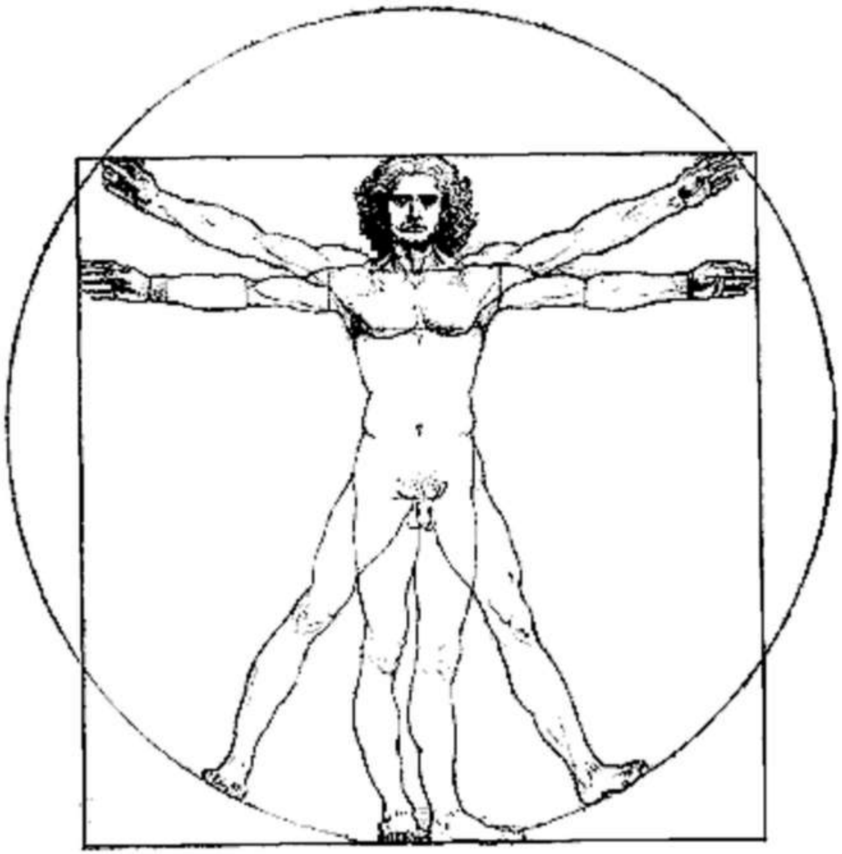
Embryology lecture 4:

A sense of proportion

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,

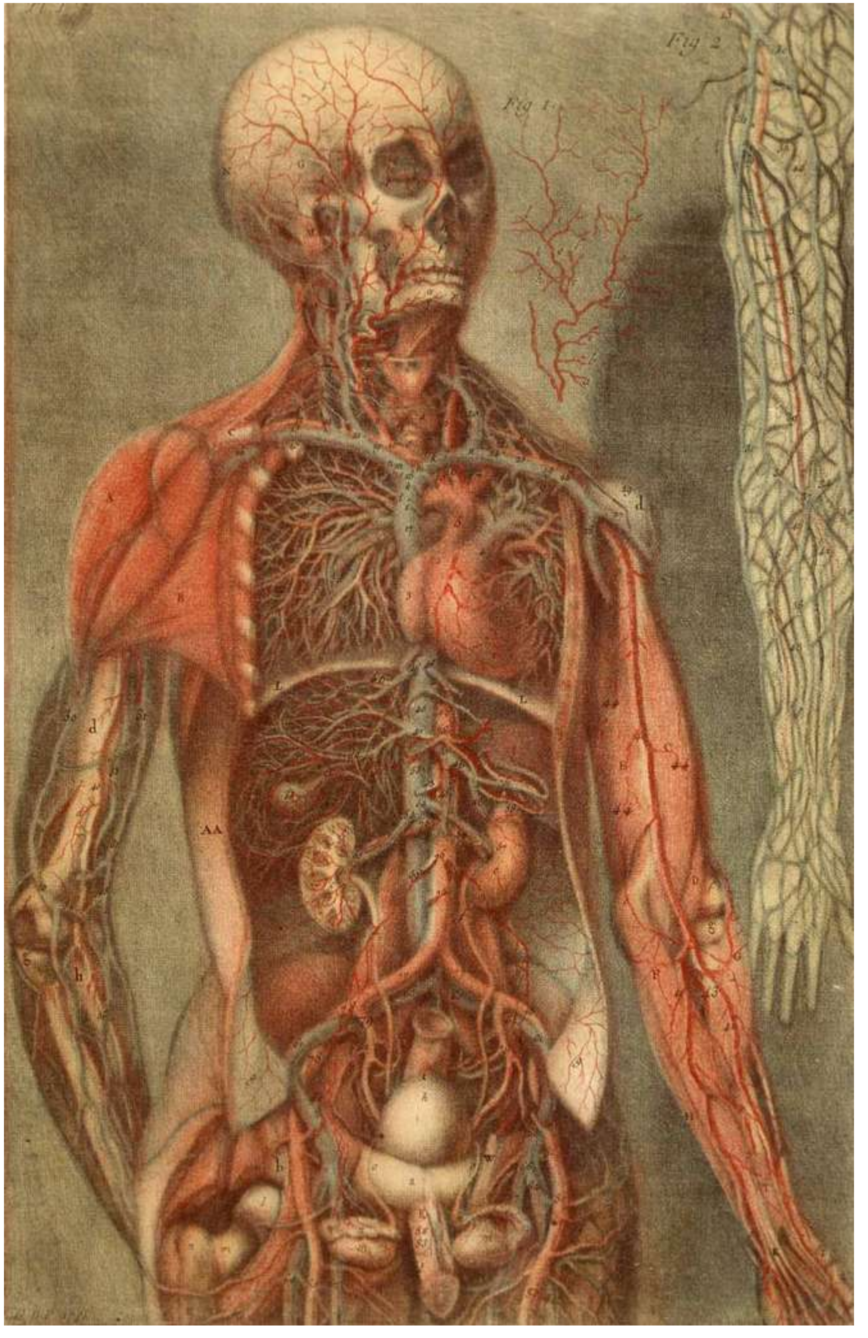
length of an ear = 1/3 length of the face

etc, etc

(don’t bother learning these)

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.



