SPECIAL ARTICLE

CLINICAL GENETICS: GHANAIAN GRATITUDE FOR BRITISH AND HUNGARIAN CONTRIBUTIONS
A Personalized Historical Perspective

FELIX I. D. KONOTEY-AHULU
Kwegyir Aggrey Distinguished Professor of Human Genetics, University of Cape Coast and Consultant Physician Genetic Counsellor in Sickle & Other Haemoglobinopathies, Ten Harley Street, London W1G 9PF

Conflict of interest: *None declared*

E-mail:*felix@konotey-ahulu.com*

There is, surely, a place for expression of gratitude by an African for British and Other Contributions in Acquired and Genetic Disease Research in his country of birth. Professor Stephen K Addae has comprehensively documented, with expressions of gratitude here and there, the "Evolution of Modern Medicine in a Developing Country: Ghana 1880-1960".[1] Wellcome Witnesses to Twentieth Century Medicine has already published "British Contributions to Medicine in Africa after the Second World War" [2] but these contributions majored on Acquired Disease, with little said about Clinical Genetics.

ACQUIRED DISEASE

For the former (Acquired Disease) my greatest gratitude goes to Dame Cicely Williams who, as a colonial medical officer working in the Gold Coast (Ghana) learnt the name *kwashiorkor* in my tribal language of the pathological condition she described when I was a toddler.[3, 4] Years later in Medical School in London I read textbooks which said kwashiorkor meant "red hair in the African tribe". Not true, I found myself whispering in class. In Krobo/Dangme-Gã 'Kwashiorkor' is a "sibling positional word" which describes the symptomatology that a child born very close to an elder sibling develops.[5] I met Dame Cicely Williams in person on September 1 1986 at Somerville College, Oxford University where the Vice Chancellor of the University of Ghana, Professor Akilagpa Sawyerr, went to visit in order to confer on the 93 year-old an honorary degree of Doctor of Science. I thanked Dame Cicely for making our tribal word known world-wide. She let me take a photograph with her which was later published in Lancet.[6]

CLINICAL GENETICS

In Clinical Genetics my gratitude to three expatriates knows no bounds. Two were British, G M Edington and Hermann Lehmann, and one was Hungarian, Bela Rigelhann who was for many years my laboratory backbone at the Korle Bu Teaching Hospital, Accra Ghana. The achievements of Edington and Lehmann were enormous. They were the first to describe sickle cell haemoglobin C disease outside the USA [7] the first to show that Upper Ghana and Burkina Fasso (then called Upper Volta) had the highest incidence of Haemoglobin C in the world [8] they were the first (with our own Bill Laing) to show that 1 in 3 healthy Ghanaians (and indeed West Africans) were either sickle cell trait ('AS') or Haemoglobin C trait ('AC') [9] as my own parents were; they were also the first to describe the phenomenon of Hereditary Persistence of Foetal Haemoglobin ($F_{Hereditary}$) mistaking it initially for beta thalassaemia.[10, 11] When I visited Professor George Edington on his death bed at University College Hospital in Gower Street he was still able to discuss the pathology of sickle cell disease. Remarkable man he was, whom I had once visited in Zaria, and who had given me a copy of his MD University of Glasgow thesis, enabling me for the first time to see how an MD was written. No less remarkable was Professor Hermann Lehmann of Cambridge University who not only joined Professor Bela Ringelhann and me in Ghana for countrywide surveys and lectures in Ghana but he also sent his trusted laboratory technician Pamela Kynoch to us to standardize our techniques.

