MBChB Yr 2: renal module

Module Organizer info:

Name:	Prof. Jamie Davies
Role:	Professor of Experimental Anatomy
Preferred mode of address:	'Jamie' or 'Professor Davies'; your choice
Preferred pronoun:	(I don't really care).
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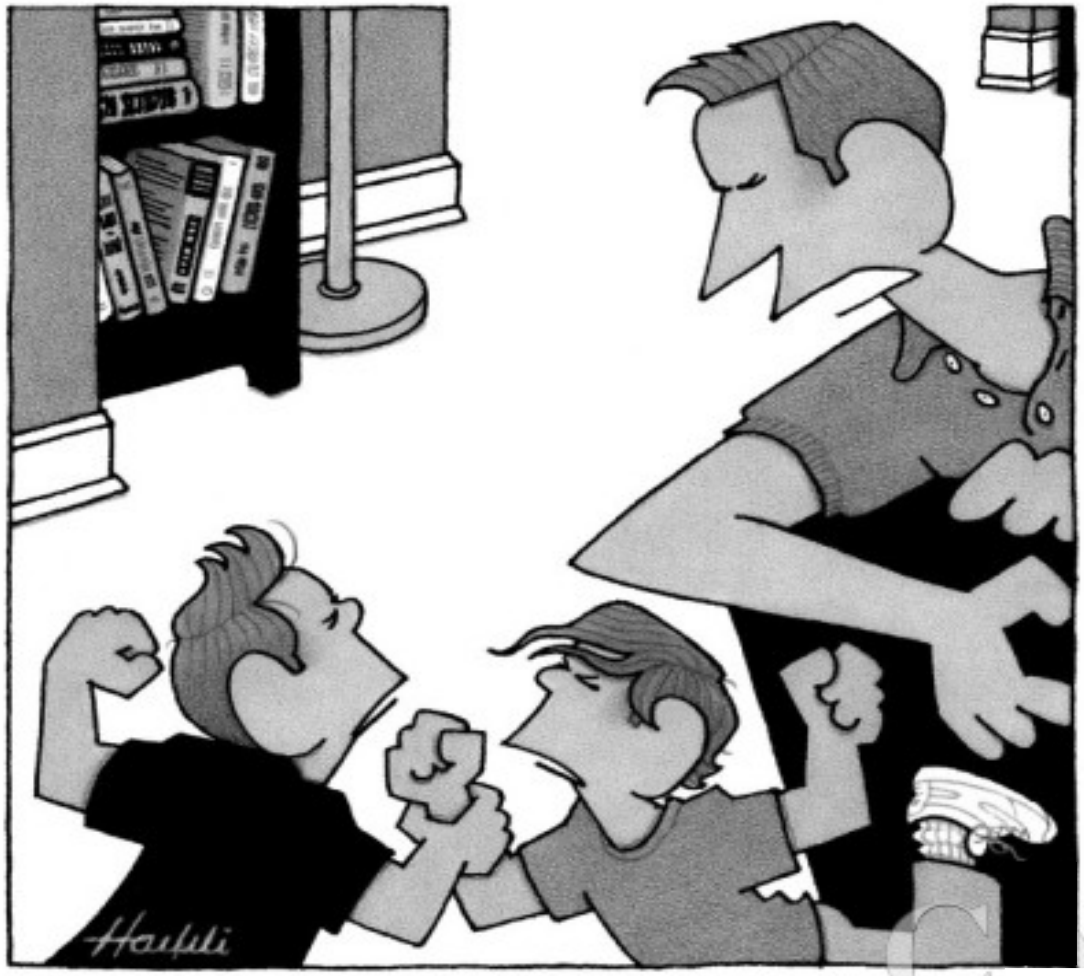
Outline of the module (actual order of events may differ for you).

Rena/ Uro anatomy and physiology	5 lectures	Jamie Davies
	1 workshop (IRT)	Jamie Davies & May Sallam
Meaning of Proteinurea	1 Lecture	Peter Mathieson
Clinical aspects of Na^+/ H_20	2 lectures	Paddy Gibson
Acute and chronic renal disease	3 lectures	Jeremy Hughes and John Neary
Renal transplantation	1 lecture	Jeremy Hughes
Drugs affecting kidney	1 lecture	Simon Maxwell
Acid-base disorders	1 lecture	Peter Rae
The Lower Urinary Tract	1 lecture	Alan McNeil
UTIs	1 CAL, 1 lecture	Clinical skills team
Urinalysis and intimate examination	1 practical	Clinical skills team
Science to Clinical Practice	1 session	Jeremy Hughes et al.



"Listen up and listen up good, 'cause I'm only going to say this a million times."