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.

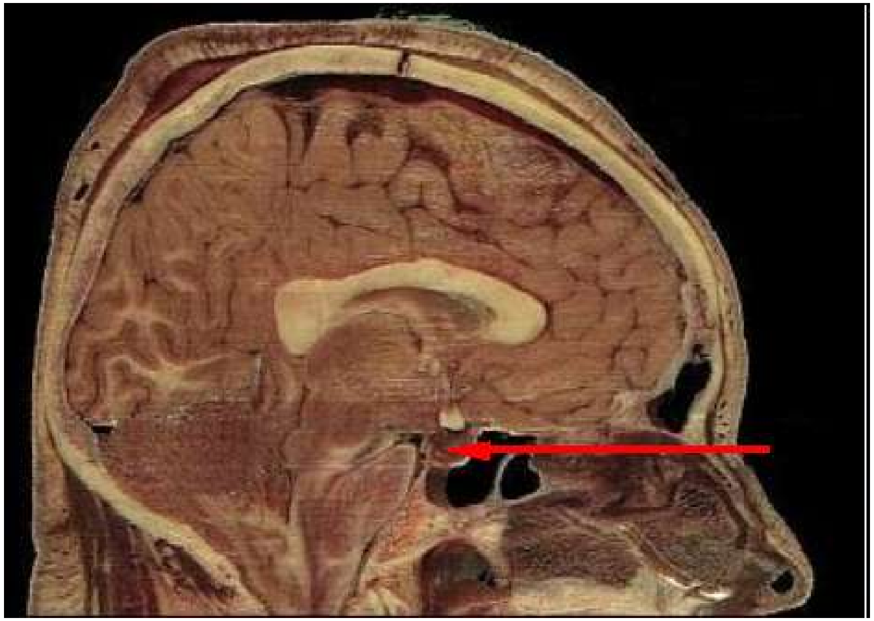
Outliers:

Some are Vitruvian in proportion:

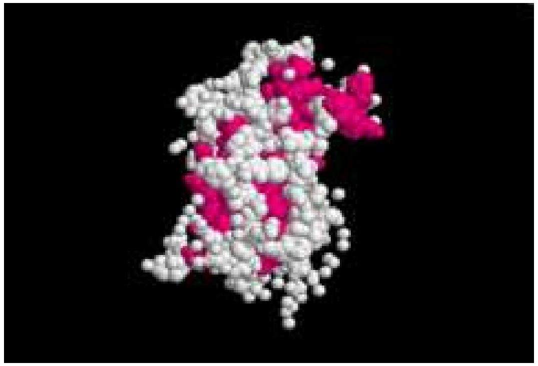
And some are not:

Pituitary tumours are associated with gigantism

Anna Haining Bates and her parents (who are typical in size)



