

The adult with Sickle Cell Disease

Prof F.I.D Konotey-Ahulu, the Dr Kwegyir Aggrey Distinguished Professor of Human Genetics, University of Cape Coast, Ghana, continues his series on the sickle cell disease patient, by concentrating this month on the adult with sickle cell disease.

If one only had textbooks in medicine, or if one relied only on media comments, one would be led to believe that no sickle cell disease patients - (Ache/Ache like SS, SC, S betaThalassaemia, etc) - ever lived into adulthood. "They all die before the age of 20" is what we are continually told.

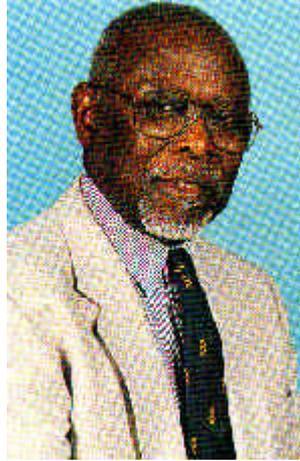
Even the internationally respected British Medical Journal had this to say recently in an editorial entitled "Genetics and developing countries": "We are unlikely to learn more about any disease than we already know about sickle cell disease. We know the gene and its mutations, the protein and its structure, and the mechanism of loss of function, yet we can do little for patients" [Barry R Bloom and Dang Duc Trach, 28 April 2001, BMJ Volume 322, pp 1006-1007].

So "we can do little for patients"?

How come the 53-year-old professor of botany, University of Cape Coast, who is "SS" (Ache/Ache) did not die at the age of 18?

How come the 52-year-old dean and professor of the Faculty of Law, University of Ghana, a former Oxford post-graduate, a known "SC" (Ache/Ache) and mother of three brilliant adults, is still doing very well if "there is little we can do for these patients"?

No, these forecasters of doom are wrong even when they are professor & dean of the Harvard School of Public Health as Barry R Bloom is. They confuse "treating a



Prof Konotey-Ahulu

patient" with "curing a disease".

Let me explain. Sickle Cell Disease, like the other hereditary conditions haemophilia and diabetes, cannot be cured but does that mean "there is little we can do for these patients"?

Why are the experts so wrong about the prognosis (the survival outlook), of the person with sickle-cell disease (Ache/Ache)?

ANSWER: Because they do not distinguish between "sickle cell disease" and the "sickle cell disease patient".

"Sickle cell disease" is pathology; it is round cells turning spiky in the blood and causing blockages; depriving vital tissues and organs of blood, and causing injury to bones, joints, kidney, lungs, brain; etc. The patient is more than mere pathology.

Circumstances

To concentrate only on the disease invites despair. The approach that does not invite

despair is to concentrate on the patient, that is the PERSON with sickle cell disease. This brings you at once to the very important factor of

"circumstances". Patients have died who have not paid enough attention to circumstances.

I remember a very brilliant 18-year-old sixth former ('SS'). He was top of his class in Ghana. After the A-level exams, fellow students were going camping and he joined them. Suddenly, there was a thunderstorm and the campers were drenched. He arrived home three days later, having to trek through the bush in severe sickle cell crisis, his body was aching, eyes were yellow, and he was dangerously ill. The young man died before he could get to hospital.

Five days earlier, he was perfectly well (in the steady state, as the healthy state of sickle cell disease is called), but 24 hours later he was "in sickle cell crisis".

What made the difference between the "steady state" when red blood cells were round and flowing easily in the body, and the very ill state of "sickle cell crisis" when cells had changed from round to spiky sickle-shape within hours in the body, obstructing blood flow and causing mayhem?

ANSWER: Circumstances.

Take also the case of an attractive 19-year-old Ache/Ache-'SC' who was at the Korle Bu Sickle Cell Clinic on a Friday morning, perfectly well. Within 4 days she was carried to hospital

desperately ill with "severe aches everywhere". This lady would have died if all we did was to listen to relatives' demand for pain killers to "make her comfortable".

I was not just dealing with a pathology called "sickle cell disease"; I was dealing with a young woman who was quite well a few days earlier. So the question I set out to answer was this: "What are the circumstances that can bring a girl from the 'steady state' to 'the crisis state' with such threatening effect?"

ANSWER: She had lied to me the previous week when I asked about her periods. She said they were normal, when in fact she was pregnant.

