Loughborough University

Submission for the Higher Doctorate Degree of

Doctor of Science (DSc)

Human growth: its assessment, evaluation and variation

by

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Contents:

Prologue

James Tanner (1920-2010) was widely recognised as the leading figure in auxological research from the 1950s to the 1990s and the field is replete with his eponymous contributions (e.g. Tanner pubertal stages; Tanner-Whitehouse skeletal maturity assessments). Having successfully completed an MSc degree in Human Biology at Loughborough University in 1973 I entered James Tanner's Department of Growth and Development at the Institute of Child Health (ICH) in London University to undertake my doctoral studies under his supervision. Tanner had been appointed as the first Professor of Child Health and Growth at the ICH in 1963 and by 1973 he was *the* leading researcher in human growth and development in Europe. His Department of Growth and Development was the primary clinical and research centre for human growth research in the UK - a position it maintained for almost 40 years. In this environment I was exposed to research projects covering both normal and abnormal growth using data emanating from ongoing and newly created longitudinal growth studies (e.g. Harpenden, International Children's Centre London, Royal Hospital School, Chard) and clinical growth data collected primarily by myself and RH Whitehouse in the Growth Disorder Clinics held twice weekly under Tanner's directorship at the Hospital for Sick Children, Great Ormond Street. Whilst the early part of my career (1973-1983) was spent in this clinical research environment I have chosen to concentrate on my output relating to normal growth, its assessment, evaluation and variation because it is the non-clinical arena in which I believe my contributions have been significant and internationally recognised.

The research papers submitted for the degree of DSc demonstrate a sustained contribution to the research field of human growth and development over more than 40 years. The significance of my publications, my contribution to the field, and my international standing have been recognised by over 13,500 citations, invitations to give numerous keynote lectures at international meetings, visiting fellowships and professorships at leading international universities, Fellowship of the Royal Society of Biology, membership of Executive Committees of the leading international societies in my field of research, and editorship, associate editorship or membership of the editorial boards of the leading international Human Biology and Auxology journals. I have been invited to give the eponymous "Tanner Lecture" at international congresses in Mexico City (2009) and Slovenia (2014) and was the inaugural recipient of the James Tanner Memorial Medal by the Society for the Study of Human Biology in Oxford in 2014.

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Summary of work submitted

Human growth: its assessment, evaluation and variation

In this submission I have chosen to divide my output into three parts; (1) the assessment and evaluation of human growth and (2) normal human growth and its variation with particular reference to South Africa and (3) the developmental origins paradigm. I have accumulated in excess of 300 published contributions in the field of human growth so for the sake of brevity I have chosen to include copies of 30 publications to support this submission. These publications represent mostly internationally reviewed articles and one book chapter. The various textbooks, most notable covering anthropometry, skeletal maturity, and research methods in the general field of human growth and development, that are used internationally by practitioners and students alike, have not been included in this submission yet they form a significant contribution to the field of human growth and development. The TW2 skeletal maturity method has been cited over 2,500 times and my reference work on anthropometric measures almost 500 times indicating the frequency with which these methods have been sued by growth researchers.

The superscripted numbers relate to the full publication list in my CV (with 'B' denoting Books and 'C' denoting book Chapters. Other superscripted numbers denote peer reviewed papers) Bold numbers in brackets denote those contributions reproduced as part of this submission.

Part 1. The assessment and evaluation of human growth and development

(Publications 1-11)

*Anthropometry (**submitted refs 1-2**):* In the early part of my sojourn at the ICH it became apparent that the literature describing the anthropometric methods used to evaluate growth were primarily based on treating the child as a small adult. The specific modifications to the methods required to deal with the growing body had not been documented. From 1978 to 1988 I published a series of papers, book chapters and a textbook that addressed this lack of description[B2,C1, C3-C5, C8, 16]. These included not only original contributions but also revisiting and modernising some established *modus operandi*, such as the International Biological Programme methods[C3-C5]. These core publications have become reference standards within the field of the anthropometry of growth having been cited in over 1200 publications; The Measurement of Human growth (1984)[B2] has received in excess of 450 citations, and The Methods of Auxological Anthropometry, published within two chapters in the reference work "Human Growth" in the 1st and 2nd editions (1978, 1984)[C1,C8] (**1**), have received over 750 citations. I have also chosen to include the latest incarnation of anthropometric methods with a 2013 invited review for the American Journal of Human Biology as part of a series of methods papers that form the basis for fieldwork recommendations[151] (**2**).