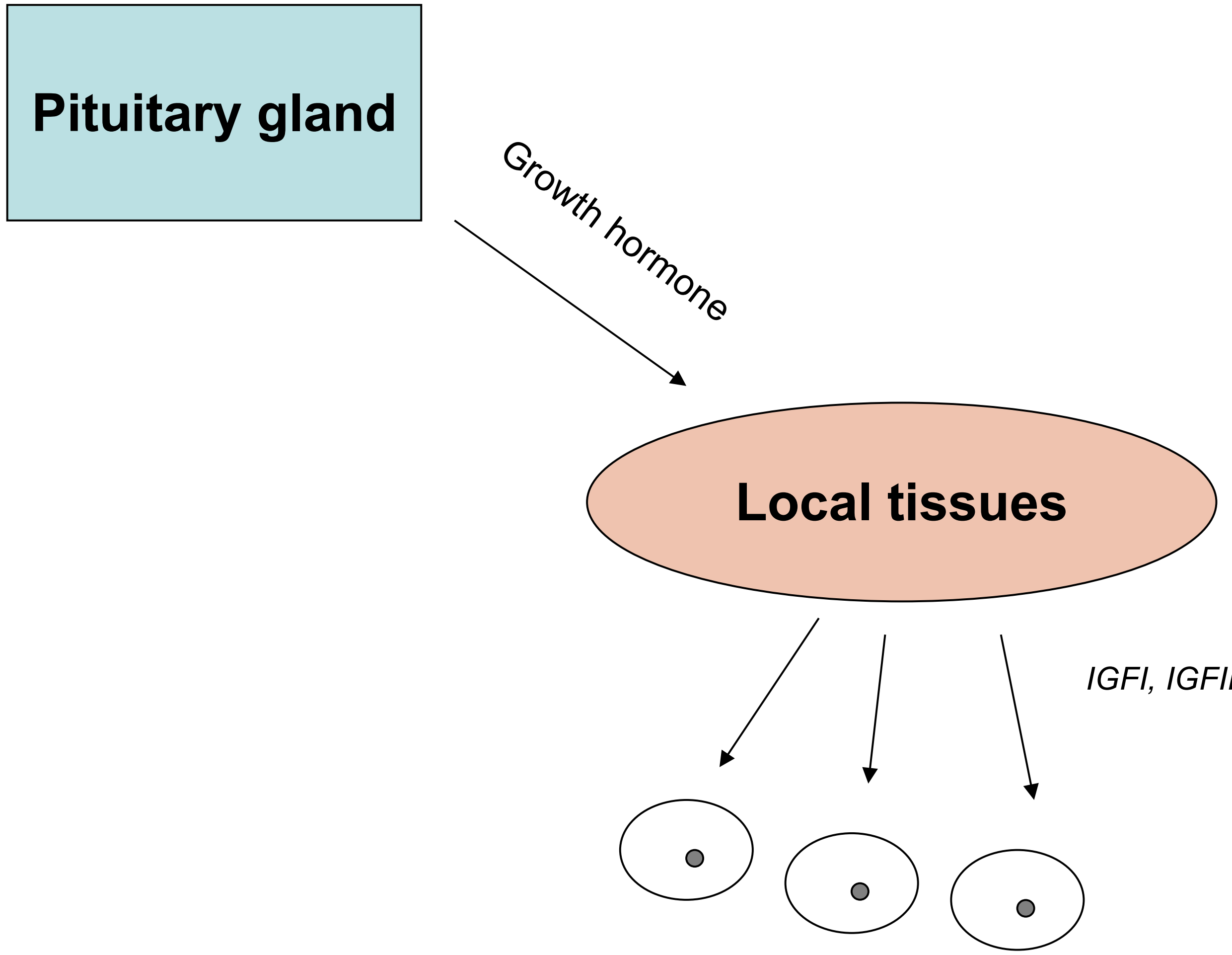
Pituitary

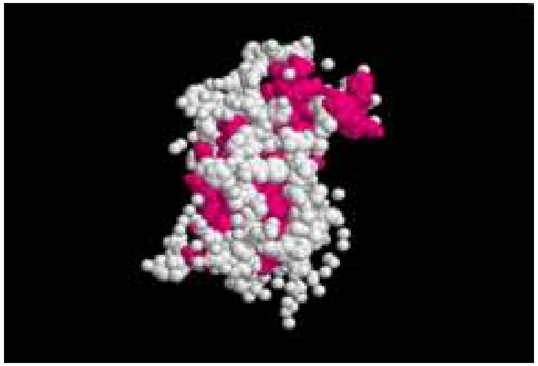


Growth hormone

Image credits: wikimedia commons

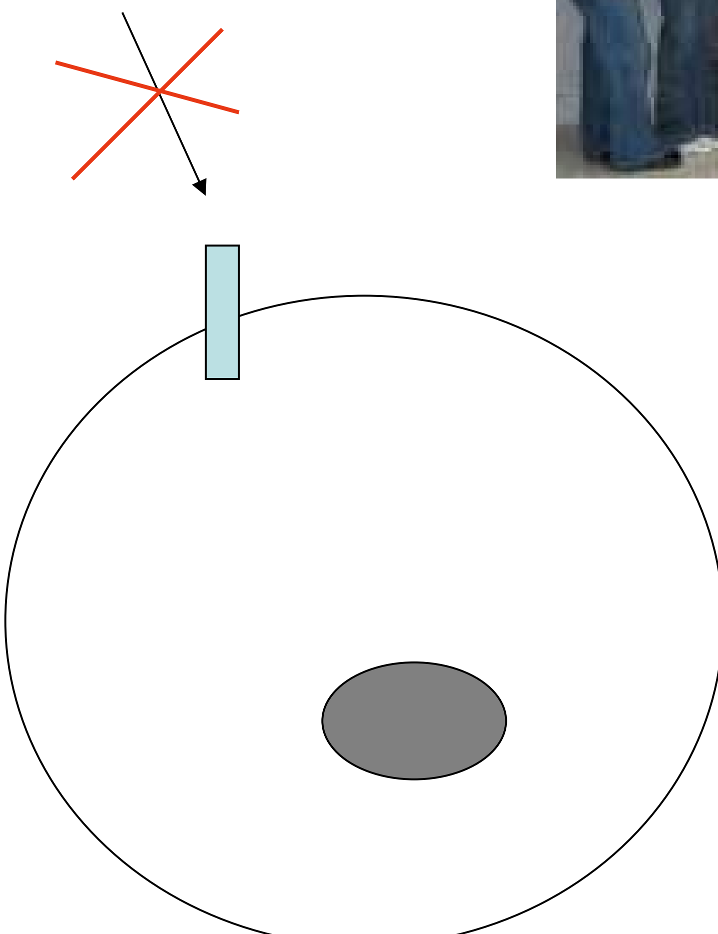