Note: your downloadable slides use these call-outs to link to extra information (eg things explained in a different way to the way I explain them in these lectures). Use the QR code if using paper copies, or click if using electronic – they go to the same place.

click

http://golgi.ana.ed.ac.uk/coursenotes/mbchbyr2/renal.html

Cartoon: *New Yorker*

Supporting Material for MBChB Yr2 Sem2 Renal Module - Renal Physiology and Development

Index:

Handout: you can download the handout for lectures 1-5, in Open Document Format. You can also download the same document in Portable Document Format (.pdf) by clicking here

Podcasts: Podcasts to support these lectures, which range from 7-15 mins, are available in the free ogg-vorbis format. Click here for an explanation of why ogg-vorbis is the best choice. You can also download them in the proprietary mp3 format. The podcasts present the same material as that covered in the renal physiology lectures, but in a slightly different way, hopefully to help you if you did not quite understand something or if you are revising for exams. You will probably not, though, be able to learn from the podcasts alone as seeing diagrams and photos is important (for this reason, the anatomy is not covered in the podcast format: you need pictures). Also, the podcasts are short, having been designed to last no longer than the walk from Pollock Halls to Teviot Place.

Recorded lectures: (all playable using VLC player, and many other platforms: please DOWNLOAD to play as this server is too slow to cope with mutliple live connections).

- Lecture 1
- Lecture 1
- Lecture 1
- Lecture 1
- Lecture 1
- A quick guide to using the GUDMAP database

Lecture slides: The slideshows from each of the lectures are available in Open Document format, readable by LibreOffice and OpenOffice: these packages are free in the full sense of the word and run on BSD, Linux, OSX, Solaris and Windows. You can also download the slideshows in pdf format. The slides never had anything to do with Powerpoint, so please do not e-mail to ask for 'the original Powerpoints', because they do not exist.

Tutorial: you can download the tutorial problems and answers in Open Document Format here or as a pdf here (but only after the last group's tutorial has run! - it will be a broken link before then).

Sample questions: you can download a short sample of questions here, and download the answers here.

The Examinator - an MCQ generator for revision purposes. Please note that you need a device with a keyboard to use this.

Edinburgh Renal Education Project: you can visit the home page of the Edinburgh Renal Education Project here.

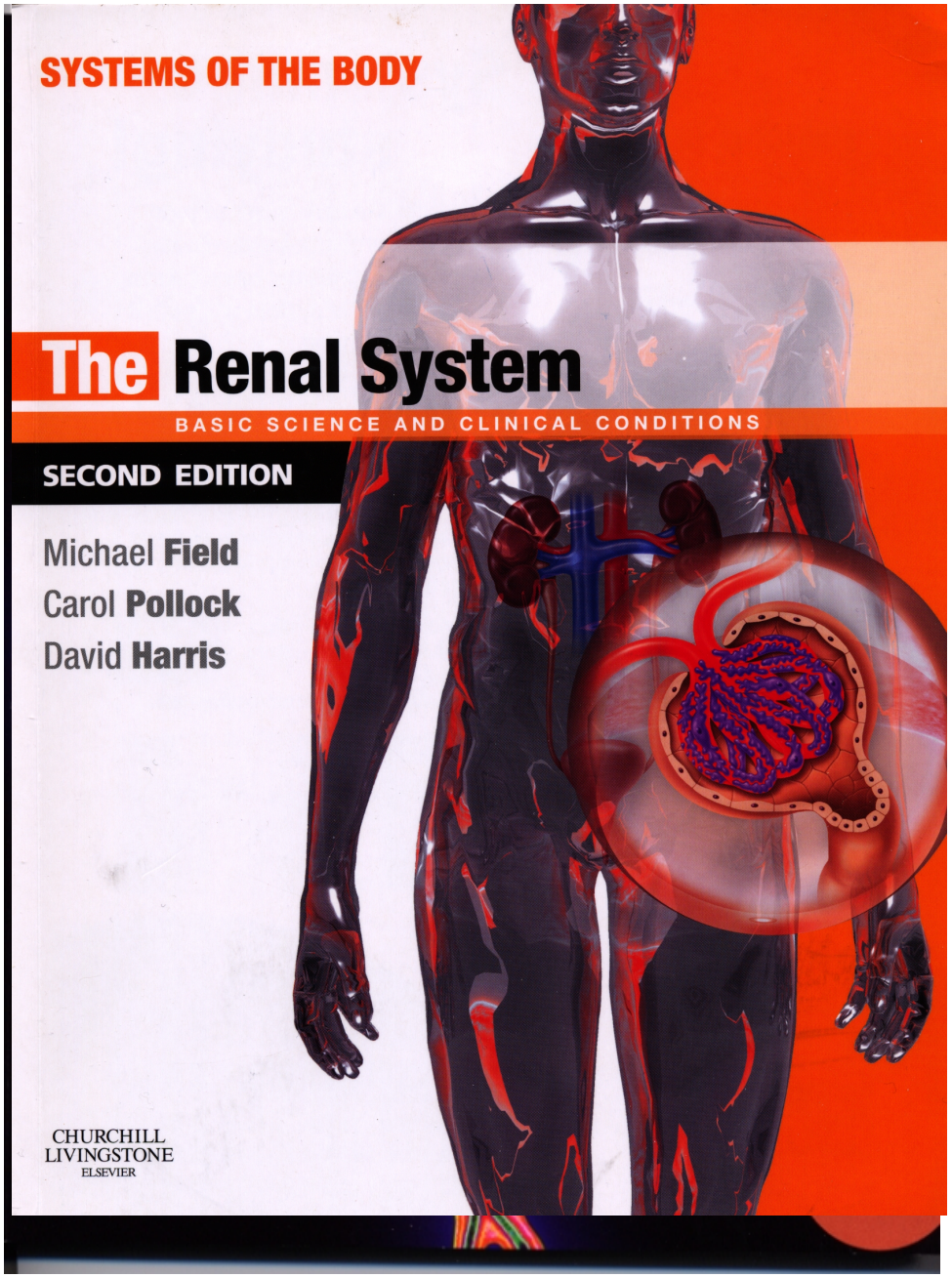
This is nothing specifically to do with the renal module, but if you are interested in running your own computer using Free software, you may find this pdf useful.

