Digit patterning is formed along the anteroposterior axis (figure 1A), with digit 1 (pollex) on the anterior side and digit 5 on the posterior side. This patterning is caused by another signalling centre called the zone of polarising activity (ZPA). The ZPA is located at the posterior of the AER, where the morphogen Shh is localised[5].

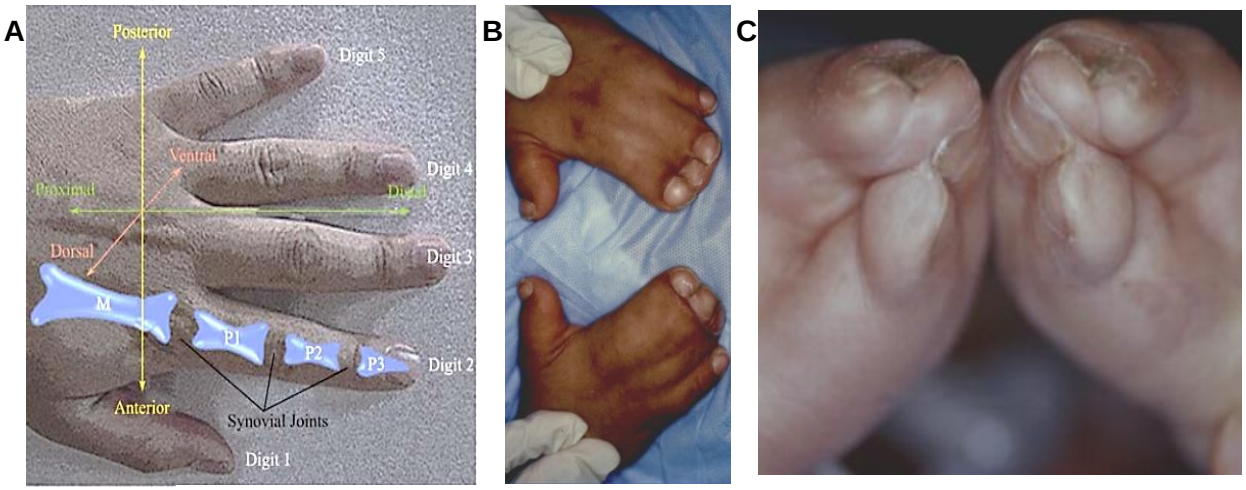

Figure 1A *– the three axis of the hand and the phalangeal and metacarpal bones of the digits.*
Figure 1B *– mild syndactyly with incomplete separation of the skin.*
Figure 1C *– more severe syndactyly with incomplete separation of the bones.*

The mechanisms controlling this digit patterning are very complex and it has long been disputed how this patterning occurs. Saunders and Gasseling show that transplantation of cells from the ZPA into the anterior part of the limb bud cause a mirror imaging effect of the digits along the anteroposterior axis[6]. This showed the importance of Shh-producing cells. Later Harfe et al report that digit one and two are depend on Shh concentration gradient while the posterior digits rely upon the length of time exposed to Shh[7]. This was determined through fate mapping of Shh-producing cells.

The elongation of the individual digits depends upon the AER and FGF signalling, as shown by the observation that up-regulating or down-regulating FGF8 can cause extra digit formation or loss of the digits[8]. Specific signals are required to form the bones of the digits and also the development of synovial joints. Bone is formed by cells leaving the AER, differentiating into cartilage, which then calcifies to form endochondral bones[9]; however the bone at the tips of the fingers (future distal phalanx) is membranous bone formed from dermis. At the sites where inter-phalangeal synovial joints should be, the cells de-differentiate to form a non-cartilaginous zone called an interzone[10]. The signals required for this interzone formation are crucial in digit patterning as this causes the separation of a single digit bone into three; the proximal, intermediate and distal phalanges (figure 1A; P1, P2 and P3 respectively).

In the embryo a key developmental stage transpires when the fingers that have just formed, become fully separated around day 54. This occurs via apoptosis of the interdigital mesenchyme. A hand anomaly called syndactyly occurs when apoptosis