Mammalian body size

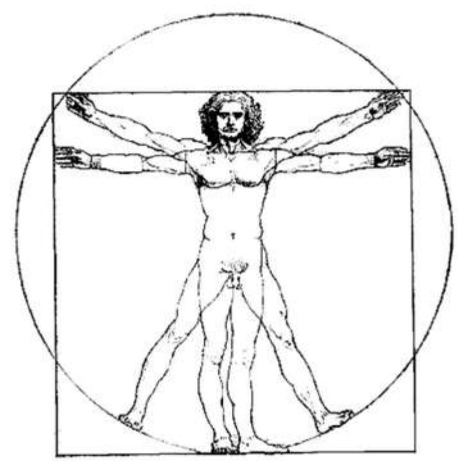




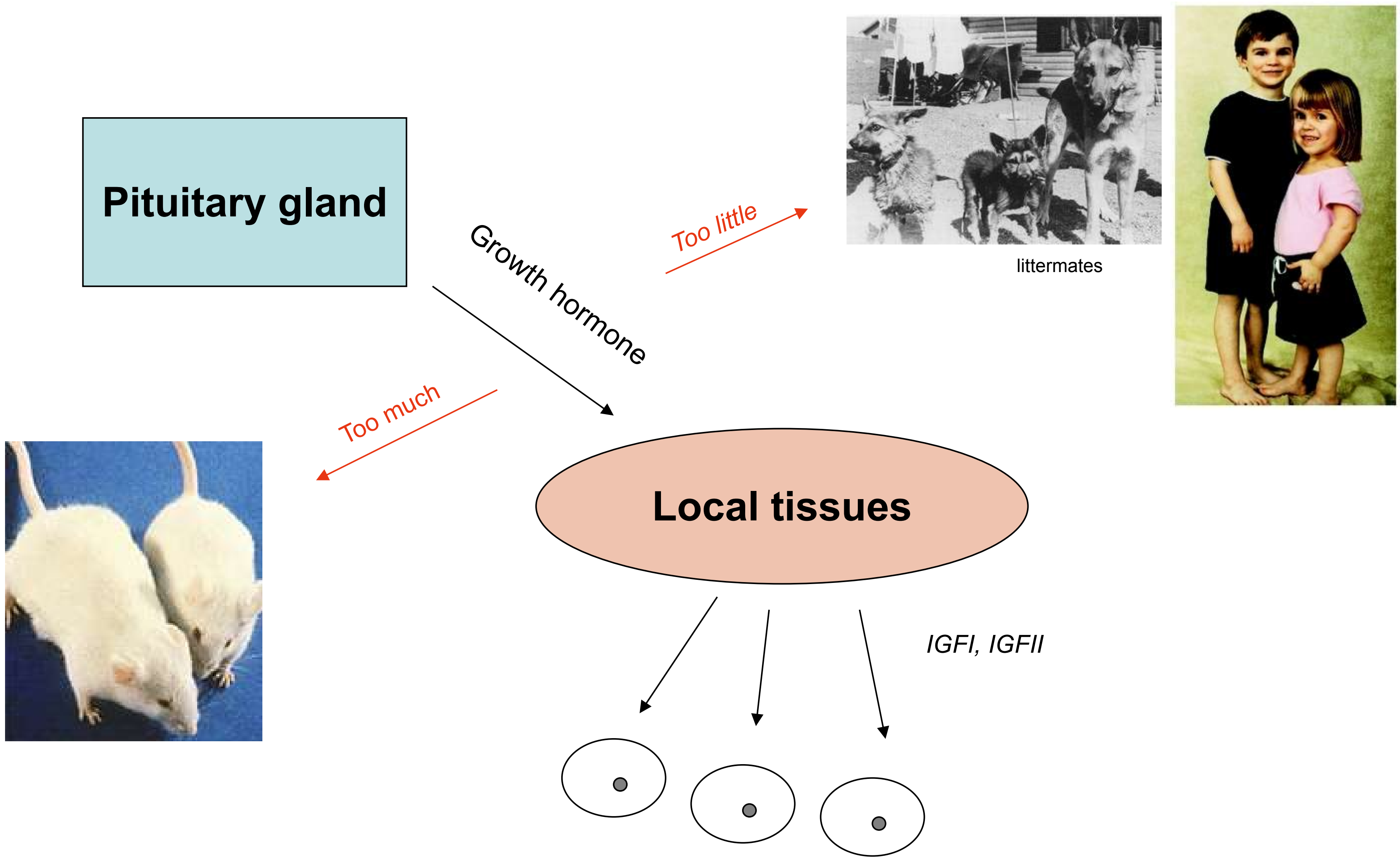
Zvi Laron, and Laron syndrome people.

