Lecture 3:

Body size and body shape.

Again, these slides contain all of the text and important images, but not all of the simply illustrative images (for copyright reasons).

Big questions:

1) How do fully-grown organisms tend to respect a characteristic size?

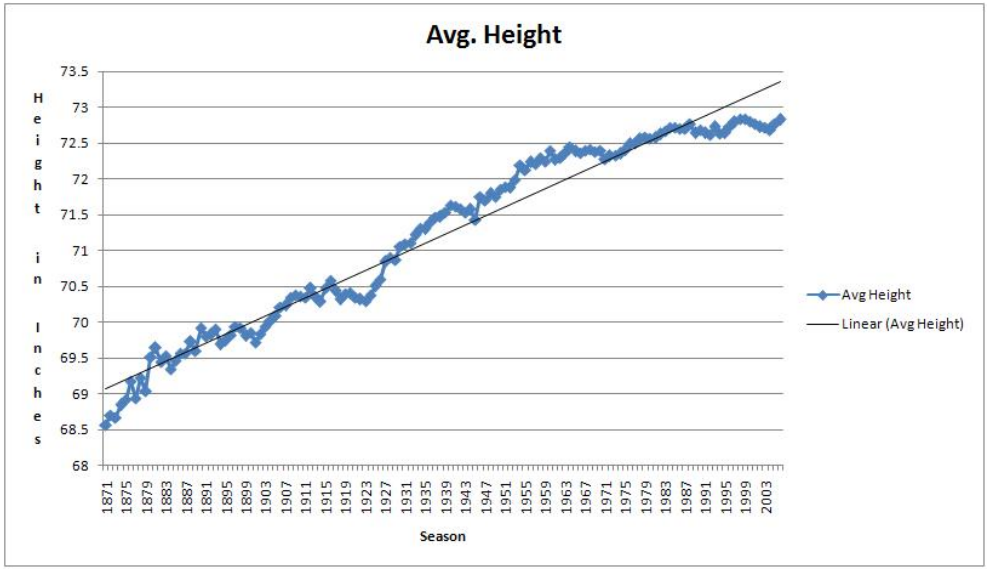
2) How do body parts grow to the right size for each other?

3) How is one body part able to be very different in size in genetically similar animals?

Environment can matter….

e.g. constrained plant growth

Good and bad nutrition in humans including foetal transfusion syndrome.



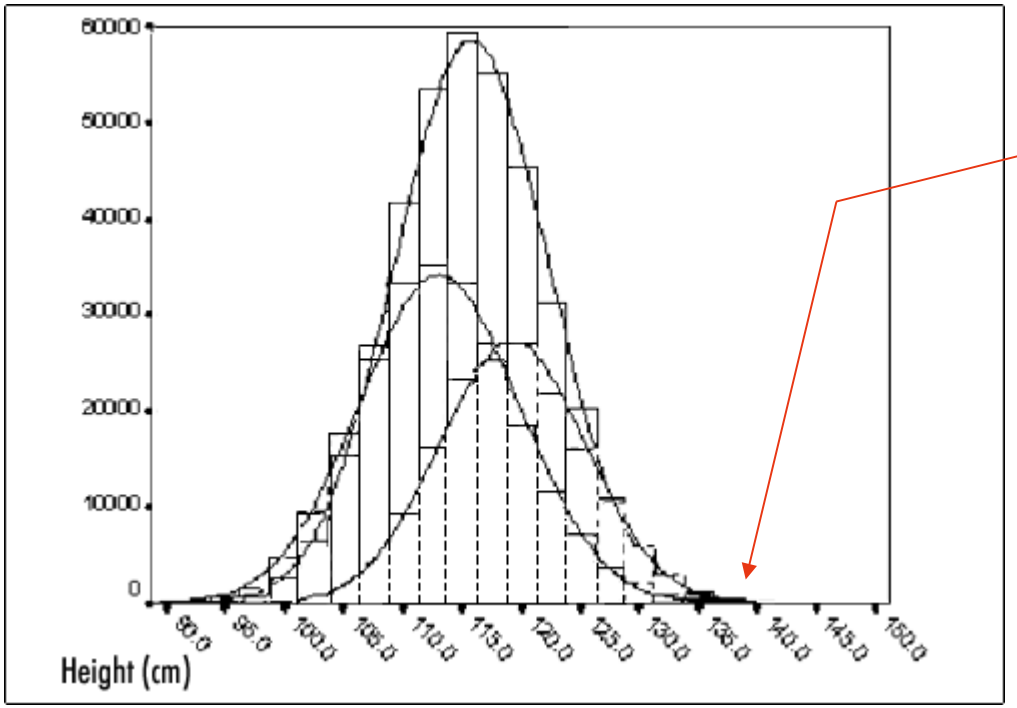
Nutrition and freedom of disease affects overall growth

Foetal transfusion syndrome:

Monozygotic twins sharing a placenta can make deep anastomoses between their placental blood systems, such that one twin receives disproportionately more nutrient than the other.

