Keynote Lecture VI

Life Course Epidemiology: Making the Connection between Development and Ageing

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Diana Kuh is professor of life course epidemiology at Royal Free and University College London Medical School and a senior research scientist for the UK Medical Research Council. Diana's first degree was in Economics at Cambridge University. Her PhD, from the London School of Economics in 1993, was on the early origins of adult health. Since 1987 Diana has worked in a small team responsible for running the MRC National Survey of Health and Development, a cohort of 5362 men and women followed up since their birth in March 1946. She has over a hundred publications, most using data from this study to investigate biological and social risk and protective factors across the life course that explain variation in adult health between individuals and different social groups. Currently, Diana is principal investigator for the study's research programmes on women's health and musculoskeletal health, and a co-investigator on the cardiovascular research programme. Diana's research involves collaborations in Europe, North America and Australia and comparative studies across cohorts, and is informed conceptually by the life course perspective. She has been instrumental in developing the field of life course epidemiology, that is the study of biological, social and psychosocial risk processes from early life that influence adult health and the development of chronic disease in later life. She has contributed to the conceptual advancement of this field through editorials, a glossary, and two co-edited books, *A life course approach to chronic disease epidemiology*, 2nd edition 2004, and *A life course approach to women's health*, 1st edition 2002, both with Oxford University Press.

The term life course epidemiology was coined in 1997 to counteract the increasing polarisation between three aetiological models of adult chronic disease risk. The prevailing model emphasised the importance of adult lifestyle, an alternative model emphasised the role of the socioeconomic environment, and the third, based on the 'Barker hypothesis', focused on nutritional programming *in utero*. Life course epidemiology studies the long-term biological, behavioural and psychosocial processes that link age related changes in biological function in later life, and chronic diseases and associated adult risk factors, with physical or social exposures in earlier life, or across generations. The effects of earlier exposures may leave imprints on the structure of function of body systems particularly during periods of rapid growth and development. Thus, researchers investigating either the fetal origins or the childhood social origins of adult chronic disease risk share a common interest in identifying prenatal and postnatal growth trajectories and other developmental characteristics that are associated with ageing and age-related diseases. Investigating these long-term associations is methodologically challenging; identifying specific exposures – such as early nutrition, infection or stress - and underlying mechanisms is even more challenging. Findings may be cohort or place specific.

Professor Kuh will briefly discuss the development of the field of life course epidemiology. Studies of cardiovascular disease and diabetes have dominated this research area but the life course approach is also relevant for many other aspects of ageing. Professor Kuh will present recent evidence from a national British birth cohort showing that ageing of the reproductive and musculoskeletal systems also have developmental origins.

Taking reproductive ageing as the first example, factors operating during development may influence age at

menopause by affecting the initial number of follicles laid down and their loss *in utero*, or during the postnatal period. Early nutritional, viral and stress exposures may all be implicated but evidence is sparse. In a cohort of 1572 women born in one week in March 1946 and followed up regularly since, lower weight in infancy, not being breastfed, and poor childhood cognitive ability, socioeconomic and psychosocial circumstances advanced timing of the menopause. These results were independent of later life risk factors, such as smoking, parity and adult circumstances, and provide evidence for a number of underlying mechanisms linking developmental experience to reproductive ageing. The association with childhood cognition has also been replicated in another cohort. These findings have implications for the interpretation of studies that show associations between menopause and adult cognitive function.

Taking midlife musculoskeletal function as the second example, there is growing evidence that birthweight is associated with adult muscle strength independent of adult body size, and that this reflects the number of muscle fibers laid down *in utero*. New evidence from the 1946 British birth cohort shows that adult muscle strength and physical capability are associated with postnatal growth and development of motor and cognitive capabilities, independent of adult risk factors. The processes that may underlie these associations are discussed. More generally, it is possible that age-related diseases share common causative mechanisms with ageing itself and with other age-related diseases, and that these mechanisms operate from early life. There are important public health implications for preventing disease, disability and frailty in an ageing population.