Growth hormone

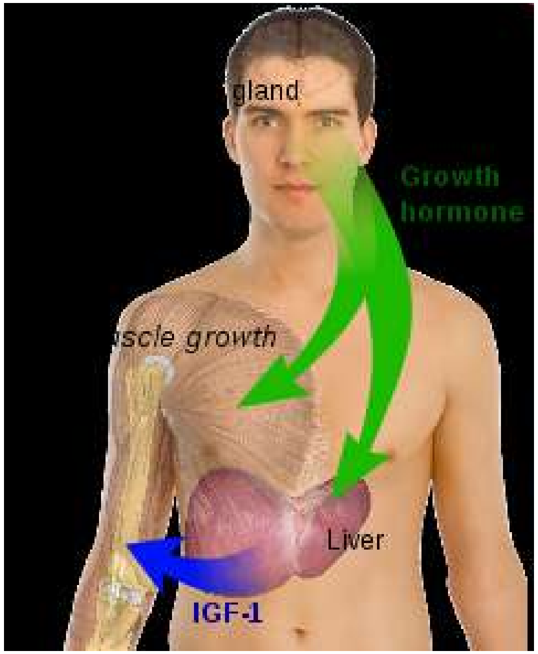




Mammalian body size



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



Mammalian body size

Pituitary gland

Growth hormone

Local tissues

IGFI, IGFII

+/+

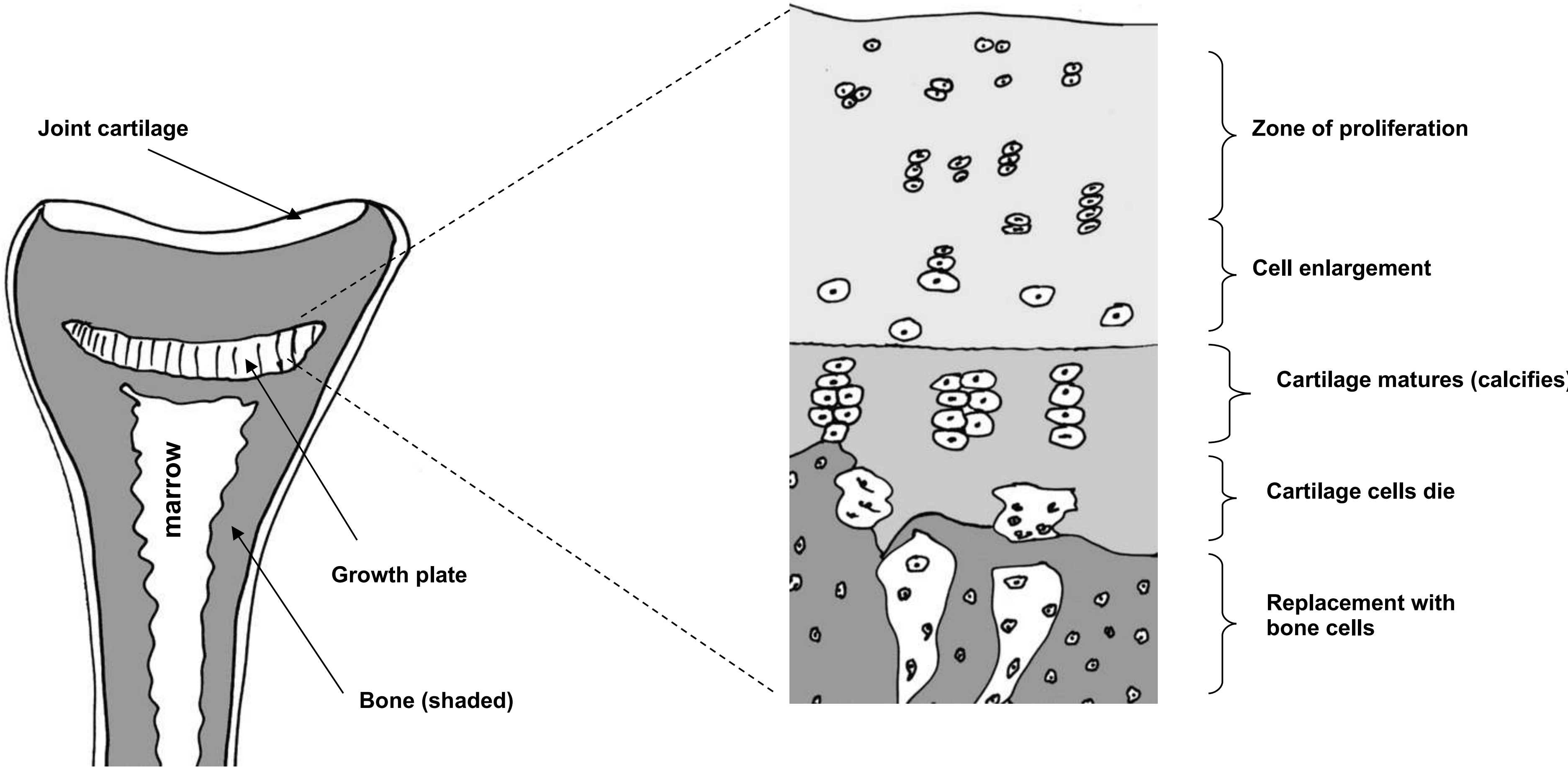
Double KO

limb growth and its limits

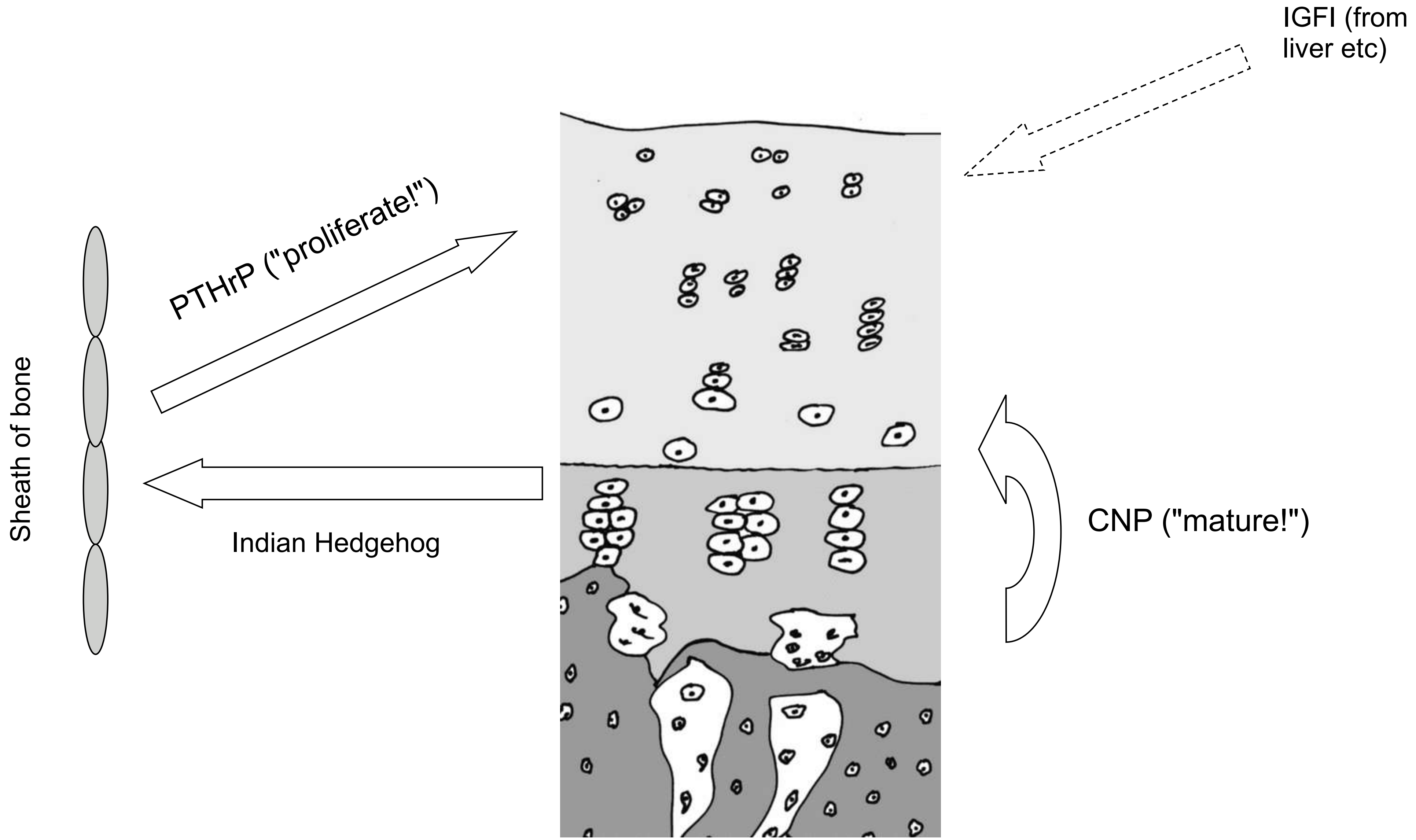
Rabbit leg experiment

- 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)