That weekend she had gone to a back-street abortionist, and had ended up with an infected womb, hectic fever, yellow eyes, painful tummy, dehydration, and she was at death's door.

Quick, get the gynaecologist, give her lots of intravenous fluids, plenty of antibiotics, oxygen, then pain-killers (not morphine or heroin please), get the womb cleared of dangerous infection, and she lived!

The lesson of these two true stories is this: The question often asked, "How long do sickle cell disease patients live?" is meaningless if "circumstances" are not mentioned.

One of the several reasons I do not use the loudly-trumpeted Hydroxyurea for my patients is that it would have helped neither the young man nor this woman.

Survival rates

It must not be imagined that sickle cell disease is the only clinical condition in which circumstances play a significant role in survival. Death came to a 16-year-old English girl who went to Scotland with school friends. She was known to suffer from asthma of which an attack occurred in the night. Alas, she had forgotten to bring her inhaler, and she died before reaching hospital.

How long do asthmatics live?

ANSWER: Circumstances dictate this.

There are thousands of adults with sickle cell disease of all Ache/Ache-phenotypes. One can discern differences in presentation and average survival rates.

While all Ache/Ache-phenotypes can have severe sickle crises, in the 'steady state' some particular "signs and symptoms" characterise certain phenotypes.

My book "The Sickle Cell Disease Patient" ["TSCDP"] details exact proportion of patients of which phenotype, sex and age who are found with which particular symptoms.

For example, anaemia (low

haemoglobin level, reflected in pale nails, weakness, feeling easily tired) was found in 99.1% of the 'SS', 55.6% of 'SC', 74.3% of 'SβThal', and 64.5% of the 'SFhereditary'. In other words, most 'SS' patients are pale and anaemic, this is why 'SS' is the type of sickle cell disease known as "sickle cell anaemia". Next with pallor are the two last mentioned disease phenotypes, and the least anaemic of the four Ache/Ache-phenotypes is the 'SC'. Indeed, many sickle cell disease (Ache/Ache-SC)

patients have never been anaemic, and this has fooled doctors. "How can a sickle cell disease patient have no anaemia?" they ask, and they wrongly label the Ache/Ache patients 'Sickle Cell Trait' (Norm/Ache).

Any 'SC' reader of this article who may have a Normal or even higher-than-Normal haemoglobin level needs to remember that circumstances of, say, dehydration and fever can precipitate a very severe sickle crisis.

Here are other signs and symptoms, indicating which phenotype more commonly has which symptom. The mere mention of a symptom does not mean all patients have it.

JAUNDICE: All sickle cell phenotypes can develop yellow eyes, but 'SS' adults are more prone to jaundice than others because distorted red cells are more easily destroyed and lose their pigment which appears on the eyes. People without sickle cells can also develop anaemia and jaundice, so

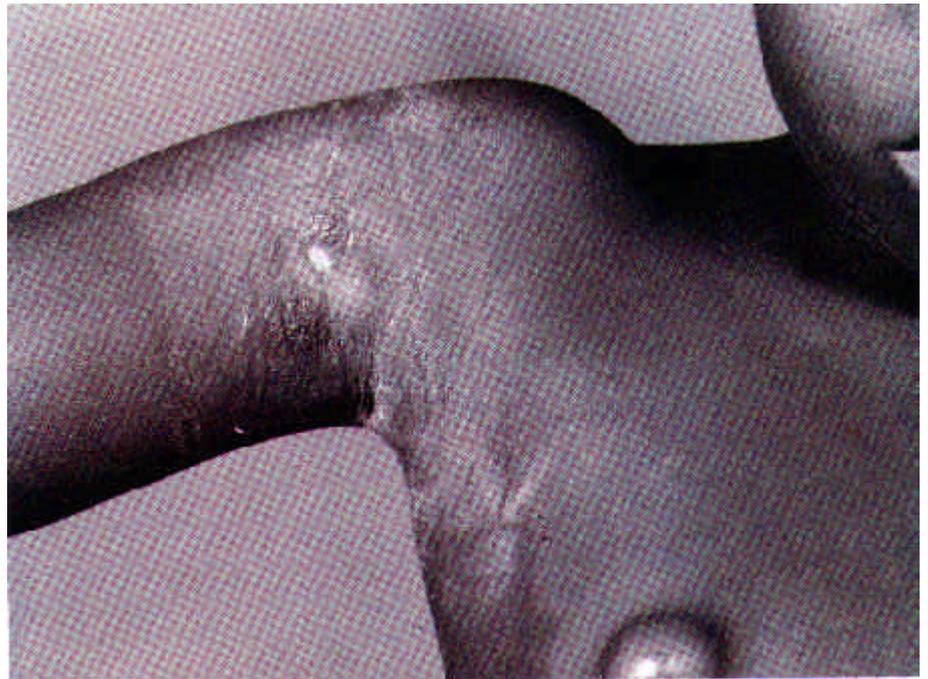
doctors and nurses should be on their guard because an 'SS' person with deepening jaundice could be suffering from infective hepatitis due to blood transfused a few months earlier. Gall stones can also make jaundice worse.