Course book:

168 pages, so not unhelpfully large for a second year, non-specialist, student.

Same material as lectures, but in a different order and CASE-BASED)

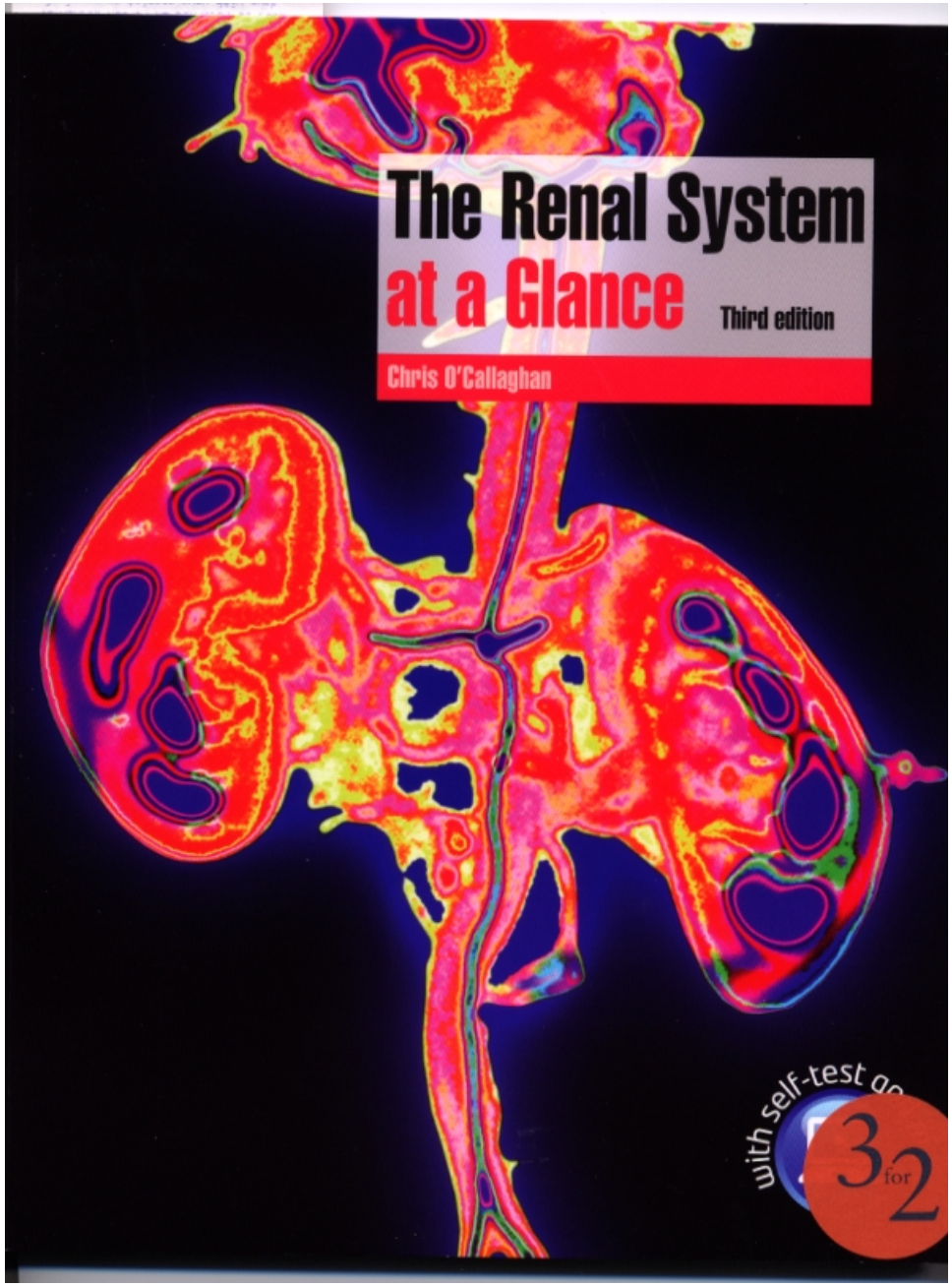
Library has STANDARD LOAN copies at Geo Sq, RIE.