But as a rule of thumb…

- Animals have a clear 'maximum size' for a species, plants and fungi may not



max

3 human races

Size is also clearly genetic control: it can vary reproducibly in different races of the same species (when both are given *ad lib* access to food etc)

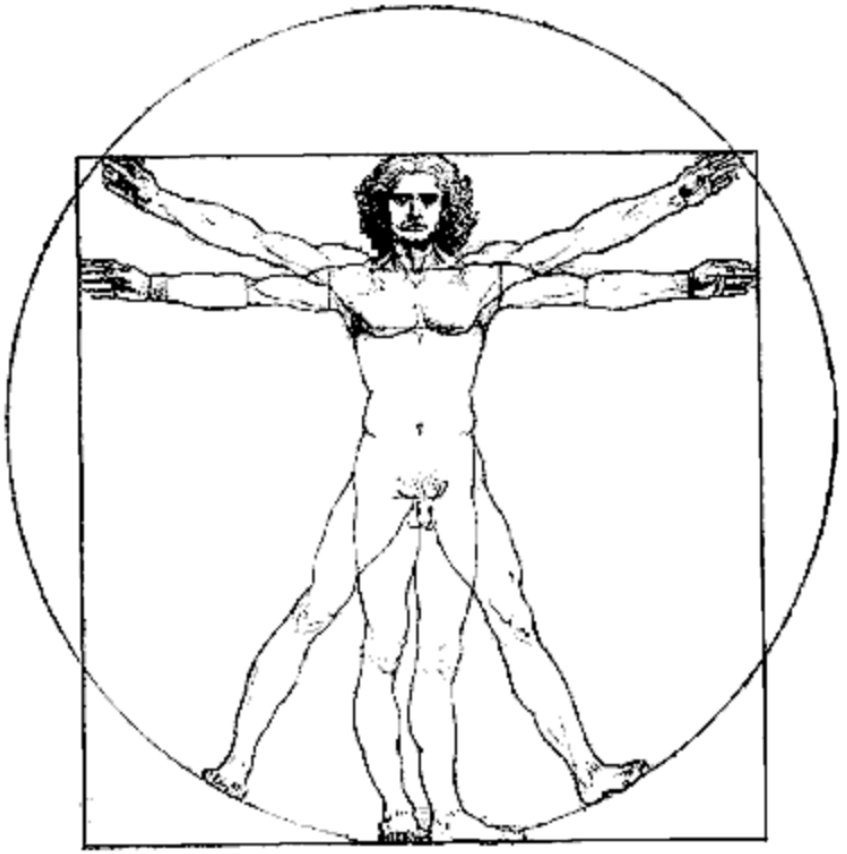
Within a species, the two sexes can show marked differences in adult size ("sexual dimorphism")

Internally, too, everything is (has to be) in proportion:

if it were not – if one organ were too small to serve the needs of others that depend on it – the body would be in trouble.

We will explore this more in Lecture 4.

Vitruvian Man



span of the out-stretched arms = height

distance from hairline to chin = 10% height

elbow to the tip of the hand = 25% height

length of foot = 1/6 height,

length of an ear = 1/3 length of the face

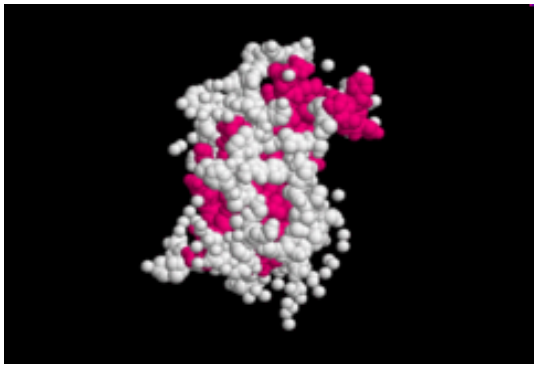
etc, etc

How is this growth control achieved?

As so often happens in medical science, our first clues came from examining outliers – exceptions to the usual norms of size and proportion.

