EDITORIAL

Aging and paediatric practice

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Scientific journals from around the world have agreed to take part this year in a global themed issue on Aging—an initiative coordinated by *JAMA*. How do we justify a contribution from the *Archives of Disease in Childhood* to this important theme? One thing that distinguishes paediatric practice is that health and disease are observed against a background of growth and development. Perhaps analogous to this is the practice of geriatrics, where biological senescence and all its psycho-social implications, form the backdrop against which health and disease are observed. Yet this philosophy becomes clouded when we consider that development and aging (or senescence) cannot be readily pulled apart. Although development implies an advantageous adaption to life, and aging implies irreversible deterioration, it is none the less true that development is not only a precursor of aging but also influences it profoundly.

A review article by *Aihie Sayer et al* on pages F162–4 poses the somewhat depressing question: Is lifespan determined in utero? It is not surprising that it might be, given the association between poor fetal growth and an increased prevalence of cardiovascular disease in adults. However, these authors draw attention to poor growth in fetal life and infancy, and the promotion of biological senescence in systems such as the eye, ear, muscle and skin. They speculate that nutritional programming of aging might come about through impaired development of tissue repair systems at cellular and molecular levels.

Programmed cell death (apoptosis), unlike necrosis, is characterised by preservation of membrane integrity and organelle structure, the occurrence of chromatin condensation and nuclear fragmentation, and the budding off of cellular fragments known as apoptotic bodies, from the Greek *apo* (away from) and *ptosis* (falling). This process occurs in diverse conditions, some physiological, such as in embryonic development and involutional processes, and others pathological, as in immune mediated cell killing and ischaemic injury. In their review article *Nicholas Mazarakis and colleagues* (pages F165–170) highlight the broad spectrum of neurological disorders in which apoptosis is a feature, including hypoxic–ischaemic brain injury in the newborn. The importance of learning more about this form of cell death is that if effective anti-apoptotic strategies were available they would be potentially applicable to a wide range of disorders.

If, as we have seen, fetal nutrition influences health in adulthood it is reasonable to ask to what extent aging—in this context biological senescence—occurs in the placenta. This subject is reviewed by *Harold Fox* on pages F171–5. He indicates that, far from senescence, the term placenta shows continuing DNA synthesis, and persisting villous growth and expansion of villous surface area. He refutes the widely held notion that, come 40 weeks of gestation, the placenta goes into a decline, both functionally and anatomically. Indeed, he draws attention to fetal macrosomia in prolonged pregnancy. He argues that the classic clinical syndrome of "postmaturity," now uncommon, is related to oligohydramnios, for which the placenta should not take the blame because there is no evidence that in late pregnancy it has a role in the production of amniotic fluid, or in the control of its volume.

The notion of "tracking of obesity" is explored in the Standard Edition of *Archives of Disease of Childhood*. Obesity of central distribution in adults is a feature of non-insulin dependent diabetes and insulin resistance, and this syndrome has been linked to low birthweight. This prompted *Mary Barker and colleagues* to examine the association between birthweight and body fat distribution in adolescent girls. Their observations, described on pages 381–3, lend support to the suggestion that a tendency to store fat on the trunk in overweight adolescent girls may be programmed by growth, or more precisely by the lack of it, in fetal life.

If we are serious about health promotion as a science we need to have a better understanding of the factors that govern the various markers for morbidity in adult life, such as obesity. The relation between parental obesity and obesity in childhood is well known. *Julie Lake and colleagues*, using longitudinal data from the 1958 British birth cohort, show that tracking of body mass index from childhood to adult life was strongest among those whose mother and father were obese (pages 376–81); indeed, such children when they reached the age of 33 years had a mean BMI 20% greater than in those whose parents were both "normal." They warn that a rising prevalence of adult obesity is likely to strengthen the tracking of child to adult BMI in the next generation.

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Improved methods of epidemiological research will most likely reveal numerous curious and provocative associations between health experiences in early childhood and the occurrence of later disease. Reduced exposure to infection in childhood has been implicated as a factor in the pathogenesis of insulin dependent diabetes (IDDM). *Caspar Gibbon et al* put this theory to the test in a brief but important paper on pages 384–5, which points to an association between decreased exposure to common infections in infancy, based on general practitioner records, and IDDM in children under the age of 16 years.

In conclusion, high quality epidemiological research during the next decade will present us with many intriguing discoveries about the influence of fetal and early childhood experience on diseases in adult life. We need also to tease out similarities of biological mechanisms of disease processes in the young and the elderly. Treatment strategies aimed at manipulating biological processes may be common to both. Stroke in the elderly and hypoxic–ischaemic brain damage in the newborn is but one example. We should also acknowledge the notion that "dependency" provokes similar psycho-social problems at the two extremes of life, including neglect and abuse. The basic science that governs the state of dependency of the very young and the elderly has similarities that might be exploited to provide improved preventive and management strategies for both, even though there will be differences in detail.

Is lifespan determined in utero?

A Aihie Sayer, C Cooper, D J P Barker

Low rates of growth in early life are now known to be associated with an increase in age related disease in later life.[1] This is thought to reflect programming, the process whereby a stimulus or insult acting at a critical period of development in early life, has lasting or lifelong importance.[2] In animal experiments that have examined the mechanisms responsible for programming, attention has focused on prenatal undernutrition and its influence on gene expression, cell division and differentiation, and tissue structure.

Fetal growth and adult disease

Epidemiological studies have shown that markers of poor fetal growth, including low early weight, thinness, and shortness at birth, are associated with increased mortality and morbidity from cardiovascular disease in later life.[1 3] Correlations have also been shown between poor early growth and the major cardiovascular risk factors—raised blood pressure,[4] raised plasma fibrinogen[5] and serum cholesterol concentrations,[6] impaired glucose tolerance[7] and reduced arterial compliance.[8] These associations were first established by studies in Hertfordshire, where from 1911 to 1948, every newborn baby was weighed and followed up to the age of 1 year. The prevalence of non-insulin diabetes and impaired glucose tolerance, for example, falls threefold between men who weighed 5.5 pounds at birth and those who weighed 9.5 pounds.[7] These associations have been replicated in several different countries including the United States[9] and India[10] as well as in Britain. The associations are independent of adult lifestyle, and are not limited to cardiovascular disease. Chronic obstructive pulmonary disease[11] and reduced bone mineral content[12 13] are both associated with reduced growth in utero and during infancy. The major determinant of fetal growth is nutrition[14–16] and the fetal origins hypothesis proposes that fetal undernutrition programmes the long term adverse sequelae of small size at birth. Cardiovascular disease, impaired glucose tolerance, chronic obstructive lung disease and bone loss are age related disorders, but the link between fetal nutrition and aging has scarcely been explored.

Postweaning and diet restriction studies

Nutrition is known to affect aging. The prolongation of lifespan by postweaning diet restriction was first shown in rodents in 1917[17 18] and the results have been replicated in many species, most recently primates.[19] Several dietary manipulations with varying reductions in calorie and protein intake have been found effective.[20] One study considered racial differences in renal and hepatic aging between Japanese and Caucasian people. Increased changes were seen in the Japanese histological specimens. It was suggested that the relatively low protein diet eaten by the Japanese was responsible for retarded development and accelerated aging.[20] There has been just one controlled diet restriction study in humans.[21] Healthy subjects over 65 years of age, living in a religious institution for the aged, were given their usual diet containing 2300 calories on odd days and 1000 calories from milk and fruit on even days. Control subjects continued with the usual diet every day. The experimental subjects spent significantly less time in an infirmary than controls and six of them died compared with

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