Alternative Course book:

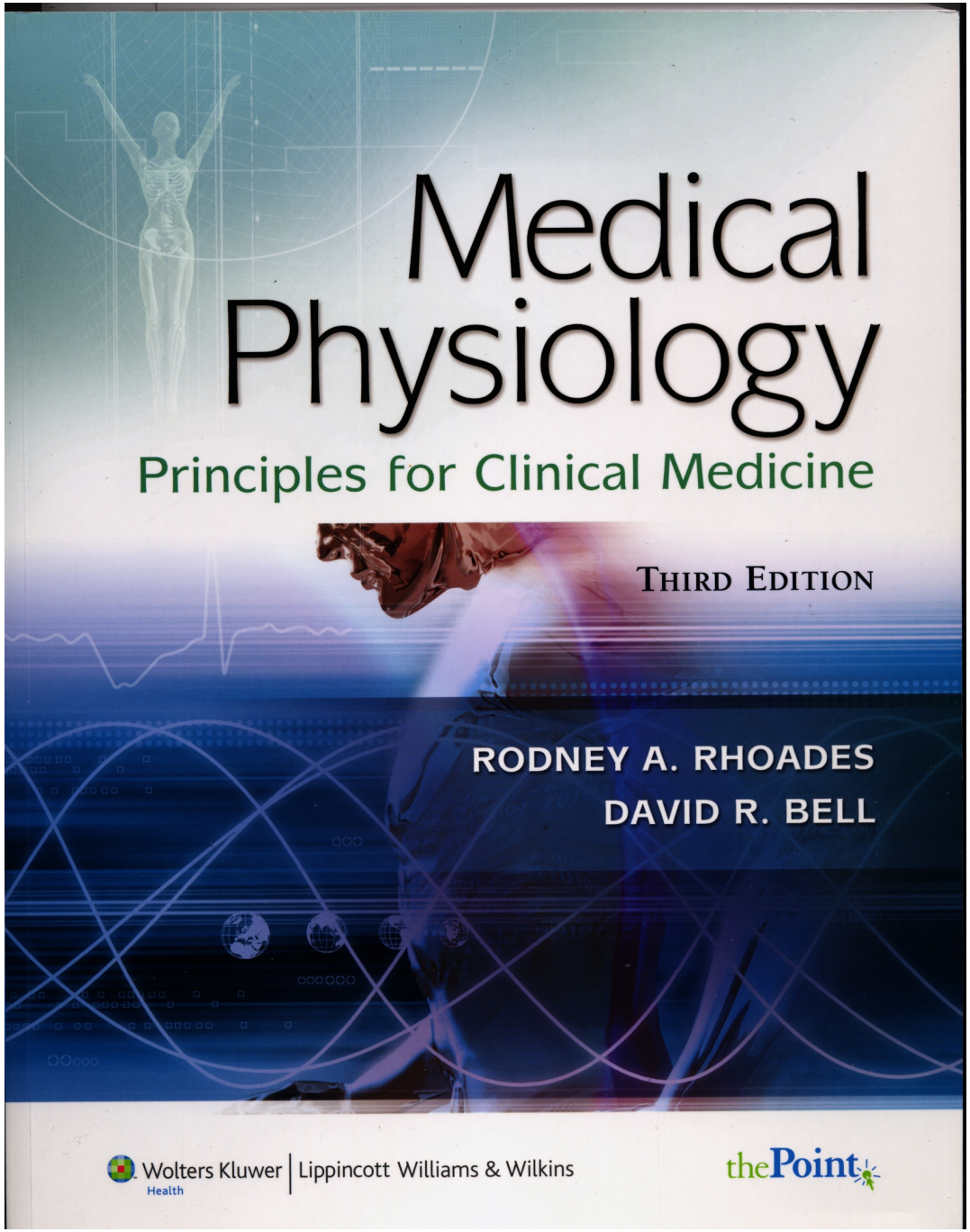
(Just over 100 pages, so not unhelpfully large for a second year, non-specialist, student)

Library has reserve copies at Geo Sq, RIE and WGH.