Pituitary tumours are associated with gigantism

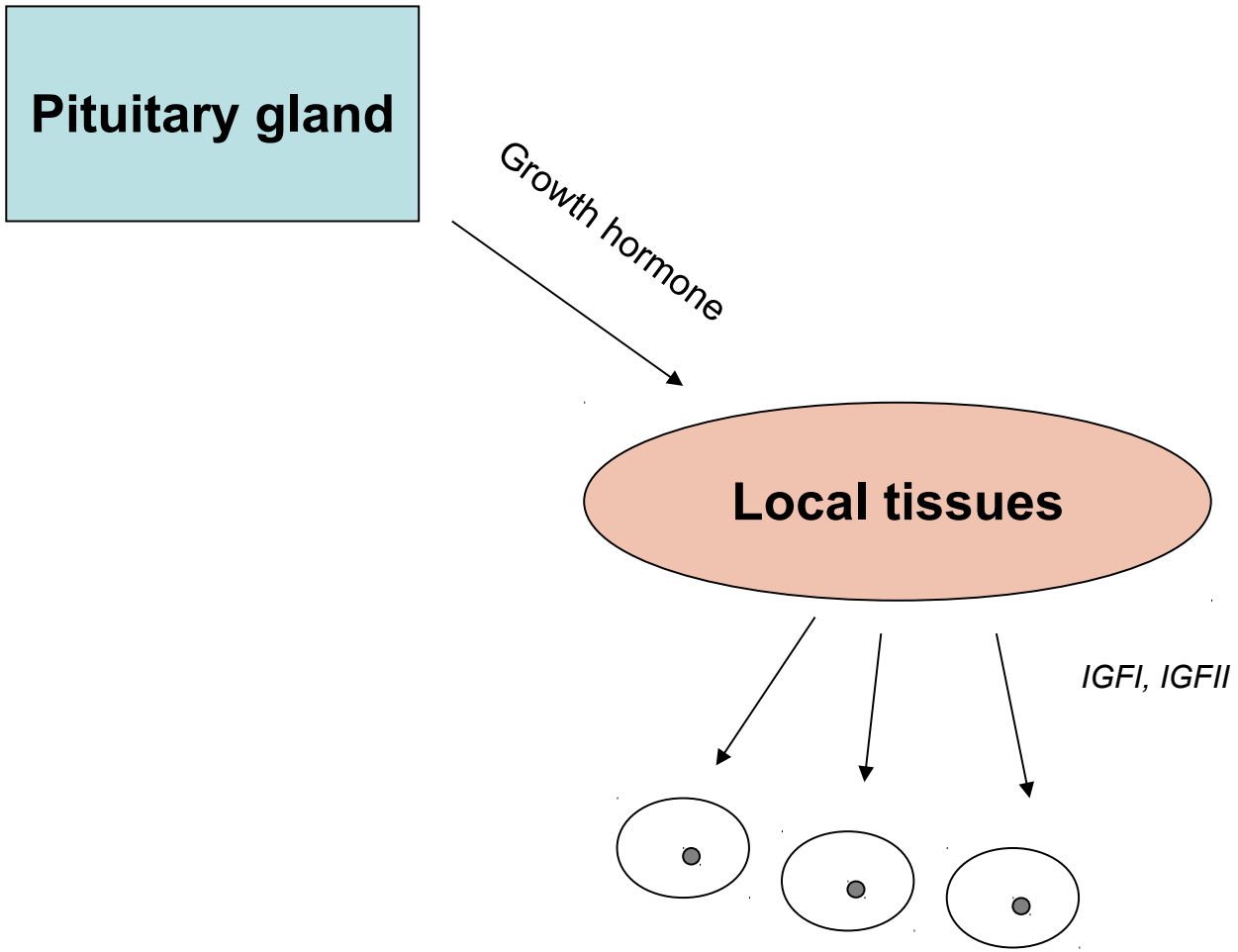
Anna Haining Bates and her parents (who are normal sized)