*Skeletal maturity (**refs 3-4**)*: I have also been instrumental in the development of the Tanner-Whitehouse methods for the assessment of skeletal maturity and the prediction of adult height[B1,B3-B5]. As with anthropometry it was evident in the early 1970s that the first bone specific scoring method to assess skeletal maturity, the Tanner-Whitehouse method (TW1), which had been developed a decade previously, was in need of a major revision and update. I achieved this with the joint publication of the TW2 method in 1983[B1] and again 20 years later I worked directly with James Tanner on a further update to produce TW3[B5]. These works are fundamental to the characterisation of the skeletal maturity of children; they are used in paediatric and research scenarios globally, and have been cited over 2,500 times. A variety of other publications have dealt with measurement and evaluation issues in human growth and

the assessment of maturation (**3,4**). My internationally recognised expertise in the field of the measurement of human growth is reflected in the seven entries I have authored in The Cambridge Encyclopaedia of Human Growth and Development published in 1998; these include contributions on Measurement and Assessment; Radiographic Assessment, Fat and Fat Patterning; Adulthood and Developmental Maturity; Skeletal Development; and Epiphyseal Fusion[C14-C20].

*Growth charts (**refs 5-8**)*: Throughout my research career the question of using the most appropriate reference charts to sensitively and specifically appraise the normality or otherwise of the growth of children has been a recurring question. I worked extensively with the UK growth charts, both general and clinical, produced by Tanner and Whitehouse in the 1960s and 1970s[7,23,32,45,76-78,81,100,117,131,153]. My work in South Africa in the 1980s and 1990s resulted in publications in which I discussed the use and value of national and international growth charts[23,32,45,60](**5,6**) and my acknowledged expertise in this discussion resulted in me being invited to join the WHO Working Group on the Growth Reference Protocol that discussed and developed the latest WHO growth standards (2007) (**7,8**). These standards are now used globally to assess the growth and development of infants, children and adolescents from birth to adulthood.

Age estimation: The relationship between maturity and age has been an area of interest to successive governments as they attempt to determine whether unaccompanied minors entering the UK are entitled to various welfare benefits. This discussion has been ongoing since the mid-1970s when the influx of Ugandan Asians was prompted by Idi Amin's regime. I was first approached at that time to proffer my opinion in a paper in Science and Public Policy[17](**9**). Most recently with the influx of migrants to continental Europe this area of Auxology has again become relevant and my expertise has again been sought to provide a scientific background to the relationship between maturity and age[164,168] (**10,11**).

Other publications listed in my CV cover different aspects of the assessment and evaluation of human growth ranging from the development of new assessment methods[B7,C7,C9,C11,C21,C24-C31,C34,C36,C38] to the variation in evaluation of the process of growth and development from using both established and novel methods of data acquisition and analysis[B7].

Part 2: Normal human growth and its variation with particular reference to South Africa.

(Publications 12-21)

*Normal growth (**refs 12-15**)*: My earliest publications (1973-1983) related to research questions concerning both normal and abnormal growth. My PhD research documented the secular trends in growth during the 20th century revealed by an extensive analysis of London County Council data collected from cross-sectional surveys conducted from 1904 to 1966[4] (**12**). This was to be the first of a number of papers spanning the next 30 years that documented secular trends in the UK and South Africa with evidence from pre-existing and newly initiated growth studies and skeletal collections[29,30,35,38,40,44,57,96,101,116,119,127]. In addition, I tackled a number of specific questions relating to various aspects of the pattern of human growth: the relationship between body size and menarcheal age in 1976[2]; the existence, timing, duration and magnitude of the mid-growth or juvenile spurt was elucidated in 1980[8](**13**); the pattern of change in VO_2max during adolescence in 1981[12], the growth of limb segments[18](**14**) and the relative importance of the growth of the anatomical leg to secular changes in height in Japan 1982[19](**15**).