Bela Ringelhann and I described the remarkable work British researchers did in the 20th Century in West Africa and the Mediterranean [12] mentioning among others the discovery of Haemoglobin Korle Bu [13] assumed to be the first known example of intragenic cross-over, and confirming the fairly high prevalence of the African type of alpha-thalassaemia interacting with abnormal haemoglobins [14] and G6PD Deficiency.[15]

Secret of Success of the work in Ghana was the way these expatriates encouraged full Ghanaian participa-

tion in the research process with contributions from Alexander Bruce-Tagoe, George Yawson, Koblah Gbedemah, George Bonney, C T Acquaye, Silas Dodu, Reginald Addae, Frank Djabanor, Carl Reindorf, Ann Rudwick, Eunice Kuma, Francis Nkrumah, and the Nursing Staff including Mary Walker.[15-37] Professor Lehmann arranged for me to join him in Christ's College Cambridge as Schofield Fellow to enable me complete writing my MD Thesis.[38] It was there I first met Professor Max Perutz. Later (on 31st May 1972) in Philadelphia, I considered it a great privilege to be asked to deliver the Keynote address at the Martin Luther King Jr Award Ceremony for Sickle Cell Disease with other recipients on the same platform as Linus Pauling, Max Perutz, Hermann Lehmann, Roland Scott, J V Neel, Graham Serjeant, A C Allison, James Bowman, Samuel Charache, Charles Whitten, etc. Quite honestly, I suspected it was because I was a black African that the Black Foundation chose me for the keynote address with such Nobel laureate heavyweights on the platform! Reading my speech in advance the organizers decided I needed 4 bodyguards for the short period I was in Philadelphia [39] because I revealed the injustice of sickle cell traits who won Gold Medals at the Olympic Games at Mexico City (8000 ft plus) and who came down to sea level to be charged 150% for health insurance cover because they were supposed to die at 4000 feet while exercising.

British Encouragers: I list below the names of British Clinical Geneticists who have also been an encouragement to me and other Africans. (i) Sir David Weatherall to whom I and others referred difficult problems of beta-thalassaemia phenotypes (ii) Professor Alan Emery who was the first to reassure me at an international Genetics Conference in Hungary that my Male Procreative Superiority Index (MPSI) [40 41] which linked male procreation to gene proliferation in Africa was not 'rubbish' as some at the conference had implied. My own family forebears where polygamy was the norm going back nine generations, was replete with beta-globin gene variants [42] Professor Emery also invited me to give the MacArthur Postgraduate Lecture at the University of Edinburgh (iii) Professor George Fraser travelled to Ghana to study hereditary deafness in the Deaf Village Adamorabe where almost the entire village was deaf. Unfortunately while sightseeing in Accra, George disappeared down a hole and had a Pott's fracture.[43] While in a hospital bed George had time to look at my MPSI concept, and also said it was "not nonsense".

When The Lancet announced my appointment as Director of the Ghana Institute of Clinical Genetics (May 25 1973, page 1064), thanks to The Managing Trustees of The VALCO Fund and The Ministry of Health, with Dr Michael Baddoo as Director of Medical Services, the following British Specialists promptly wrote to me encouraging me: Professor Hermann Lehmann, Professor Paul Polani, Professor Alan Emery, Professor Peter S Harper, Professor Alan Fleming, Dr Andrew Stevenson, Mr David Patey, and from the USA Professor Roland Scott, from Hungary Professor Bela Ringelhann, and from the African Continent Professor B O Osuntokun, Professor Kofi Duncan, Professor G M K Kpedekpo, Professor F T Sai, Dr Saakwa-Mante, Mr Edward Akufo-Addo who later became President of the Republic of Ghana.

Clinical Genetics without Ethics is Eugenics. The two living British Clinical Geneticists who hardly write major texts without mentioning Ethics in some detail and who proved a great encouragement to us Africans were Professor George Fraser [44] and Sir David Weatherall.[45] We want, if possible, to place on the record Africa's gratitude to these expatriates. The World Health Organization (WHO) and International Atomic Energy Agency (IAEA) supplemented with generous research funds the maintenance funds of the Managing Trustees of the VALCO Fund, enabling the then Ghana Institute of Clinical Genetics to pursue successfully its aim of SERVICE, EDUCATION, RESEARCH, in that order, rather than reverse that order as often happens in most research institutions. [46 47]