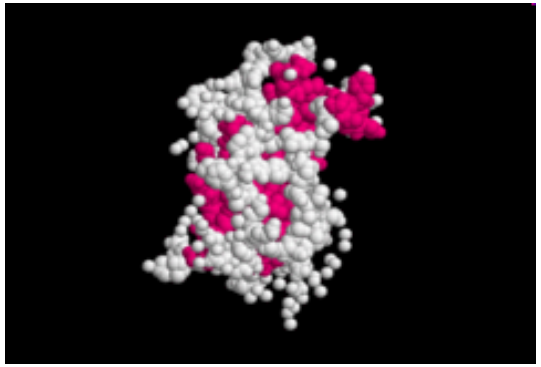


Growth hormone

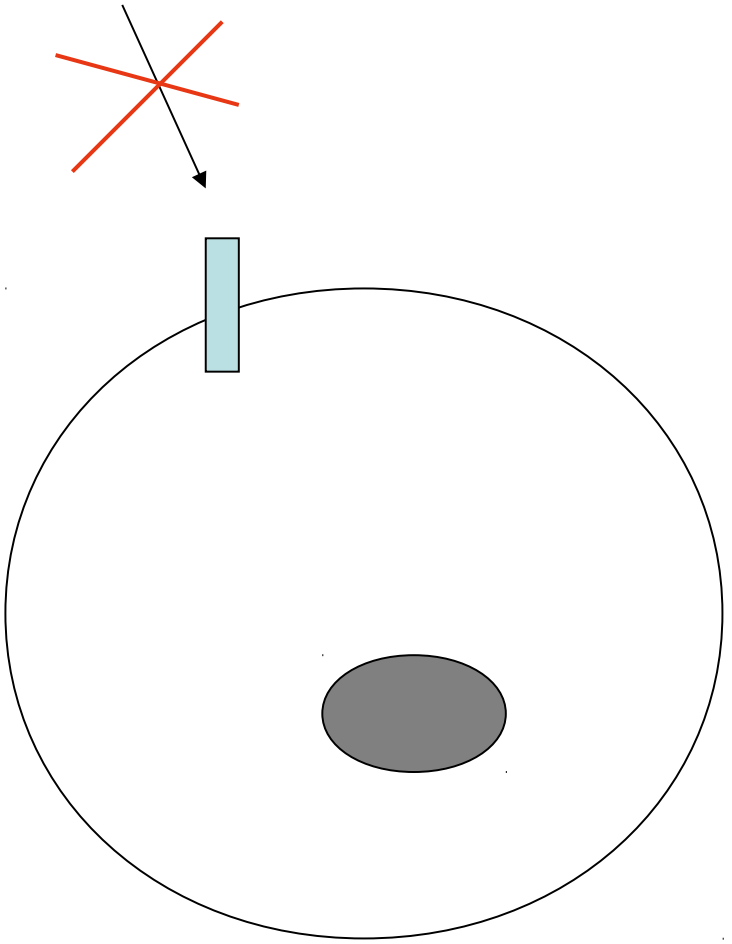
Image credits: wikimedia commons

Mammalian body size

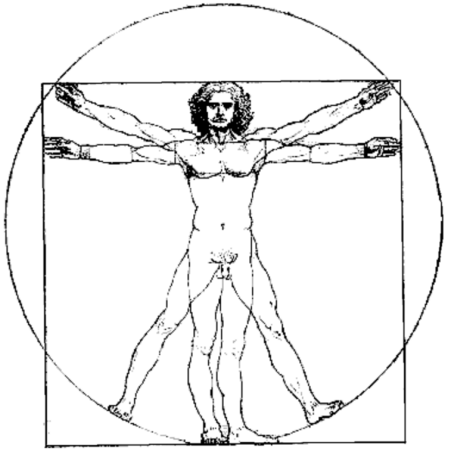




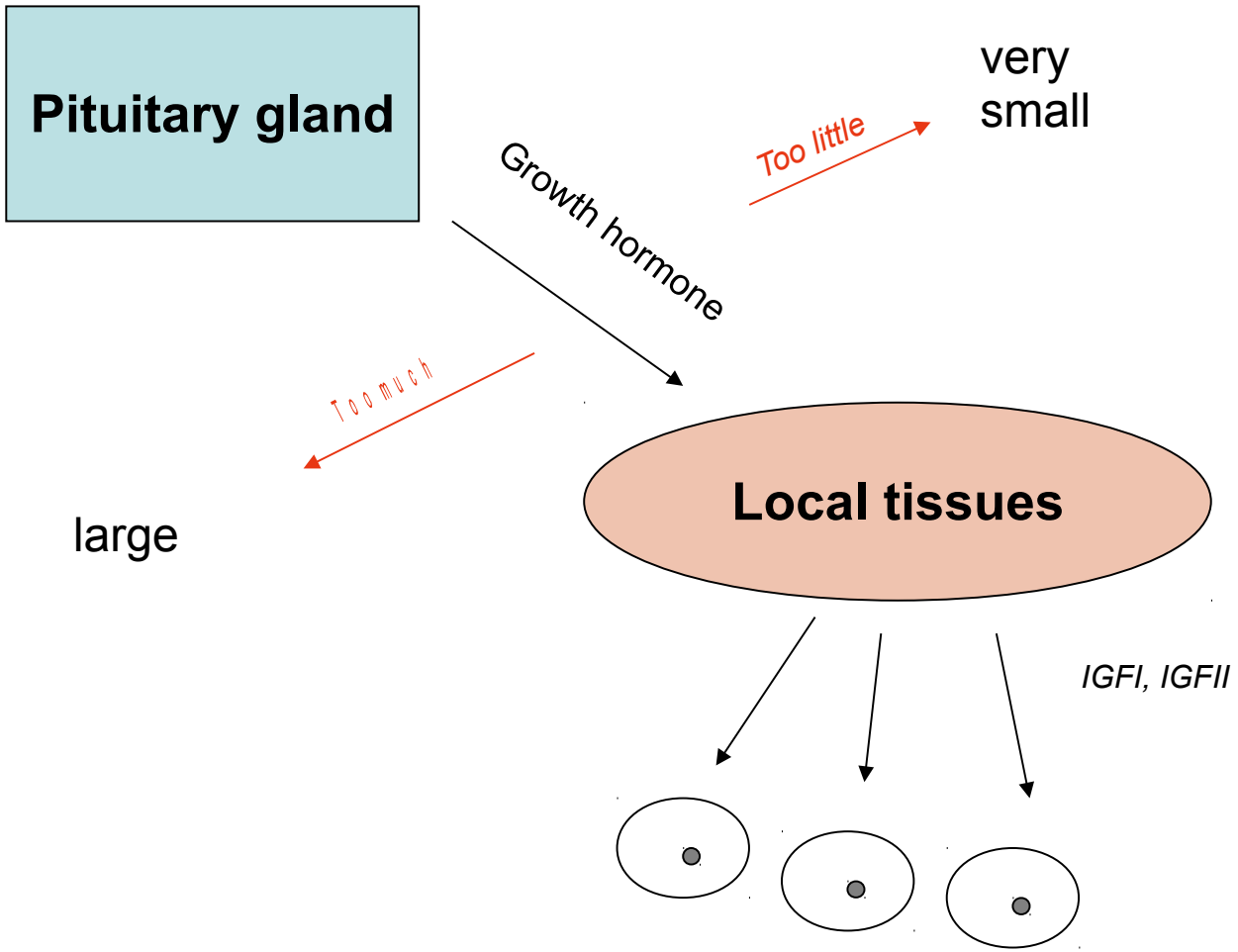
Growth hormone



Laron syndrome – small but in normal proportions.

