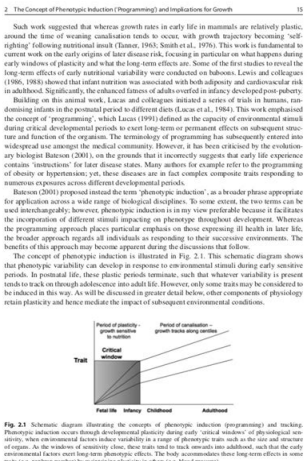

2 The Concept of Phenotypic Induction ('Programming') and Implications for Growth 15

Such work suggested that whereas growth rates in early life in mammals are relatively plastic, around the time of weaning canalisation tends to occur, with growth trajectory becoming 'self-righting' following nutritional insult (Tanner, 1963; Smith et al., 1976). This work is fundamental to current work on the early origins of later disease risk, focusing in particular on what happens during early windows of plasticity and what the long-term effects are. Some of the first studies to reveal the long-term effects of early nutritional variability were conducted on baboons. Lewis and colleagues (1986, 1988) showed that infant nutrition was associated with both adiposity and cardiovascular risk in adulthood. Significantly, the enhanced fatness of adults overfed in infancy developed post-puberty.

Building on this animal work, Lucas and colleagues initiated a series of trials in humans, randomising infants in the postnatal period to different diets (Lucas et al., 1984). This work emphasised the concept of 'programming', which Lucas (1991) defined as the capacity of environmental stimuli during critical developmental periods to exert long-term or permanent effects on subsequent structure and function of the organism. The terminology of programming has subsequently entered into widespread use amongst the medical community. However, it has been criticised by the evolutionary biologist Bateson (2001), on the grounds that it incorrectly suggests that early life experience contains 'instructions' for later disease states. Many authors for example refer to the programming of obesity or hypertension; yet, these diseases are in fact complex composite traits responding to numerous exposures across different developmental periods.

Bateson (2001) proposed instead the term 'phenotypic induction', as a broader phrase appropriate for application across a wide range of biological disciplines. To some extent, the two terms can be used interchangeably; however, phenotypic induction is in my view preferable because it facilitates the incorporation of different stimuli impacting on phenotype throughout development. Whereas the programming approach places particular emphasis on those expressing ill health in later life, the broader approach regards all individuals as responding to their successive environments. The benefits of this approach may become apparent during the discussions that follow.

The concept of phenotypic induction is illustrated in Fig. 2.1. This schematic diagram shows that phenotypic variability can develop in response to environmental stimuli during early sensitive periods. In postnatal life, these plastic periods terminate, such that whatever variability is present tends to track on through adolescence into adult life. However, only some traits may be considered to be induced in this way. As will be discussed in greater detail below, other components of physiology retain plasticity and hence mediate the impact of subsequent environmental conditions.

Fig. 2.1 Schematic diagram illustrating the concepts of phenotypic induction ('programming') and tracking. Phenotypic induction occurs through developmental plasticity during early 'critical windows' of physiological sensitivity, when environmental factors induce variability in a range of phenotypic traits such as the size and structure of organs. As the windows of sensitivity close, these traits tend to track onwards into adulthood, such that the early environmental factors exert long-term phenotypic effects. The body accommodates these long-term effects in some traits (e.g. nephron number) by maintaining plasticity in others (e.g. blood pressure)