REFERENCES

1. Addae SK. Evolution of Modern Medicine in a Developing Country: Ghana 1880-1960. Durham, Durham Academic Press Ltd, 1997. [ISBN 1-900838-05-2] 523 pp.
2. Reynolds LA, Tansey EM (eds) (2001) British contributions contribution to medical research and education in Africa after the second world war. Wellcome Witnesses to Twentieth Century Medicine, vol 10. London: The Wellcome Trust Centre for the History of Medicine at UCL, 93 pages.
3. Williams CD. A nutritional disease of children associated with a maize diet. *Archives of Disease in Childhood* 1933; **8:** 423
4. Williams CD. Kwashiorkor – a nutritional disease of children associated with a maize diet. *Lancet* 1925; **ii:** 1151-1152.
5. Konotey-Ahulu FID. Kwashiorkor. *Brit Med J* 1991; **302:** 180-181
6. Konotey-Ahulu FID. Issues in kwashiorkor. *Lancet* 1994; **343:** 548
7. Edington GM, Lehmann H. A case of sickle cell haemoglobin C disease and survey of haemoglobin C incidence in West Africa. *Trans. Roy. Soc. Trop. Med. Hyg* 1954; **48:** 332-336.

8. Edington GM, Lehmann H. Expression of the sickle cell gene in Africa. *Brit Med J* 1955; **1:** 1308-1311
9. Edington GM, Laing WN. Relationship between Haemoglobin C and S and malaria in Ghana. *Brit Med J* 1957; **2:** 143-145
10. Edington GM, Lehmann H. Expression of the sickle cell gene in Africa. *Brit Med J* 1955a; i: 1308-1311
11. Edington GM, Lehmann H. Expression of the sickle cell gene in Africa. *Brit Med J* 1955b; ii: 1328
12. Ringelhann B, Konotey-Ahulu FID. Hemoglobinopathies and thalassaemias in Mediterranean areas and West Africa: historical and other perspectives 1910 to 1997. *Atti dell'Accademia delle Scienze di Ferrara* 1998; **74:** 267-307 [A Century Review]
13. Konotey-Ahulu FID, Gallo E, Lehmann H, Ringelhann B. Haemoglobin Korle Bu (alpha2 beta 73 Aspartic acid to Asparagine), showing one of the two amino acids of Haemoglobin C Harlem. *J Med Genet* 1968; **5:** 107-111
14. Konotey-Ahulu FID. Alpha-Thalassaemia nomenclature and abnormal haemoglobins. *Lancet* 1984; **i:** 1024-1025
15. Ringelhann B, Dodu SRA, Konotey-Ahulu FID, Lehmann H. A survey for haemoglobin variants, thalassaemian and G6PD Deficiency in Northern Ghana. *Ghana Med J* 1968; **7:** 124-128.
16. Kamuzora H, Ringelhann B, Konotey-Ahulu FID, Lehmann H and Lorkin PA. The gamma chain in a Ghanaian Adult, homozygous for hereditary persistence of fetal haemoglobin. *Acta Haemat* 1974; **51(3):** 179-184. PMID: 4218432 [PubMed – indexed for MEDLINE] http://lib.bioinfo.pl/pmid:4218432
17. Bethlenfalvay NC, Motulsky AG, Ringelhann B, Lehmann H, Humbert JR and Konotey-Ahulu FID. Hereditary Persistence of Foetal Haemoglobin Delta Beta Locus: Further family data and genetic interpretations. *Amer J Human Genet* 1975 Mar; **27(2):** 140-154. http://lib.bioinfo.pl/pmid:1124762 or http://www.pubmedcentral.nih.gov/picrender.fcgi?artid=1762752&blobtype=pdf PMID:1124762 [PubMed – indexed for MEDLINE]