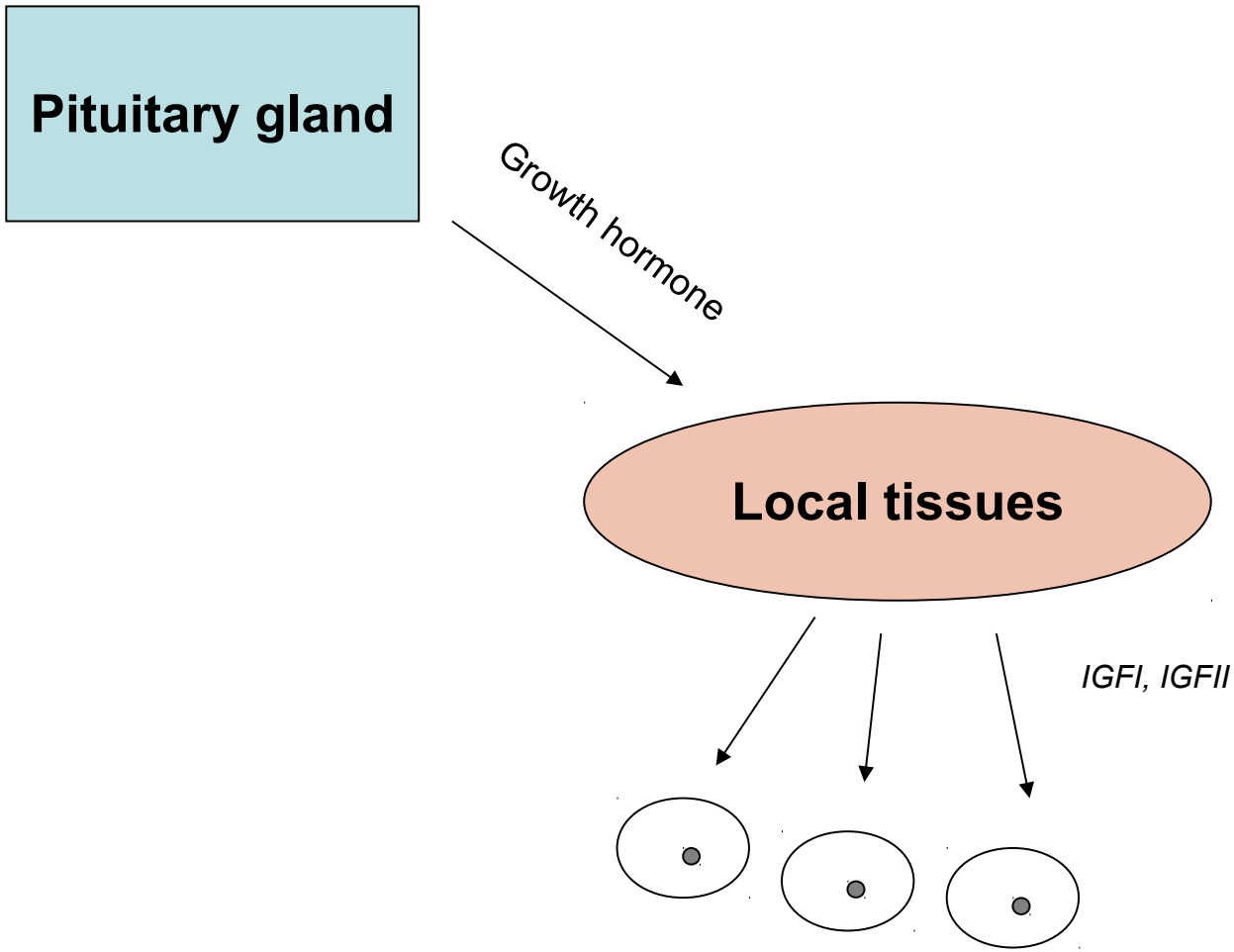


Mammalian body size



Growth hormone itself affects post-natal muscle growth directly, but other tissues only indirectly.

Mammalian body size



Single knockouts are small, double knockouts are very small (often too small to live).