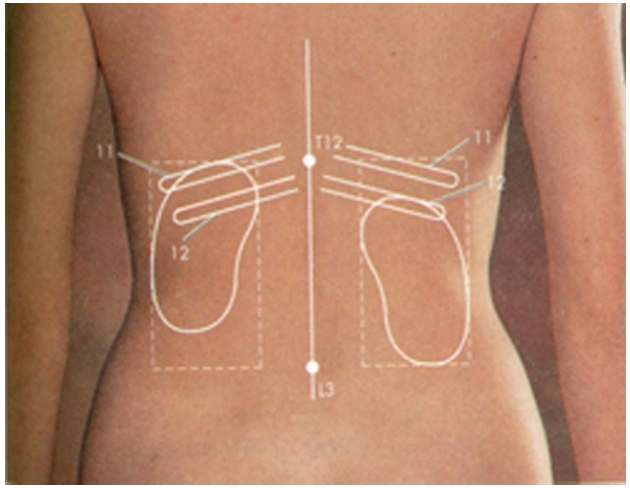


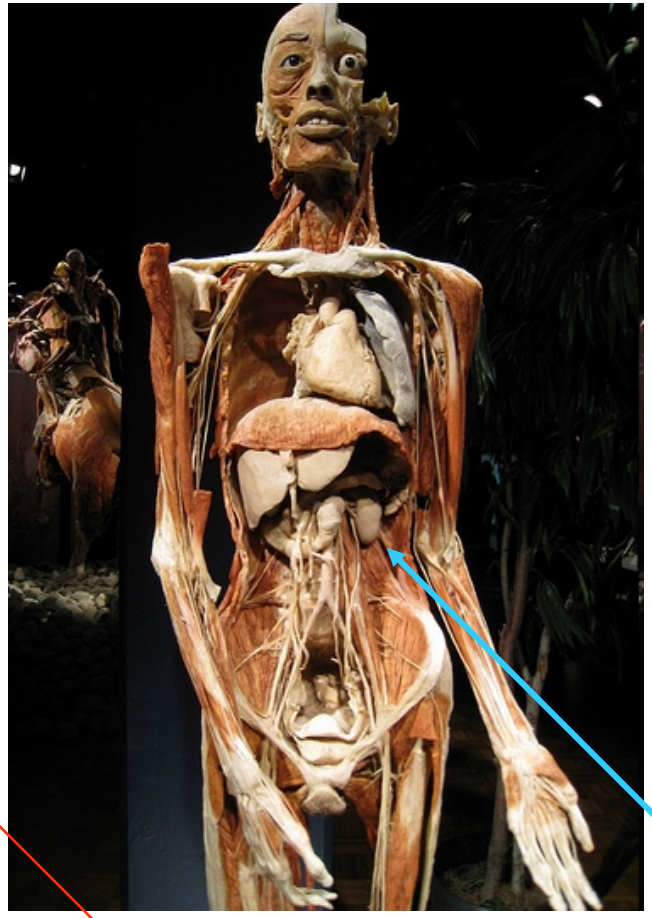
If you want better explanations (less brief), then try Chapter 22

(This is a superb book generally).

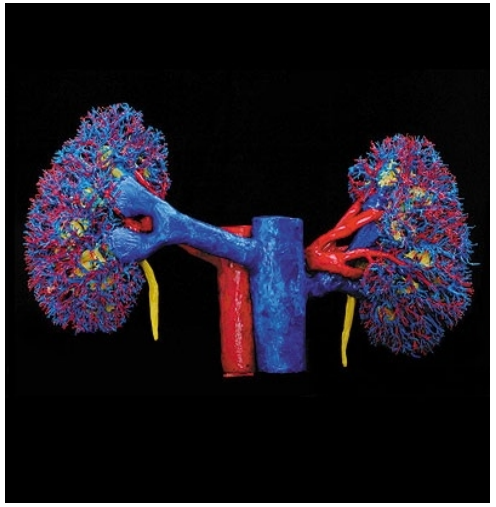


The star of this module: the kidney





Source: Body Worlds



20% of cardiac output

Left kidney

FUNCTIONS:

Filtration of blood,

Detoxification (incl drugs),

Regulation of blood pressure,

Regulation of blood pH,

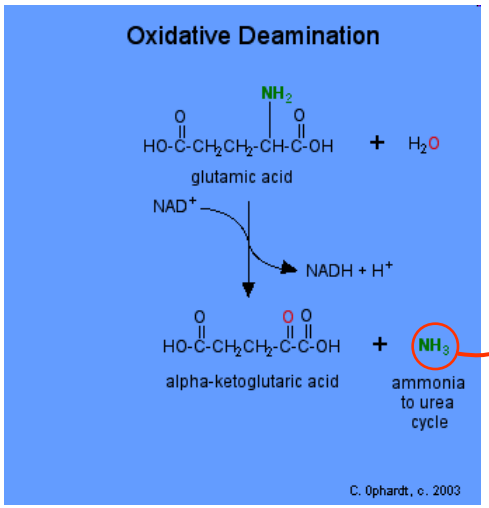
Regulation of haematopoiesis

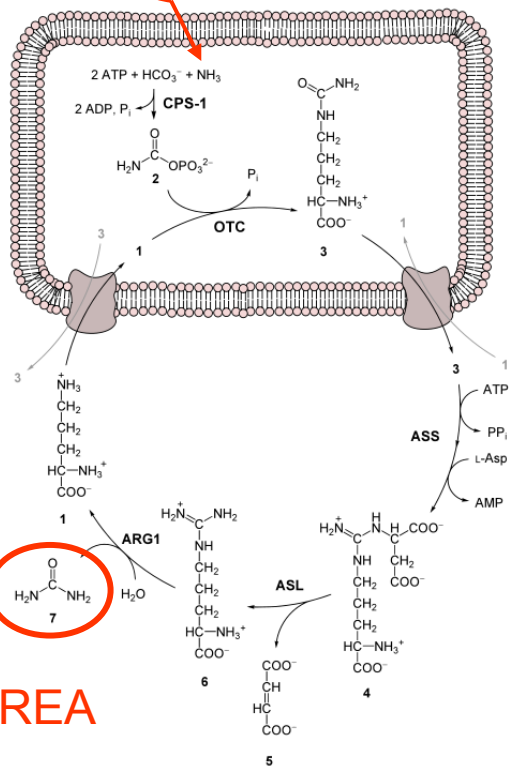
Making vitamin D

This module will be mostly about these, but don't forget the other functions!