*South Africa (**refs 16-21**)*: I spent from 1984 to 1997 in the Department of Anatomy and Human Biology in the Medical school of the University of the Witwatersrand, South Africa. During this time I initiated three longitudinal growth studies at Vaalwater, Ubombo, and in Soweto-Johannesburg[36,38,40-47,49,51,52,55,58,63,68](**16, 21**). A major part of my raison d'être for working in South Africa was to make contributions in the human growth and development of the disadvantaged black population. Prior to my research there had been few South African studies of the normal growth of such children; most studies had been investigations initiated by concerns over maternal and child health and malnutrition and almost all were of a cross-sectional design and had been conducted in urban areas. It was clear in 1984 that the end of apartheid was in sight and as a result the draconian laws, known as the "pillars of apartheid", that controlled freedom of residency, occupation, education, health care, and marriage were breaking down. The South African census of 1983 predicted that 14 million black Africans would move into urban areas by the year 2000 and that urban areas would double in size by 2010. There was a clear and obvious need for baseline information on the growth of black children for two reasons (1) to monitor the effects of almost 40 years of disadvantage under apartheid and (2) to be able to monitor the positive changes that might result in a post-apartheid, non-racial, democratic South Africa. Vaalwater and Ubombo were two rural areas with different characteristics[38,40,43-46,49,51,52,63]. The former was a farming area, mainly growing tobacco, in the northern Transvaal not far from the Botswana border and the latter a traditional rural area of subsistence and cattle farmers in the Eastern Transvaal near the Mozambique border. I initiated longitudinal studies in both areas and published a series of articles that formed the first baseline data on normal growth and pubertal development of rural black children (**17**). The third longitudinal study was a birth cohort study called Birth to Twenty (Bt20) that was specifically initiated to investigate the effect of the urban environment on child health and growth. Bt20 started on late April 1990 and is now recognised as the longest running and most detailed study of child growth and health in sub-Saharan Africa. It forms one of the COHORTS studies and is widely recognised for the contribution it has made to our understanding of the growth of African children in rapidly urbanising environments[36,41,42,55,58,65,68-70,74,75,82,83,87,89,91,94-98,101,104,106,111,115,116,118-121,128,130,132,136,138,139,141,148,149,157](**18 -20**).

In précis, these studies have documented the differences in the pattern of growth exhibited by black African and White children towards the end of apartheid and subsequently the positive secular trends that have occurred (**16-21**). Importantly publications relating to the increased rates of pubertal development (menarche, puberty), skeletal maturity (bone age) and growth have been landmark studies[38,40,44,49,51,52,57,63,16,119,127,157,162]. In addition, and subsequent to my departure from South Africa in 1997, the Bt20 study has been used for a variety of landmark papers concerning child health and growth in the global setting of developing and transitional countries [96,101,140].

Part 3: The developmental origins paradigm

(Publications 22-30)

*Developmental Origins of Health and Disease (**refs 22 – 30**)*: My return to the UK in 1997 coincided with growing interest in the developmental origins of non-communicable diseases of lifestyle (NCDs) advocated by the late Professor David Barker. Barker proposed that the pattern of fetal growth was in response to the intrauterine environment and that insult during this time resulted in adaptation by the fetus which led to increased post-natal risk for NCDs. Some of my papers during this time explored the existence of critical periods in human growth during infancy and childhood[80](**30**) and, combined with studies of infant growth from Bt20,

were significant in identifying early infant growth as being critical in the acquisition of risk for NCDs[69,70,74,75,80,83,91,97,106,128,136](**22-25**). Within the developmental origins paradigm, the existence of significantly increased risk for NCDs amongst South Asians has received considerable attention. In 2007 I was involved in the development of another birth cohort study in Bradford (Born in Bradford; BiB) to specifically address the question of the aetiology of NCD risk in the bi-ethnic population of that city[145-147,156,159,163,165,169,177](**26-29**). Through analyses carried out by two of my PhD students we have been able to explore the growth of this mixed ethnic sample during intrauterine life (**28,29**) and infancy (**26**). The importance of this work is in understanding the greater risk that South Asians display in relation to the acquisition of NCDs (**30**).

I believe that this submission represents published work of high merit in the research fields of human growth and development/Auxology. The publications indicate both an internationally recognised expertise in my field of research and a sustained contribution to understanding within this field.

Statement on publications submitted

Only a small subset of my 300 publications is included in this submission. The submitted papers relate primarily to the key research areas summarised in the preceding section: anthropometry, skeletal maturity, growth charts, age estimation, normal growth and its variation, South Africa, Developmental Origins of Health and Disease. In all cases the publications were solely or jointly prepared by myself and PhD students or research associates and collaborators. All the papers benefitted fully from my intellectual input but my contribution to each paper varied from 100% of the actual writing and preparation of the manuscript where I am first author to a significant but lower percentage where I am a co-author or senior author.