Rabbit leg experiment

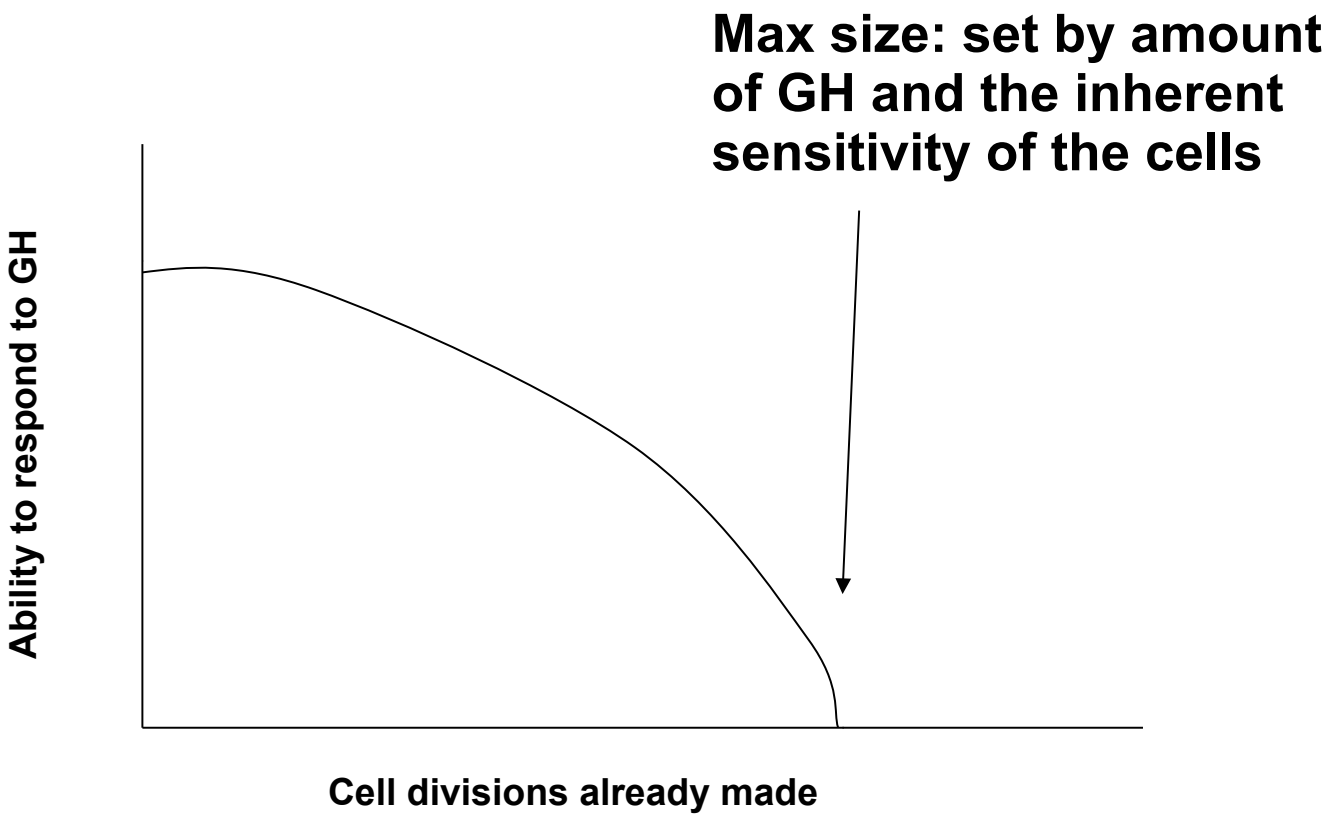
- Inhibit the growth of *one* leg of a young rabbit
- Contralateral leg grows normally (-> lop-side bunny)
- Release the inhibition -> inhibited leg catches up.

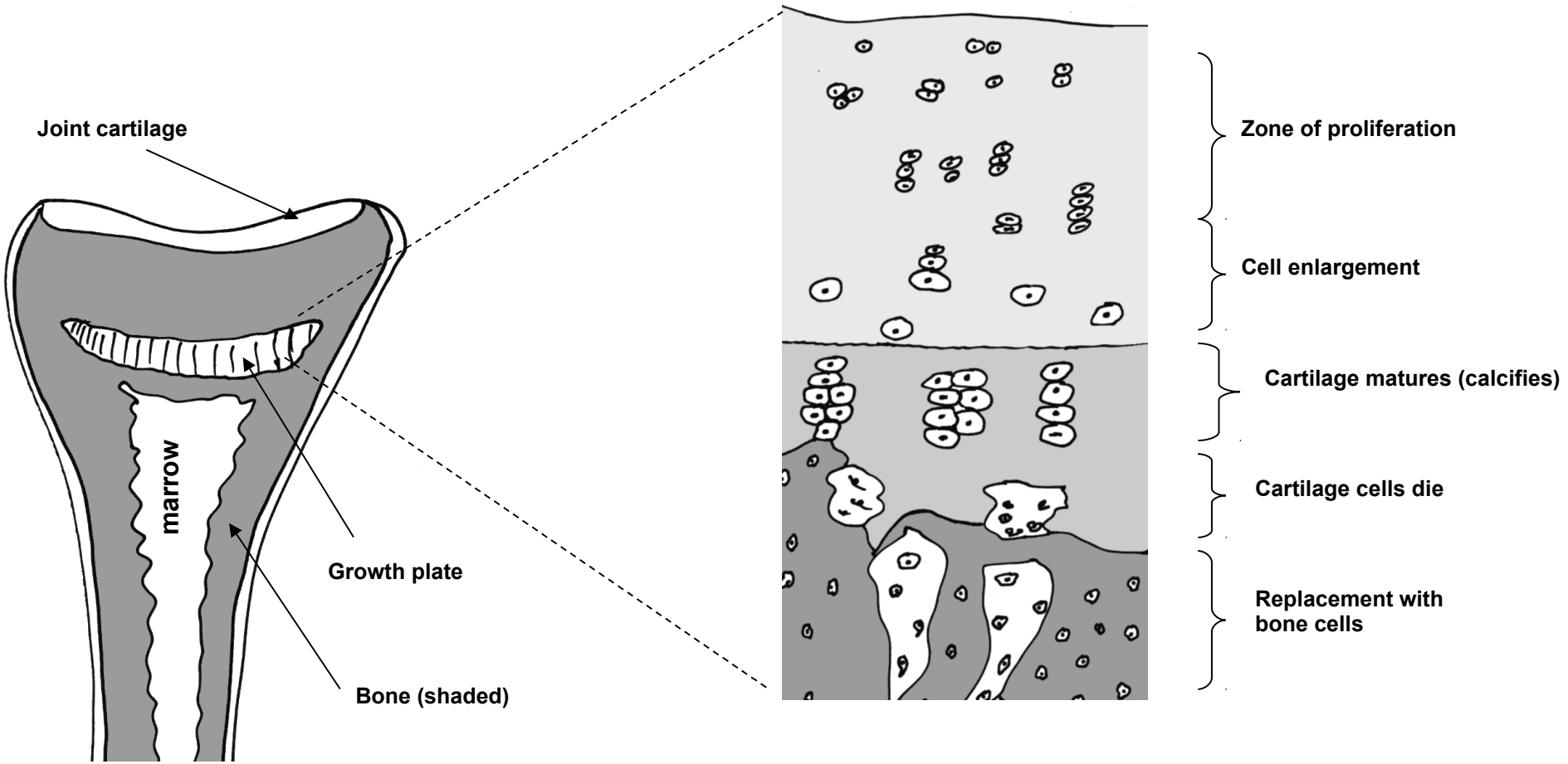
-> The leg 'knows' how big it must be (it is not just a matter of grow until time x)