18. Kamuzora H, Ringelhann B, Konotey-Ahulu FID, Lehmann H and Lorkin PA. Further investigations of the y-chain in a Ghanaian adult, homozygous for hereditary persistence of foetal haemoglobin: Isolation of GB-3 peptides and Gy:Ay ratio determination in human Hb.F. *Acta Haematological* 1975; 53(5): 315-20. http://lib.bioinfo.pl/pmid:808072 [PubMed – indexed for MEDLINE]
19. Gbedemah KA, Acquaye CTA, Konotey-Ahulu FID and Reindorf CA. Haemoglobin phenotype patterns in more than 1,000 consecutive newborn babies in Ghana. *Ghana Med J* 1976; 15: 253-256.
20. Bonney GE and Konotey Ahulu FID. Polygamy and genetic equilibrium. *Nature* 1977; 265: 46-47 (January 6 1977). doi:10.1038/265046a0 http://www.nature.com/nature/journal/v265/n5589/abs/265046a0.html …n5589/pdf/265046a0.pdf PMID: 834239 [PubMed – indexed for MEDLINE]
21. Acquaye CTA, Oldham JH and Konotey-Ahulu FID. Blood-donor homozygous for hereditary persistence of fetal haemoglobin. *Lancet* 1977 April 9; **1(8015):** 796-
22. Acquaye CTA, KA Gbedemah, Konotey-Ahulu FID. Glucose-6-Phosphate Dehydrogenase Deficiency Incidence in sickle cell disease patients in Accra. *Ghan Med J* 1977; **16:** 4-9.
23. Ringelhann B, Konotey-Ahulu FID, Yawson G, Bruce-Tagoe AA, Miller A and Huisman THJ. Alpha-Thalassaemia in West Africa. In Szabo G and Papp Z (Eds). Medical Genetics, *Excerpta Medica* 1977; 614-616.
24. Ringelhann B, Acquaye CTA, Oldham JH, Konotey-Ahulu FID, Yawson G, Sukumaran PK, Schroeder WA and Huisman THJ. Homozygotes for the hereditary persistence of fetal haemoglobin: The ratio of G to A chains and biosynthetic studies. *Biochem Genet* 1977 Dec; **15(11-12):** 1083-1096. PMID: 603615 [PubMed – indexed for MEDLINE]
25. Altay C, Ringelhann B, Yawson GI, Bruce-Tagoe AA, Konotey-Ahulu FID, James L, Gravely M and Huisman THJ. Haemoglobin alpha chain deficiency in black children with variable quantities of haemoglobin Bart's at birth. *Paediatrics Research* Feb 1977; **11:** 147-152. PMID: 840505 [PubMed - indexed for MEDLINE] http://www.pedresearch.org/pt/re/pedresearch/pdfhandler.00006450-197702000-00017.pdf.
26. Ringelhann B and Konotey-Ahulu FID. Thalassaemia Africana - an independent mutation? *New Istanbul Contribution to Clinical Science* 1978 Dec; **12(3-4):** 264-271. PMID: 756537 [PubMed – indexed for MEDLINE]
27. Mears JG, Ramirez F, Leibowitz D, Nakamura F, Bloom A, Konotey-Ahulu FID and Bank A. Changes in restricted human cellular DNA fragments containing globin gene sequences in thalassaemias and related disorders. *Proc Natl Acad Sci USA* 1978 Mar; **75(3):**1222-1226. PMID: 274714 [PubMed – indexed for MEDLINE]

http://www.pubmedcentral.nih.gov/picrender.fcgi?artid=411442&blobtype=pdf
http://lib.bioinfo.pl/pmid:274714