The specific papers submitted are tabulated below (Refs 1-30). The "CV Refs" refers to the numbering my list of publications within my *Curriculum Vitae*.

Refs	CV Refs	Publications (full bibliographical details)
		Anthropometry
1	C1	**Cameron N.** The methods of auxological anthropometry. In: Falkner F, Tanner JM, editors. Human Growth. New York: Plenum; 1978. p.35-90.
2	151	**Cameron N**. Essential anthropometry: Baseline anthropometric methods for human biologists in laboratory and field situations. American Journal of Human Biology 25(3):291-9. 2013
		Skeletal maturity
3	25	**Cameron, N**., 2003. Assessment of maturation: bone age and pubertal assessment. In: Glorieux, F., *et al*. (edd.), 2003. *Pediatric bone*. Oxford: Academic Press, pp. 325–338.
4	50	**Cameron N**. The Tanner-Whitehouse II skeletal maturity method: Rationale and applicability. Clinical Pediatric Endocrinology, 2(Suppl. 1); 9-18. 1993
		Growth charts
5	78	Wright, CM, Booth, IW, Buckler, JMH, **Cameron N**, Cole, TJ, Healy MJR, Hulse JA, Preece MA, Reilly JJ, Williams AF. Growth reference charts for use in the United Kingdom. Archives of Diseases in Childhood 86;11-14. 2002.
6	77	**Cameron N**. British growth charts for height and weight with recommendations concerning their use in auxological assessment. Annals of Human Biology 29(1);1-10. 2002.
7	71	Victoria, CG, de Onis, M, Garza, C, Cole, T, Frongillo, EA, **Cameron N**, Shekar, M, Yip, R, Bhatnagar, S, Burger, H, Delgado, HL, Dada, OA, Gross, B, Hofvander, Y, Lavin, PA, Tang, GH. Growth patterns of breastfed infants in seven countries. Acta Paediatrica 89(2);215-22. 2000.
8	81	WHO Working Group on the Growth Reference Protocol and the WHO Task Force on Methods for the Natural Regulation of Fertility. Growth of healthy infants and the timing, type, and frequency of complementary foods. American Journal of Clinical Nutrition 76:620-627. 2002.
		Age estimation
9	17	**Cameron N**. The estimation of chronological age in children. Science and Public Policy, 9,20-27. 1982

10	164	**Cameron N**. Can maturity indicators be used to estimate chronological age in children? Annals of Human Biology 42(4):302-7. 2015
11	168	**Cameron N**. The European refugee crisis and biological age-Is it right to use skeletal maturity as an estimate of chronological age? Annals of Human Biology 17(1);1-2. 2016
		Normal growth and its variation
12	4	**Cameron N**. The growth of London schoolchildren 1904-1966; an analysis of secular trend and intra-county variation. Annals of Human Biology 6;505-525. 1979
13	8	Tanner JM, **Cameron N**. Investigation of the mid-growth spurt in height, weight, skinfolds and limb circumference of children from the London County Council Survey 1966-1967. Annals of Human Biology, 7, 565-577. 1980
14	18	**Cameron N**, Tanner JM & Whitehouse RH. A longitudinal analysis of the growth of the limb segments in adolescents. Annals of Human Biology, 9,211-220. 1982
15	19	Tanner JM, Hayashi T, Preece MA & **Cameron N**. Increase in length of leg relative to trunk in Japanese children and adults from 1957 to 1977; and comparison with British and Californian-born Japanese. Annals of Human Biology, 9,411-424. 1982
		South Africa
16	43	**Cameron N**. Human growth, nutrition and health status in Sub-Saharan Africa. Yearbook of Physical Anthropology, 34;211-250. 1991
17	52	**Cameron N**, Gordon-Larsen P and Wrchota EM. A longitudinal analysis of adolescent growth in height, fatness and fat patterning in rural South African black children. American Journal of Physical Anthropology, 93; 307-321. 1994
18	98	Richter L, Norris SA, Pettifor JM, Yach D, **Cameron N**. Cohort Profile: Mandela's Children: The 1990 Birth to Twenty Study in South Africa. International Journal of Epidemiology 36(3);504-511. 2007.
19	68	**Cameron N**, De Wet T, Ellison GTH and Bogin B. Growth in height and weight of South African urban infants from birth to five years: the Birth To Ten Study. American Journal of Human Biology, 10 (4); 495-504. 1998
20	162	Cole TJ, Rousham EK, Hawley NL, **Cameron N**, Norris SA, Pettifor JM. Ethnic and sex differences in skeletal maturation among the Birth to Twenty cohort in South Africa Archives of Diseases in Children. 100(2):138-43. 2015.
21	82	**Cameron N**. Physical growth in a transitional economy: the aftermath of South African apartheid. Economics and Human Biology. 1(1):29-42. 2003
		Developmental Origins of Health and Disease
22	92	**Cameron N**, Preece MA, Cole TJ. Catch-up growth or regression to the mean? Recovery from stunting revisited. American Journal of Human Biology 17(4):412-7. 2005
23	69	Crowther NJ, **Cameron N**, Trusler J and Gray IP. Association between poor glucose tolerance and rapid post-natal weight gain in 7 year old children. Diabetalogia. 41;1163-1167. 1998
24	74	Crowther, NJ, Trusler, J, **Cameron, N**, Toman, M, Gray, IP. Relation between weight gain and beta-cell secretory activity and non-esterified fatty