Possible explanation

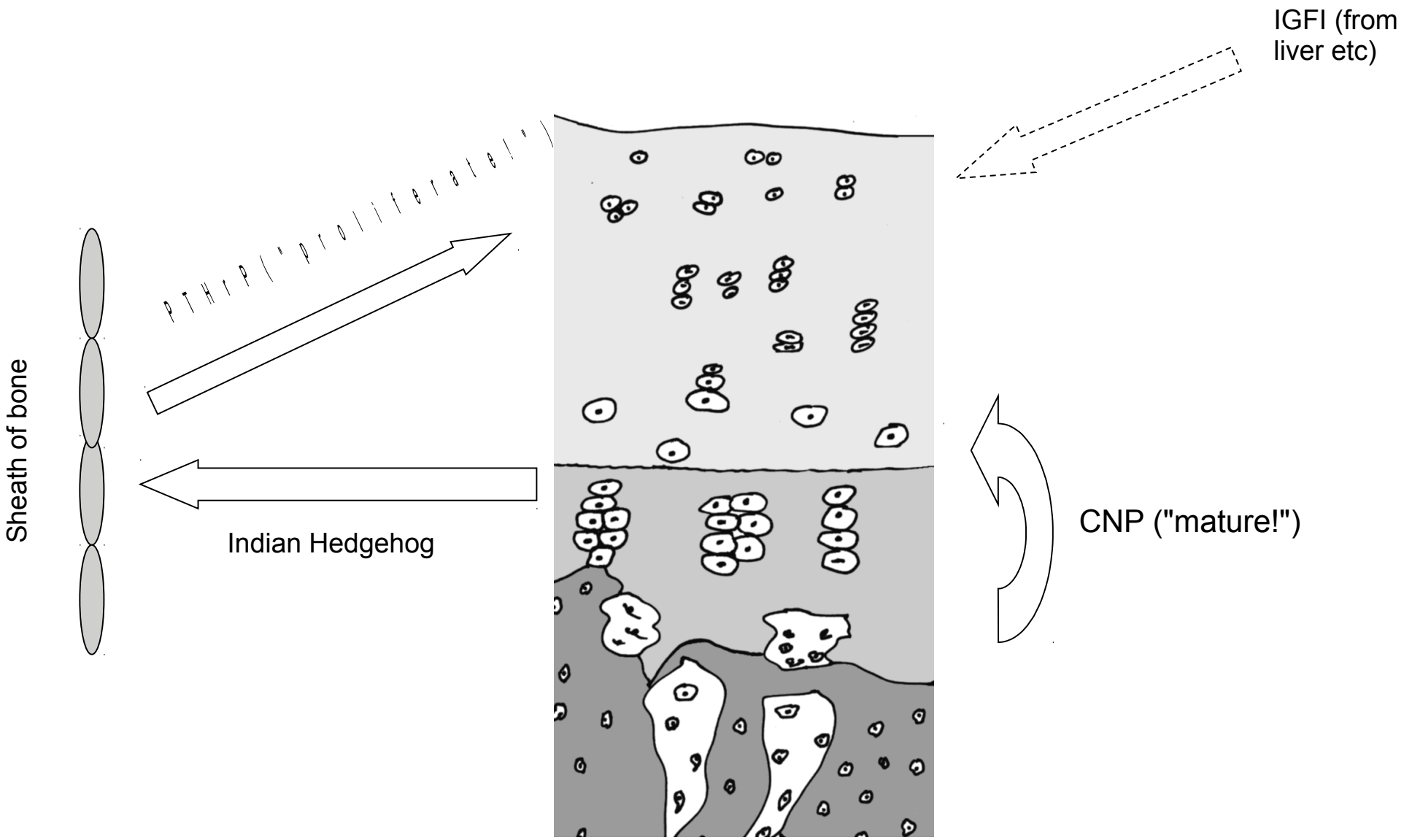
- The ability of the growth plate of the long bone to respond to GH declines with the number of cell divisions it has made.

(the stalled leg made fewer divisions early, so retained the ability to "listen to" GH and catch up.)