GROWTH & DEVELOPMENT:

'SS' adults can be all sizes, short, average height, or taller than average. Puberty tends to be delayed in the 'SS', but things improve later. Brain function is not affected, otherwise we would not have the Ache/Ache professors I mentioned earlier, or the many other patients with genius.

ABDOMEN: Some patients have a big tummy because the liver and spleen enlarge.

The 'SS' adult tends to have a larger liver (on the right), while the 'SC' has the larger spleen (on the left). A large spleen can easily be ruptured with disastrous results when kicked in the tummy, so SC' people should avoid violent sport. The 'SS' adult tends to have a shrunken spleen, but as the spleen is necessary for



Bone infection (Osteomyelitis), which occurs equally in the phenotypes 'SC' and 'SS', can go on for many years



'SS' adults are more prone to Jaundice (yellow eyes)

fighting infection, these spleen-less 'SS' adults are prone to infection.

LEG ULCERS: These are around the ankles usually on the inside of the leg. They can be painful, and slow to heal. As the 'SS' has the lower Haemoglobin level, leg ulcers are more common in them than in the 'SC'.

OSTEMOYELITIS: Bone infection occurs equally in the phenotypes 'SC' and 'SS', and often follows an attack of Salmonella infection (Typhoid fever). The limb becomes hot and swollen and continues to ache after recovering from sickle cell crisis. A "boil" may point and burst. Such infection can go on for many years if the bone is not opened up and scraped, with the removal of dead bone and treatment with powerful antibiotics

HIP NECROSIS: A painful hip, found in all phenotypes is due to blood flowing too slowly in the vessels of the joint, causing sickling and blockages in the bone surface which sloughs off. The limb shortens and the joint stiffens. The problem can be so severe that women have been known to have difficulty parting their legs for sexual intercourse.

Paradoxically, some of these developed their hip necrosis after prolonged labour with their legs parted for hours during child-birth. Blood flow in the joint was drastically slowed down, leading to bone infarction.

Prolonged bed rest has the same effect. If patients admitted in sickle cell crisis are not made to get up and walk about within 48 hours or so (depending on what brings on the crisis in the first place), but are kept in bed for days on end, sometimes weeks, and even months, when eventually they manage to get up, they will find they cannot walk properly due to avascular necrosis of the head of the femur.

When patients beg me to keep them in bed "a bit longer", I show them the photographs of hip necrosis in my book, and

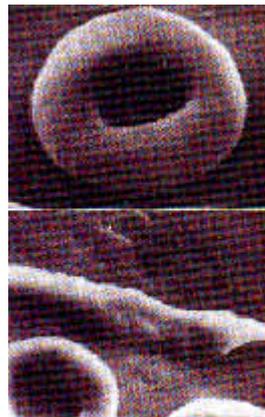
ask them: "Do you want to walk properly, or do you want your hip to seize up?" They soon get up, help distribute meals to the other patients. Home the next day. [TSCDP pages 236-242].

NOSE BLEEDING: This affects all phenotypes, and is related to dry weather such as the Harmattan in West Africa. Patients are advised not to nose pick.

HAEMATURIA (blood in the urine): Bleeding from the kidney tends to be more common in the 'SC' phenotype. Because these 'SC' patients are robust and do not have anaemia, some doctors have described them as "sickle cell trait patients bleeding from the kidney". There are millions of people all over the world passing blood in the urine for one reason or other. For example, Bilharzia is the commonest cause of passing blood in the urine in African countries. An African 'Ache/Ache' person ('SS' or 'SC', etc) who comes to hospital with haematuria should never be assumed to be bleeding from the kidney due to "sickling infarction". Examination of the urine may show the Bilharzial Schistosome eggs. 'Bilharzia haematuria', and 'Sickle cell renal infarctive haematuria' can occur together. Bilharzia can lead to urinary tract infection, which leads to kidney infection, which in turn leads to kidney "infarction" (part of kidney deprived of blood). Shining a torch into the bladder (cystoscopy) discovers blood oozing from the left ureter in the case of sickle cell bleeding. Bilharzial bleeding comes from the bladder, while sickle cell bleeding is from the kidney. Usually the left one bleeds first.