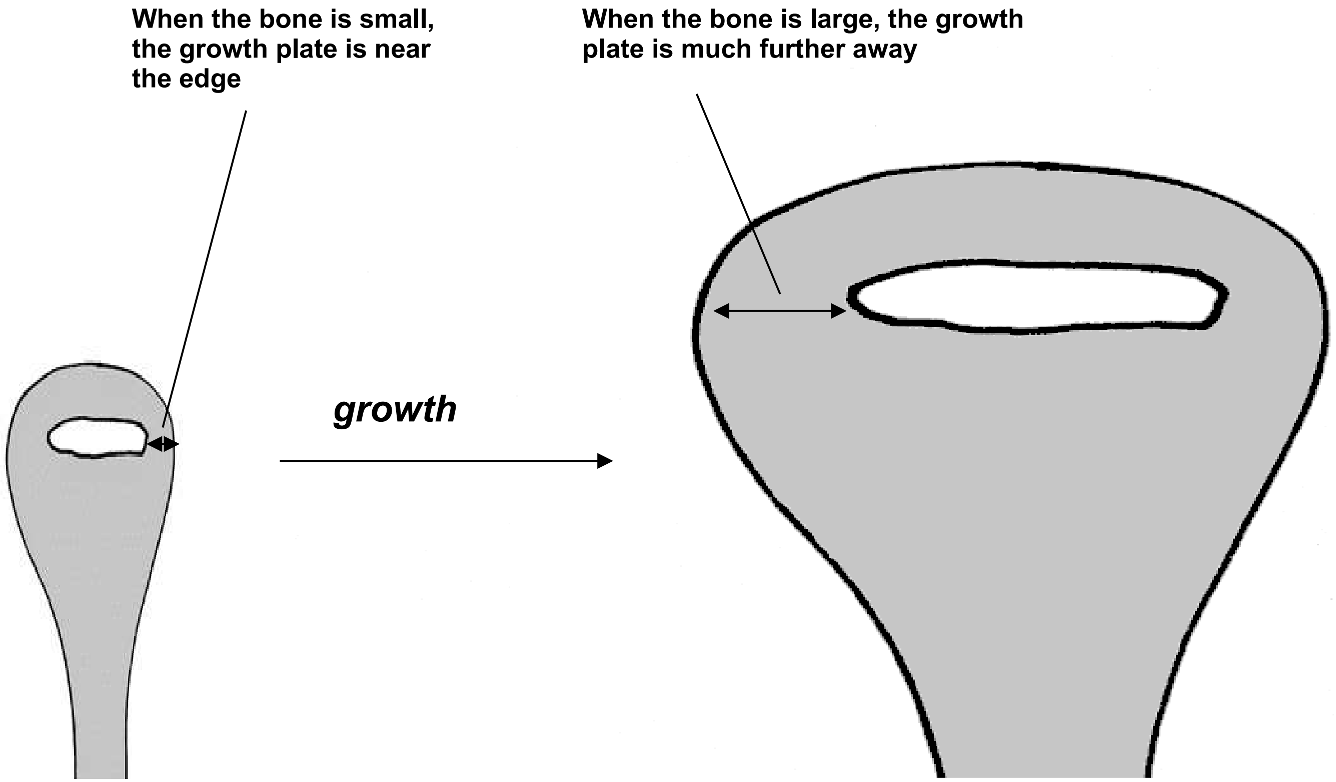

Joint cartilage
marrow
Growth plate
Bone (shaded)
Zone of proliferation
Cell enlargement
Cartilage matures (calcifies)
Cartilage cells die
Replacement with
bone cells

The growth plate maintains itself using internal and external signals



You will not be tested on these protein names: just see the underlying logic

A possible explanation for rate of growth falling away with size



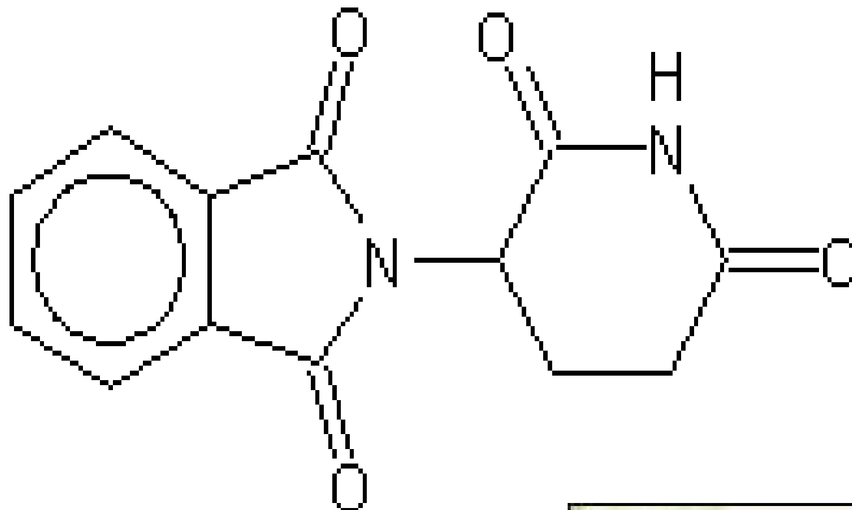
Non-Vitruvian phenotypes

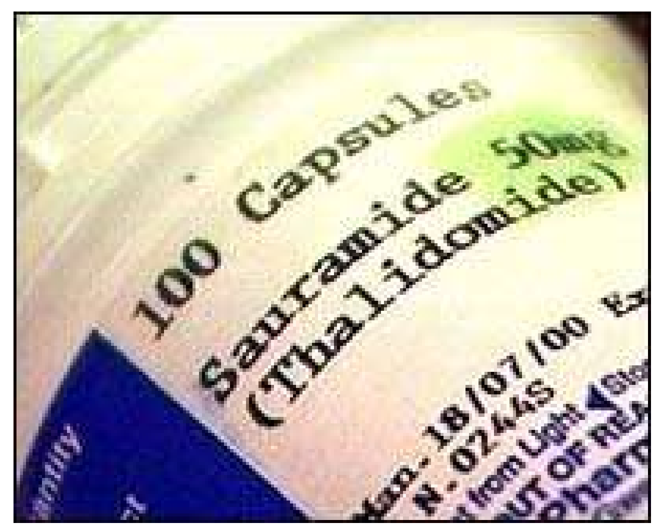
Limb growth has a peculiar vulnerability: it takes place very rapidly, and makes high demands for oxygen.

It therefore needs the vascular system to grow very quickly into the elongating limbs.

Limb growth is therefore uniquely vulnerable to anything that impairs vascular growth.

Anyone recognize this?



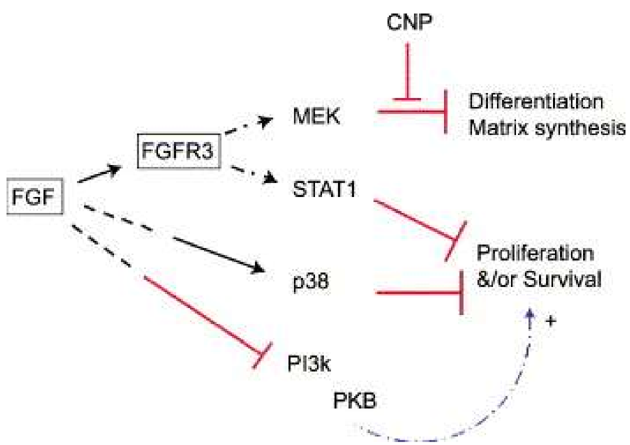


Phocomelia ('seal limb')

How about genetic 'non-Vitruvian' conditions?