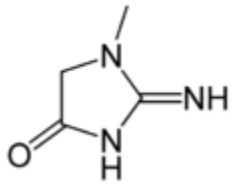
The problem:

1) The blood fills up with waste products and toxins that need to be cleared from the body





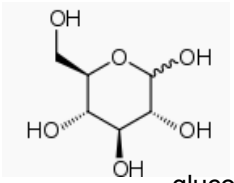
UREA



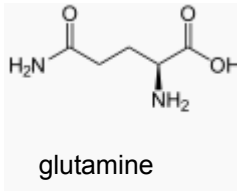
creatinine

(From muscle)

2) The blood is full of goodies about the same size as waste products and toxins (or smaller, in the case of water), that are precious and must not be lost from the body

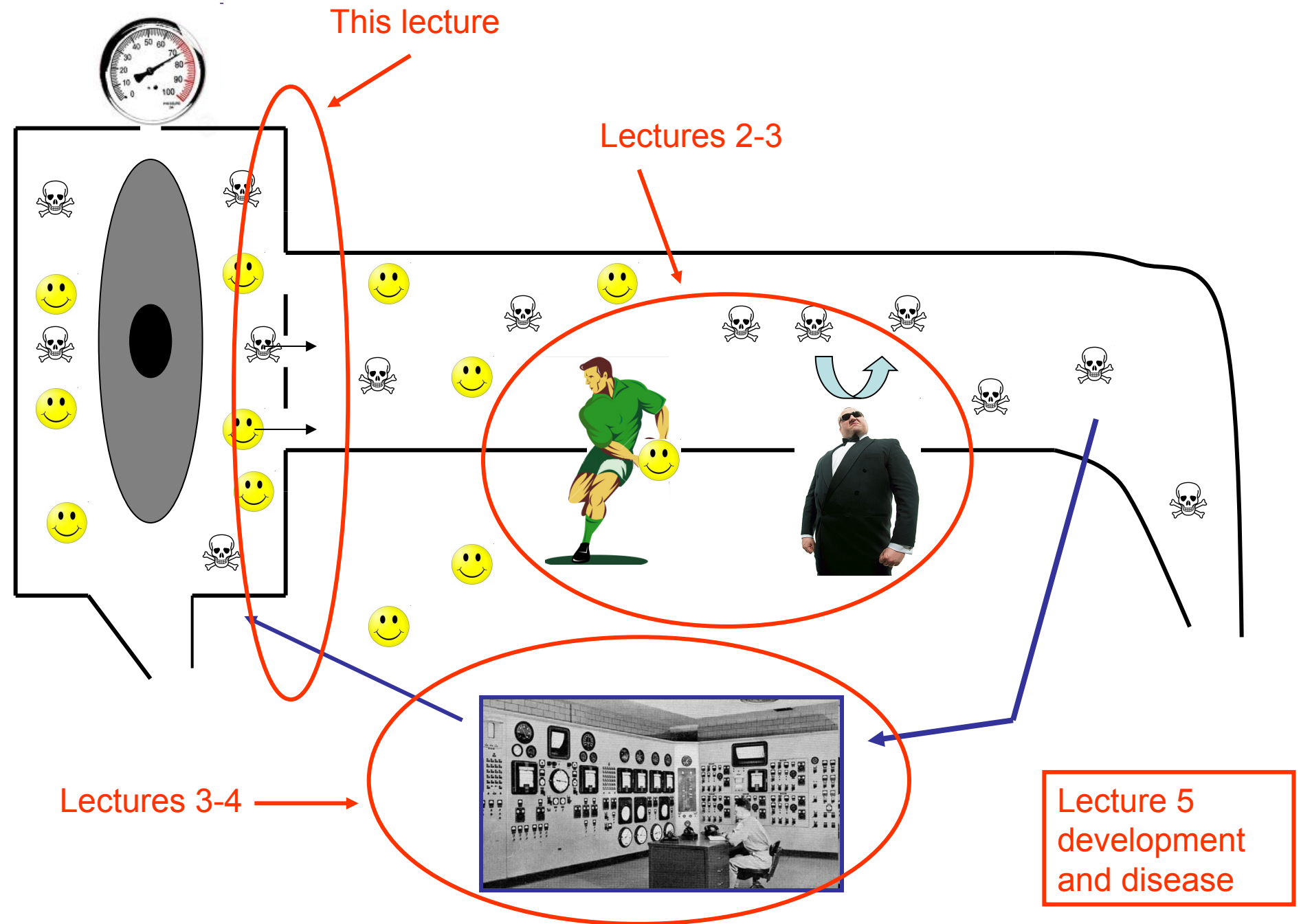


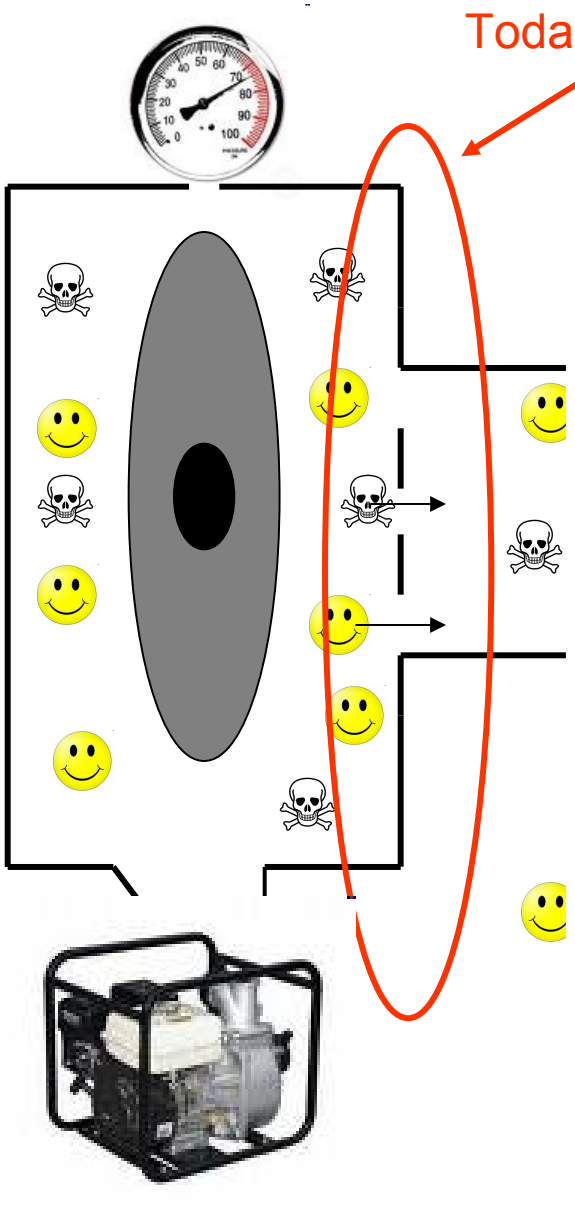
glucose



glutamine

etc, etc

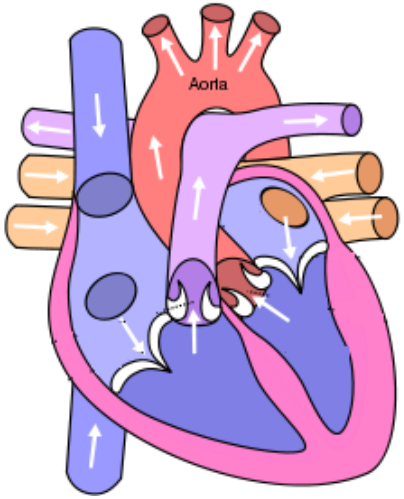

This lecture
Lectures 2-3