How about the 'Sickle Cell Trait' and bleeding from the kidney?

ANSWER: We shall come to the "Sickle Cell Trait" (Norm/Ache-'AS') in a subsequent article, but before then try answering this question: "If an English person (Norm/Norm-'AA), or German, without sickle cell trait, can bleed from the kidney, why should not a Turk, or Nigerian, or Indian, or Greek, all with Sickle Cell Trait ('AS') also bleed from the kidney?"



(TOP) The round red blood cells of the 'steady state'; and (above) 'the sickle cell crisis state' when red blood cells turn into spiky sickle shape.

PRIAPISM: Persistent erection of the penis starting at night is a complication of sickle cell disease. If it is not dealt with promptly, it can lead to difficulty in erection in later years [TSCDP pages 226 -235].

STROKES: Here is an example of circumstances precipitating a stroke in a sickle cell disease person. A 55-year-old 'SC' man went into hospital for an operation scheduled for 9 am. Emergency operations earlier held up the surgery for six hours. Meanwhile the nurses put "nil by mouth" on the patient's door so from the previous night, until 3pm when eventually the patient went in for surgery, he was deprived of fluids. The operation was "successful", but the patient suffered a stroke and could not speak. A totally avoidable tragedy because "Nil by mouth" does not mean "Nil into the vein". Deprive an 'SC' or 'SS' of fluids, and the viscosity of the blood shoots up, blood flow slows down drastically, red cells change to sickle shape resulting in brain tissue infarction, and a stroke. Urgent fluid replacement, plus oxygen to reverse the sickling could have averted the disaster, but the patient was under a general anaesthetic and nobody knew there was anything wrong until he woke up!

GALL STONES: As mentioned in the previous article, 'SS', 'SC', and the other

phenotypes, are all prone to these pigment stones, but the 'SS' more so. The stones can cause abdominal pains especially after eating fatty food.

GNATHOPATHY: This is a term I coined for describing a slight protrusion of the upper jaw seen in some Ache/Ache people. The 'SS' phenotype is more prone to gnathopathy because the bone marrow over-activity from severe anaemia is greater in the 'SS'. Proportion of patients with gnathopathy (grades 1, 2, 3) is in my book [TSCDP pages 178-188].

EYE BLEEDS: Visual impairment, including blindness occurs occasionally more often in the 'SC' phenotype than any other because the "thickness" (viscosity) of the abnormal haemoglobins 'S' and 'C' combination is greatest. Dehydration, flying, straining hard (known also as the Valsalva Manoeuvre such as occurs in the second stage of labour when pushing the baby out, or shouting, or exercising, or lifting a heavy object) can increase the pressure in the brain and cause bleeding into the eye. Bleeding can be slight in which case all the patient notices is a sensation of "cobwebs" or "smoke" in the line of vision. A heavy vitreous haemorrhage can cause sudden blindness as shown here: An athletic Ghanaian soldier on military exercises leapt over a fairly high wall. He told me: "Upon landing heavily on the ground, I saw a curtain coming down my right eye from top to bottom. Within seconds the curtain fell completely, and I was blind".

This account is typical. Upon landing heavily, the young 'SC' soldier began to bleed into the eye. Our eyes are so wonderfully created that things seen "up" are actually "down", and vice versa. So when the inner chamber of the eye which is like a hollow bowl begins to fill with blood from below upwards, the mind's eye actually sees a curtain coming down from above. The level of the blood welling upwards is like the edge of a curtain falling. This story was enough for me to ask the soldier: "Do you suffer from Nuidudu?" "Yes" he said, being of the Ewe tribe. If he had been Yoruba, I would have asked "Do you have Aromolegun or

Lakuregbee?", the tribal names of sickle cell rheumatism.

But how did I know he was 'SC-phenotype'?

ANSWER: Because he was robust enough to do military exercises. We admitted him to hospital, checked the blood, and sure enough he was 'SC'. Bed rest caused much of the blood to clear, and in a fortnight he began to regain his sight without surgery.

