Joint hypermobility in children

The late Dr Barbara Ansell frequently stated that 'hypermobility is tricky in children'. That joint hypermobility should more frequently occur in children than in adults is undisputed. This is normally attributed to the stabilization of joint collagen that occurs as a result of increased cross-linking between adjacent molecules as disulphide bridges form with ageing. However, this is not the whole picture because most authorities agree that joint laxity increases up to a maximum at the time of adolescence, only decreasing thereafter. Presumably the stretching effect of growth on collagen predominates over decline, additional 'spurs' of hypermobility apparently accompanying each of the growth spurts in either sex and the onset of menstruation in females. The first seminal description of hypermobility as a syndrome and frequently recognized as a cause of symptoms, often severe, came from Dr Ansell and her colleagues in 1967 [1]. It has also long been recognized that symptoms arising from hypermobile joints in children can mimic pauciarticular inflammatory polyarthritis [2], a situation also found in adults [3].

Compartmentalization within medicine can be a mixed blessing. Although the advent of paediatric rheumatology, now recognized increasingly as a subspecialty, provides obvious benefits to many children and their parents, the case for a clear separation between the management of children and adults is least strong in the field of inherited abnormalities, particularly those of connective tissue. Often the review in the same clinic of three generations within a single affected family may be necessary to clearly delineate and quantify the clinical phenotype. This, in turn, paves the way for molecular genetics.

Research into hypermobility is also changing, in large part influenced by advances in molecular medicine. Traditionally the syndrome was notified, quantified and then ignored. Early scoring systems, notably those from Carter and Wilkinson [4] and the 1973 modification of this by Beighton et al. [5], concentrate on an appraisal of the joint laxity, reducing it to a single figure. Although this was of value in epidemiological studies (and still is), this approach ignored the fact that collagen is not only ubiquitous throughout the body but exists in many different forms at different sites and that, in turn, 'joint hypermobility' might simply be a phenotypic marker for problems likely to occur elsewhere. The Brighton 1998 criteria for the diagnosis of the syndrome [6] attempted to address this, retaining the earlier quantification of joint laxity but adding additional clinical features increasingly recognized with joint hypermobility. The ARC information pamphlet attempts to define four possible contributing factors to joint hypermobility, not only at the knee [10] but also at the hand [11]. Therefore the possibility that proprioception alone might be the cause of the delayed walking arises; it is also conceivable that impaired proprioception in the fingers might handicap writing skills. It has recently been shown [12] that enhancement of proprioception in patients ameliorates symptoms; perhaps exercises to enhance proprioception might also improve function. It would also be interesting to determine whether, on the basis of subsequent follow-up (or study of adults from the same family), it was this group who ultimately were particularly susceptible to premature osteoarthritis.

The paper also only partially dissect the influence of race on phenotype. Earlier work from South Africa [5] has convincingly shown that even where different ethnic groups live in the same climate and circumstances, there is wide divergence in the joint laxity observed. The Europeans are most stiff; the Bantu tribes of intermediate joint laxity and those originally from the Indian subcontinent of most marked joint laxity. In the global village that is London only 99 out of 125 were classified as Caucasian, the remainder almost constituting a small United Nations. A small proportion was of 'mixed' parentage. In Caucasians the genes for joint laxity are thought to have greater penetration in females (though...
this may in part be hormonal). Study of the mixed group might clarify whether this held true in those of more diverse ethnic origin. Worldwide, small pockets of extreme hypermobility have existed since antiquity, e.g. Hippocrates' description of the Scythians who had so much hyperextensibility of the elbows that they proved inefficient as bowmen. Recent interest has concentrated on northern Iraq [13] and the Yoruba of Nigeria [14]. This might also skew the results in an urban population and it would be of interest to know if the joint laxity was maintained in a new environment.

The study is devoted to the benign joint hypermobility syndrome, deliberately excluding more serious specific inherited abnormalities of connective tissue such as Ehlers-Danlos syndrome, Marfan’s syndrome, osteogenesis imperfecta and (presumably) skeletal dysplasias. There also seem to be no representatives with Stickler’s syndrome, an abnormality of type II collagen causing ocular and musculoskeletal abnormalities, which is inherited as an autosomal dominant condition and estimated to occur in 1 in 10 000 live births [15]. In spite of this, the authors find and comment on considerable overlap between benign hypermobility and mild variants of these other conditions. A separate literature already attests to some mosaicism between these various discrete conditions. The prevalence of osteogenesis imperfecta is normally given as 1 in 20 000 [16]; the prevalence of type I Ehlers–Danlos syndrome as 1 in 20 000; and that of type IV Ehlers–Danlos syndrome (the vascular variant) as 1 in 100 000 [17]. If these prevalence rates are accepted, such conditions are unlikely to have contributed significantly to this particular series, but the possibility remains that there may be several more mild variants of these rarer conditions, all with varying degrees of penetrance within the same family.

Perhaps, sensibly, the study therefore sidesteps the question most frequently asked by the accompanying parents, which concern the chances of other children being affected if they enlarge their family. It also makes no mention of a further problem associated with this group, which is the propensity to easy bruising and even fracture on minimal trauma, which sometimes leads to an erroneous diagnosis of child abuse when the injuries first present in the casualty department. This information is perhaps more likely to have contributed significantly to this particular series, but the possibility remains that there may be several more mild variants of these rarer conditions, all with varying degrees of penetrance within the same family.

The field remains complex and interesting, rejuvenated by the recent dramatic advances in molecular genetics. These have recently been summarized eloquently by Pope [18], the number of recognizable genetic abnormalities expanding by the month if not the day. In general, clinical documentation of the phenotype resulting from these molecular abnormalities has been a limiting factor, so descriptive studies of this sort, which behave us to collect more detailed clinical information not just in affected children but in their affected parents and grandparents thus crossing the rheumatological age divide, become all the more important.

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References