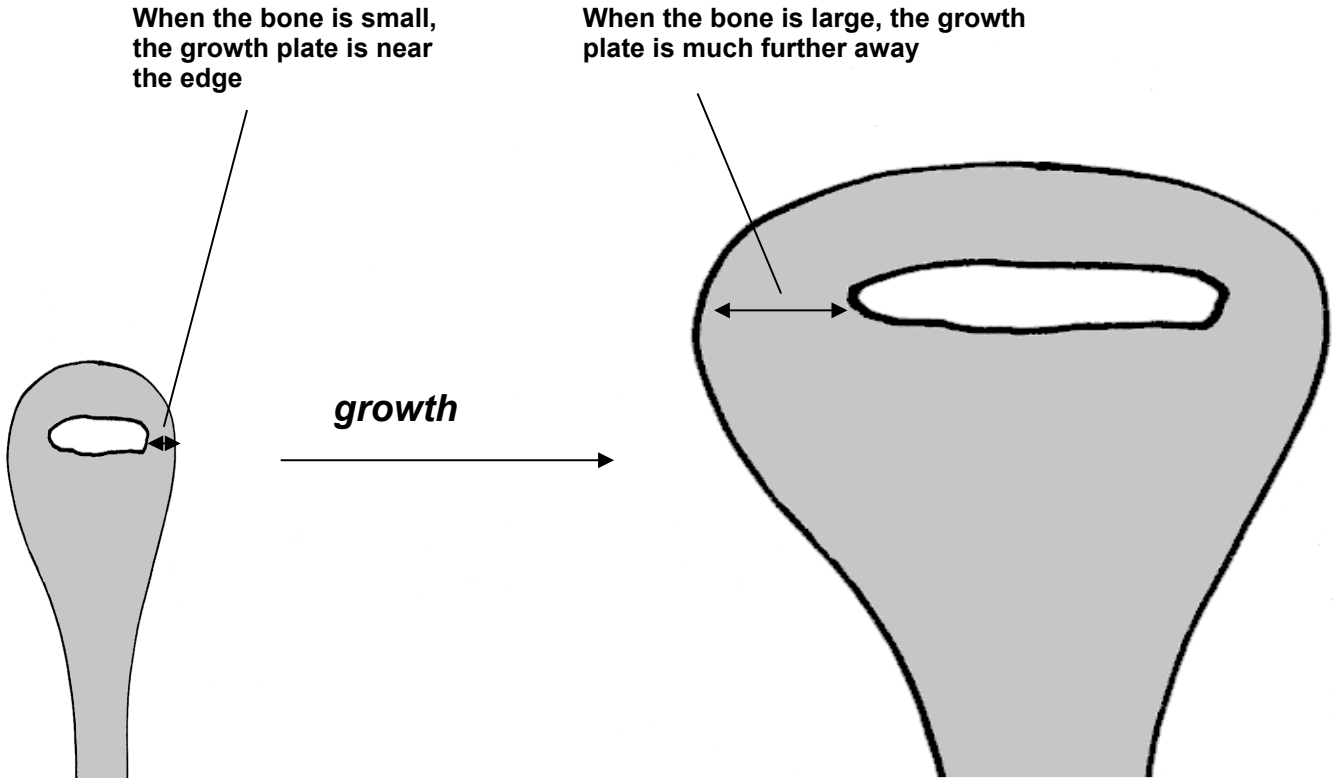

Max size: set by amount of GH and the inherent sensitivity of the cells
Ability to respond to GH
Cell divisions already made


Joint cartilage
marrow
Growth plate
Bone (shaded)
Zone of proliferation
Cell enlargement
Cartilage matures (calcifies)
Cartilage cells die
Replacement with bone cells

The growth plate maintains itself using internal and external signals

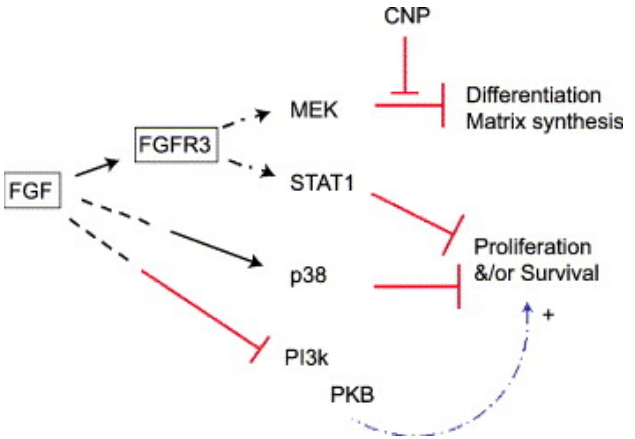


A possible explanation for rate of growth falling away with size



Achondroplasia: activating mutation in FGFR3

FGF signalling via FGFR3 usually inhibits both proliferation and differentiation of chondrocytes (it's complicated).



Activating mutations in FGFR3 cause growth plates full of chondrocytes, and premature closure of the growth plates.

In contrast, *fgfr3*-/- mice show over-long bones

References: Pubmed PMID: 17950653, 17630040, 15748888

This kind of mutation makes two points;

1) **Some parts of the body keep growing anyway (so it is *not* that every part keep up with every other part)**

2) **The amount of skin, tendon, muscle, etc is still correct for a peculiar shortened limb, so tissues cannot be independent for each other.**