To prevent him having hip necrosis, we advised him to keep moving his legs in bed to let the blood flow, and also to cut his hair very short. Combing African hair can shake the head so hard that some 'SC' people notice "cob webs" in their line of vision after visiting the hairdresser. Driving on bumpy roads can also induce bleeding into the eye. A fuller account of the sickle cell disease eye is in Chapter 18 ('Sickle Cell Ophthalmopathy') of my book "The Sickle Cell Disease Patient" published by T-A'D Co, P O Box 189, Watford, Herts, WD1 7NJ, England.

PREGNANCY: Sickle cell disease patients of all phenotypes can conceive, and have children. There is an historical tradition of experienced midwives in African countries who, over the centuries, have delivered these women safely.

Those interested in the evidence can find this in Chapter 2 of my book where I have traced Sickle Cell Disease in my own forebears generation by generation, with the actual names of 'Ache/Ache' patients right back to 1670 AD, reproduced on my website: www.sicklecell.md

The Krobo people could distinguish clinically the 'SS' (gbagblaa) from the 'SC' (pi-gbagblaa) phenotypes. So the modern belief that 'Ache/Ache' patients cannot have children is flying in the face of historical evidence.

Having said that, the traditional midwives were the

first to admit that the expectant mother with sickle cell disease (Ache/Ache - 'gbagblaa' and 'pi-gbagblaa') has always been an obstetric risk.*** [See below]

For instance, the pregnant Sickle Cell Anaemia lady who is already short of blood, cannot afford to have post-partum haemorrhage. The baby might be born alive, but the mother could die soon later from blood loss.

Therefore, doctors and nurses need to be aware of this. If these ladies want to have a child and pass on their genes of genius, let us take extra care to help them, but strict family planning afterwards will be needed to ensure extension of their lives.

NUMB LOWER LIP: This complication of Sickle Cell Crisis which I was the first to describe can frighten patients and their relatives into thinking that they are on the verge of a stroke. Researchers wishing to know where it was first published should note this

reference: "Konotey-Ahulu F I D, Mental nerve neuropathy: a complication of sickle cell crisis. Lancet 1972, Volume 2, page 388".

The story is as follows - A post-graduate law student at the University of Ghana was admitted under my care in severe sickle cell crisis. I knew her to be 'SC'. She was perfectly well the day before admission. So what had happened?, I asked her when she calmed down on treatment. "This time", she replied, "the precipitating cause was gin". Other precipitating causes of previous crises were "swimming, staying up late, blood transfusion, malaria, and flying". Gin, as opposed to other alcohols, would always precipitate in her a violent sickle cell crisis. "The Faculty had a party for a visiting professor, and I said to myself 'gin always troubles me, but let me just see today, if it will happen again'". She took "very little", and went to bed feeling all right but, at midnight, she was seized with

pain in the back, limbs, knees, chest, neck, and left jaw. "I thought I was going to die", she said.

When she recovered after just a few days, she felt that her "lower lip burned, together with an area on the chin", as shown in the figure (p....). Three months later the 'burning area' had shrunk, and turned to numbness. This was a new phenomenon, never before described in Medicine, so I researched it and found that the mental nerve, lying close to the medial aspect of the jaw became infarcted (deprived of blood) during her crisis. It did recover completely, but it took more than 18 months. I further discovered that about 1.5% of 'SS' and 0.7% of 'SC' patients complain of this peripheral neuropathy of the mental nerve after sickle cell crisis. As dental caries can also cause sickle cell crisis, the teeth of such patients have to be examined and treated.

It is important to know about "The numb lower lip sign", if only to reassure people that they are not about to suffer a stroke. It is purely a local facial phenomenon, and as long as we know that it takes over 18 months to disappear completely, people need not be scared of it.

*[***I have no objection if some researcher reading this material quotes the tribal obstetrics information and acknowledges that it is from "F.I.D Konotey-Abulu - 'The Sickle Cell Disease Patient', Macmillan 1991 & 1992, London, and T-A'D Co, Watford, 1996, pp6-28; and also F.I.D. Konotey-Abulu - 'The Sickle Cell Diseases; Clinical Manifestations including the Sickle Crisis'; Archives of Internal Medicine, Vol 133, pp 611-619". But I do most certainly object to doctors quoting this family information with its Krobo 'gbagblaa' and 'pi-gbagblaa' phenotypes, researched and published by myself as here mentioned, and then attributing their source not to me, but to someone else across the Atlantic!]*