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.**

Why is the amount of skin always right for the leg length?

…or any other growth?

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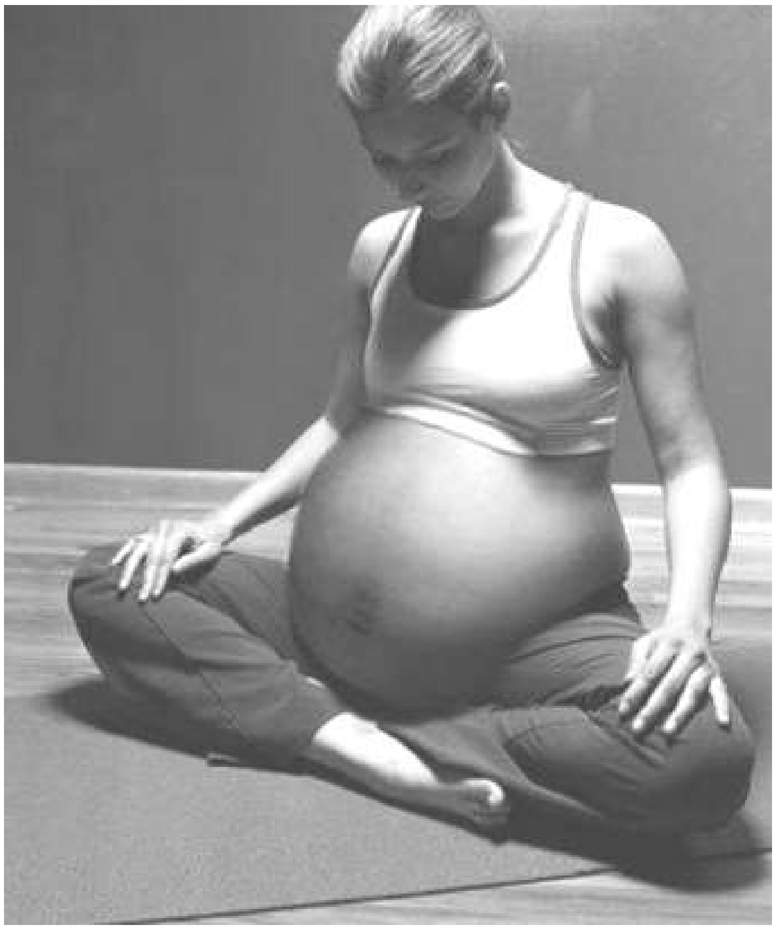
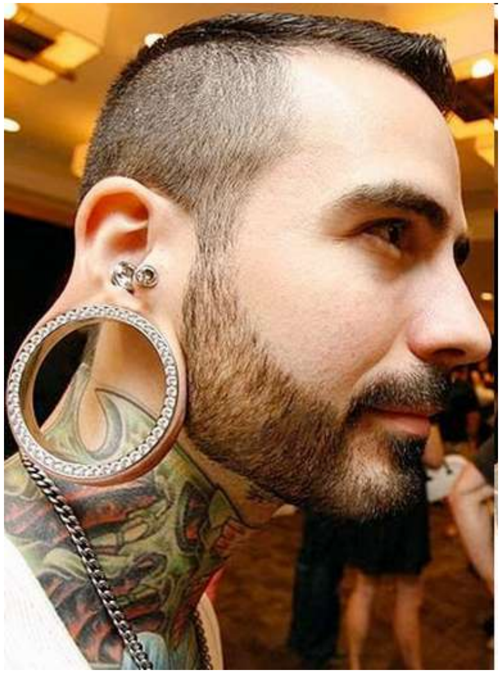
…or any other growth?



Wikimedia commons

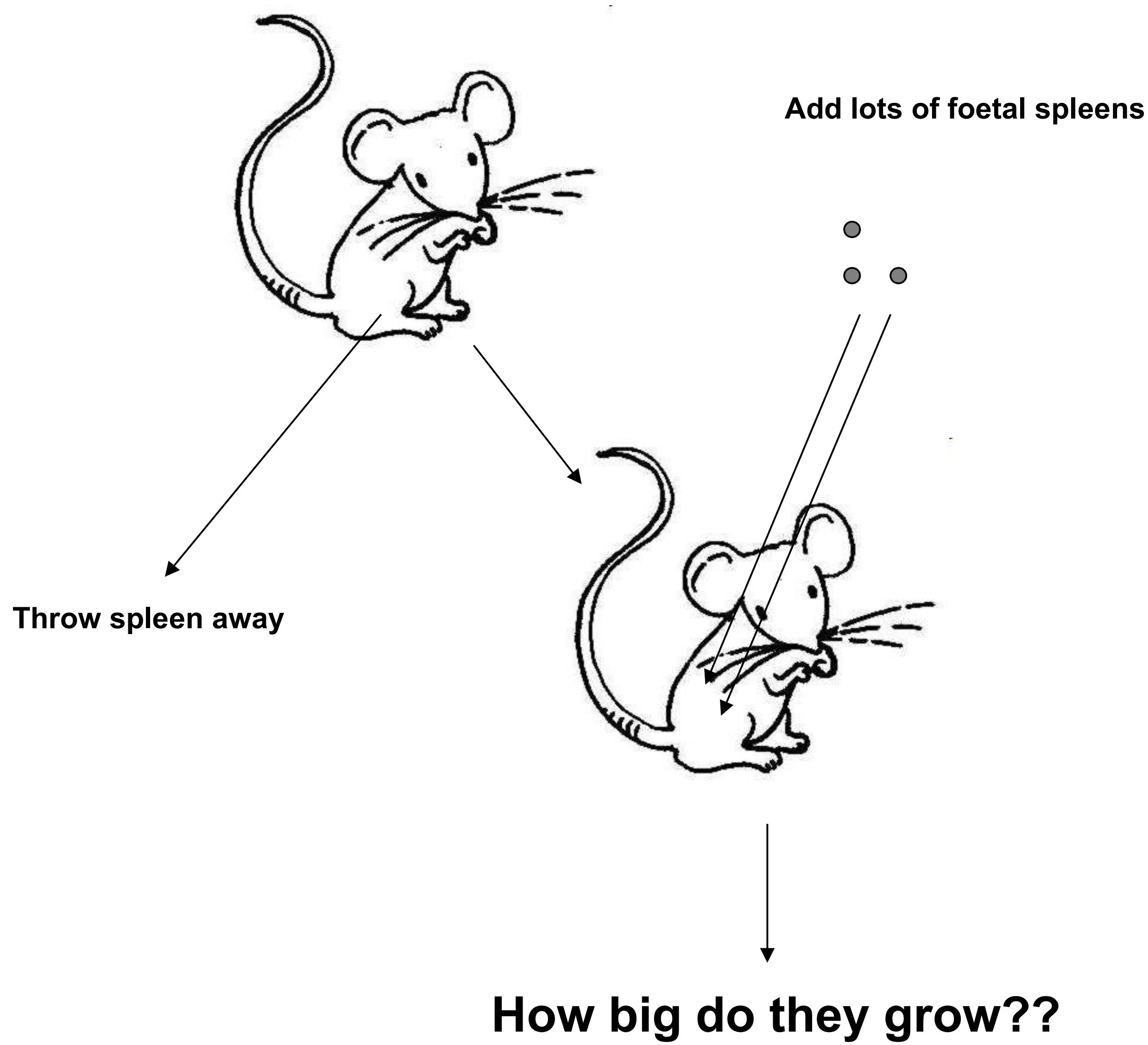
We can get a hint from the fact that applying a mechanical force (excessive stretch) to human skin drives skin growth