Lectures 3-4
Lecture 5
development
and disease



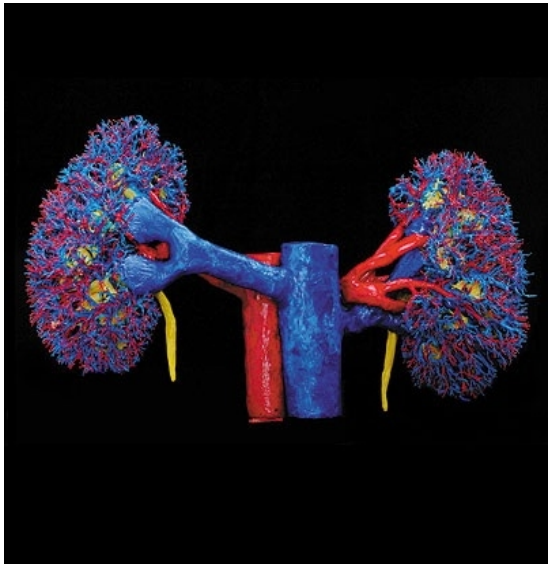
We need:

1) A pump

2) A filter



Easy! – Run the input directly from the high-pressure side of the circulation (c. 15,000 N/m^2, c. 0.1atm)



=115mm Hg, if you must use non-SI units

The filter:

"Design" problems:

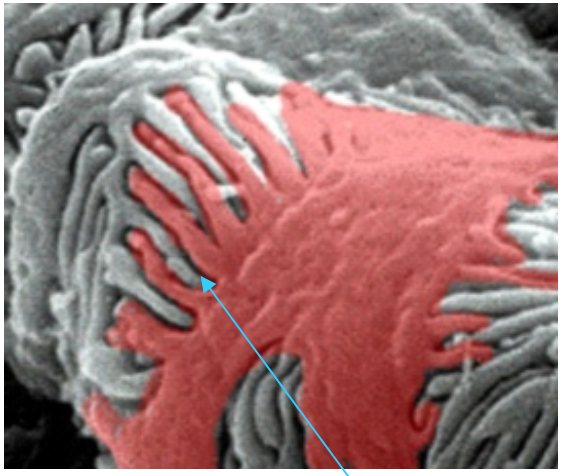
We need to make a very fine filter (cut off c. 4nm = 40Å, free flow below 18Å)

We need the filter not to clog.

We need to be able to filter a lot of fluid in a small-ish space

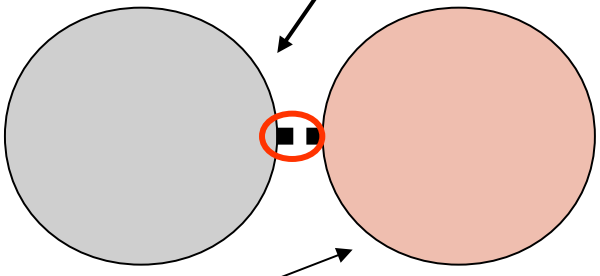
The finest filter – the slit diaphragm.