28. Bonney GE, Walker M, Gbedemah K and Konotey-Ahulu FID. Multiple births and visible birth defects in 13000 consecutive deliveries in one Ghanaian hospital. In *Proceedings of the Second International Congress on Twin Studies Part C Ed Nance W. Progess in Clinical and Biological Research* 1978; **24 Pt B:** 105-108. PMID: 724702 [PubMed – indexed for MEDLINE]
29. Addae RO. Sickle cell trait and altitude *British Medical Journal* 1972; 1: 53
30. Djabanor FFT. Sickle cell trait and altitude. *British Medical Journal* 1972; 1: 113
31. Djabanor FFT, Reindorf CA, Konotey-Ahulu FID. The effect of sickle cell disease on Ghanaian children. In First International Publication No (HSM) 1974; 73-9141: 70-87.
32. Konotey-Ahulu FID. Sickle cell trait and altitude. *British Medical Journal* 1972; 1: 177-178.
33. Owusu SK. Absence of Glucose 6 Phosphate Dehydrogenase [G6PD] in the red cells of an African. *British Medical Journal* 1972; 4: 25-26.
34. Konotey-Ahulu FID, Kinderlerer JL, Lehmann H, Ringelhann B. Haemog;lobin Osu-Christiansborg: A new beta-chain variant of Haemoglobin A (beta 52 D3 Aspartic acid to Asparagine) in combination with Haemoglobin S. *Journal of Medical Genetics* 1971; 8: 302-05.
35. Ringelhann B, Konotey-Ahulu FID, Talapatra NC, Nkrumah FK, Price B, Lehmann H. Haemogllobin K Woolwich (alpha-2 beta-2 132 Lysine to Glyucine) and its combination with Hb S and Hb C in two Ghanaian tribes. *Acta Hematologica* 1971; 45(4): 250-258.
36. Ringelhann B, Rudwick Ann L. Thalassaemia major with complete suppression of Haemoglobin A production in a Ghanaian girl. *Acta Hemtologica* 1972 1972; 47: 118-126.
37. Konotey-Ahulu FID, Kuma Eunice. Skeletal crumbling in sickle cell anaemia complicated by Salmonella typhi infection. *British Journal of Clinical Practice* 1965 Oct; 19(10): 575-578. http://www.pubmedcentral.nih.gov/picender.fcgi?artid=1846577&biotype=pdf PMID: 5830346 [PubMed – indexed for MEDLINE]
38. Konotey-Ahulu FID. The Sickle Cell Disease Patient. Natural History from a Clinico-Epidemiological Study of 1550 patients of Korle Bu Hospital Sickle Cell Clinic. Macmillan, London 1991/1992; Tetteh-A'Domeno Company Ltd, Watford. 1996.
39. Konotey-Ahulu FID. Four bodyguards and the perils of unmasking scientific truths. (Personal View) *Brit Med J* 2007; **335:** 210-211
40. Konotey-AhuluFID. Male procreative superiority Index in African populations: The fact established and quantified. In Szabo G, Papp Z (Eds) *Medical Genetics, Excerpta Medica* 1977; 600-607.
41. Konotey-Ahulu FID. Male procreative superiority index (MPSI): The missing coefficient in African Anthropogenetics. *Brit Med J* 1980; **281:** 1700-1702
42. Konotey-Ahulu FID. The Human Genome Diversity Project (HGDP): cogitations of an African Native. *Politics and The Life Sciences* (Lake Superior State University) 199; **18:** 278-283 showing Sickle Cell Disease in 9 successive generations http://www.konotey-ahulu.com/images/generation.jpg
43. Konotey-Ahulu FID. The male procreative superiority index (MPSI): It's relevance to genetical counseling in Africa. In Oliver Mayo, Carolyn Leach: Fifty Years of Human Genetics. *A Festschrift and Liber Amicorium* To Celebrate The Life and Work of George Robert Fraser. South Australia, Kent Town 2007, pp 48-50.
44. Fraser GR. Medical knowledge in the service of informed parental reproductive decision and choice: absence of implications for eugenic ideology. In Oliver Mayo, Carolyn Leach: Fifty Years of Human Genetics. *A Festschrift and Liber Amicorium* To Celebrate The Life and Work of George Robert Fraser. South Australia, Kent Town 2007, pp 287-298
45. Weatherall DJ. Ethical issues and related problems arising from the application of the new genetics to clinical medicine. In DJ Weatherall: The New Genetics and Clinical Practice. Oxford, Oxford University Press, Third Edition 1991, pp 347-368
46. Konotey-Ahulu FID. First Annual Report – 1974 of the Ghana Institute of Clinical Genetics. Korle Bu 1975 Ghana.
47. Konotey-Ahulu FID. Konotey-Ahulu FID. Report on May 1974 to May 1979. Ghana Institute of Clinical Genetics 1979, 54 pages.