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25	128	Demerath EW, Jones LL, Hawley NL, Norris SA, Pettifor JM, Duren D, Chumlea WC, Towne B, **Cameron N**. Rapid weight gain and advanced skeletal maturation in childhood. Journal of Pediatrics. 155(3):355-61. 2009.
26	143	Johnson W, Wright J, **Cameron N**. The risk of obesity by assessing infant growth against the UK-WHO charts compared to the UK90 reference: findings from the Born in Bradford birth cohort study. BMC Pediatrics. 12:104. 2012
27	146	Wright J, Small N, Raynor P, Tuffnell D, Bhopal R, **Cameron N**, Fairley L, Lawlor DA, Parslow R, Petherick ES, Pickett KE, Waiblinger D, West J; on behalf of the Born in Bradford Scientific Collaborators Group. Cohort profile: The Born in Bradford multi-ethnic family cohort study. International Journal of Epidemiology. 42(4);978-91. 2013.
28	156	Norris T, **Cameron N**. Investigating the relationship between prenatal growth and postnatal outcomes: A systematic review of the literature. Journal of Developmental Origins of Health and Disease 4(6); 434-441. 2013
29	159	Norris T, Tuffnell D, Wright J, **Cameron N**. Modelling foetal growth in a bi-ethnic sample: results from the Born in Bradford (BiB) birth cohort. Annals of Human Biology. 41(6);481-487. 2014
30	80	**Cameron N**, Demerath EW. Critical periods in human growth: relationships to chronic disease. Yearbook of Physical Anthropology 45;159-184. 2002

Submitted publications

Appendix 1

Abstracts of Conference Proceedings

1. **Cameron N**. A test of the Frisch hypothesis for critical weight and body fat at menarche. In: Compte-Rendue de la XII Reunion des Equipes Chargee des Etudes sur la Croissance et la Development de l'enfant Normal. Paris: International Children's Centre. pp 103-104. 1974

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5. Preece MA, Greco L, Savage MO, **Cameron N**, Tanner JM. The auxology of growth delay. Paediatric Research. 15:76. 1981

6. **Cameron N**. Activity, adolescence and serum hormones. Proceedings of the Society for the Study of Human Biology. Annals of Human Biology. 10;83. 1982

7. **Cameron N**. Growth at Adolescence. Proceedings of the International Symposium on Adolescent Nutrition and Food Behaviour,1982. Prince Edward Island: University of Prince Edward Island Press. 1983

8. Bailey DA, Mirwald RL, **Cameron N**. Aerobic Power and Growth in Boys with differing physical activity profiles - A dimensional assessment. Proceedings of the Workshop on Paediatric Work Physiology. Papendal, Holland. 1983.

9. **Cameron N**. Preliminary results of the application of new height prediction techniques. Anatomical Society of Southern Africa. S.Afr.J.Sc.,80; 434-435. 1984

10. **Cameron N**, Jones PRM, Mitchell J, Moodie A, Bowie,MD, Mann,MD, Hansen JDL. A longitudinal analysis of the growth and development of children following early Kwashiorkor. IVth International Congress of Auxology. Annals of Human biology,12, Suppl.No.1;56. 1985

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