born, and it would have been a pity."

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