How about 'mechanically isolated' organs?

Spleen:

TOTAL mass = mass of one normal spleen.

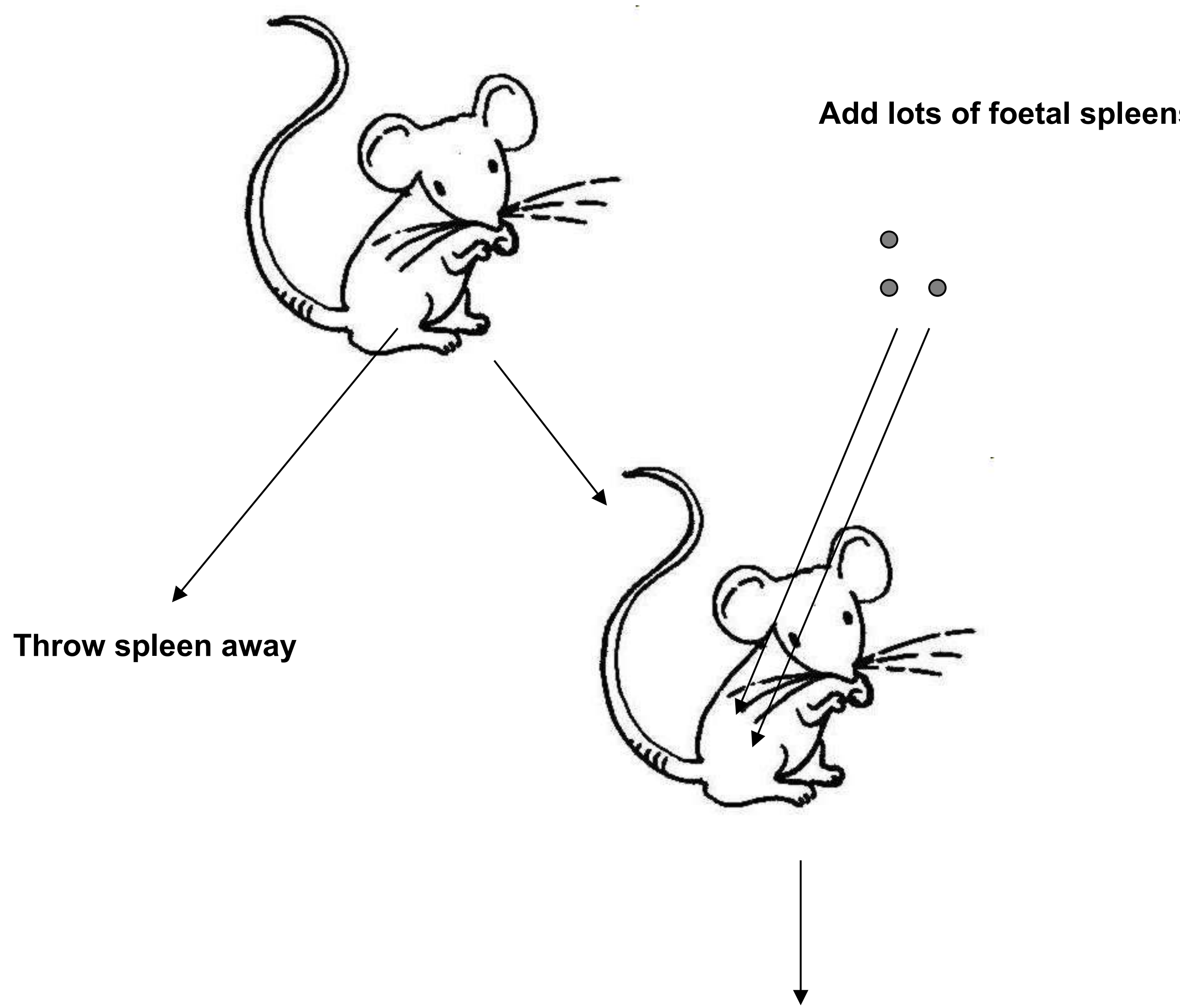


How about 'mechanically isolated' organs?

Spleen:

TOTAL mass = mass of one normal spleen.

But if you do it with a THYMUS, each one grows normal size



How big do they grow??