IMPORTANT: this understanding is relatively recent (late 1990s)– beware old texts that claim the finest filter is the GBM

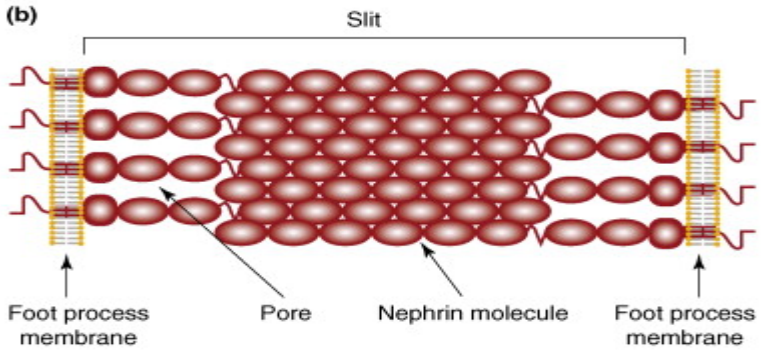


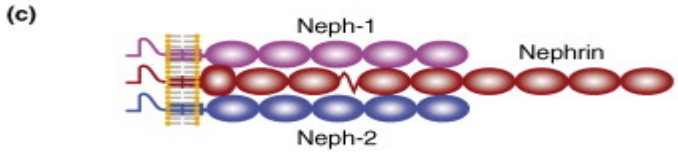
Slit diaphragm

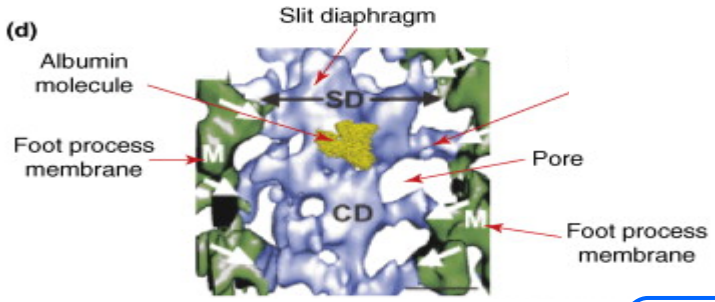
Cross-section:



Processes of adjacent cells







click

Patrakka J, Tryggvason K. (2007) Nephrin--a unique structural and signaling protein of the kidney filter. Trends Mol Med. 2007 13:396-403.

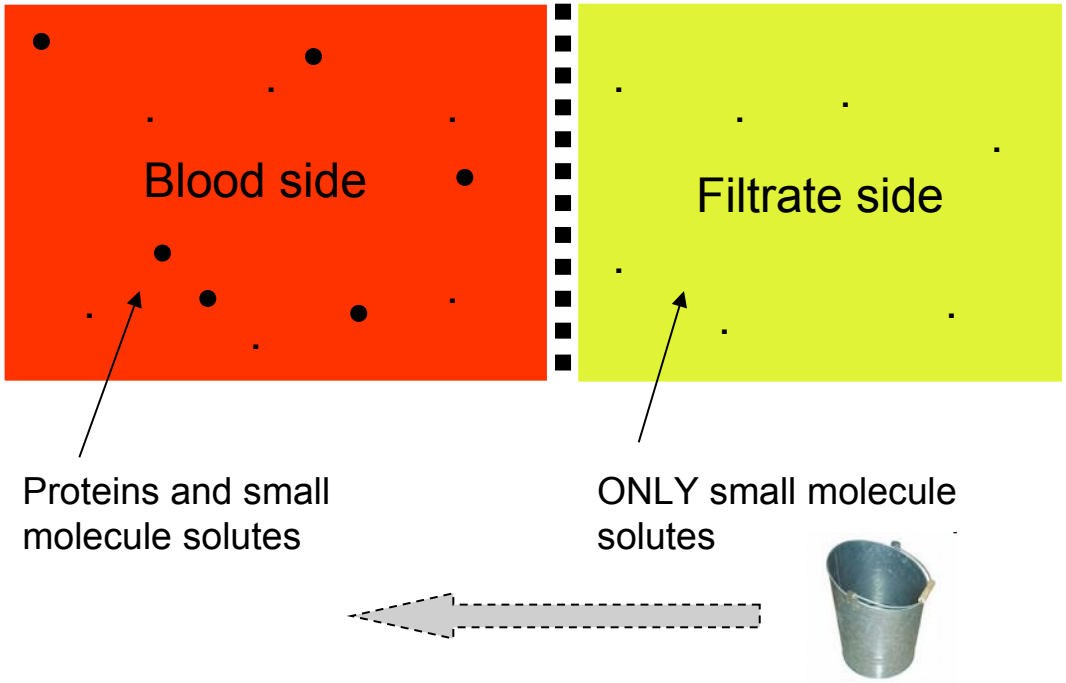
Only about 3% of the total area is actually slit (the hole itself)

-> the slit diaphragm is therefore a major source of resistance to fluid flow

You NEED this pressure.

Think about osmotic pressures:

Click



.. So we need pressure on the left to oppose it

Effect of restricting blood supply and drain:

Restrict afferent arteriole:

- Blood pressure in capillaries drops
- Filtration rate drops

Restrict efferent arteriole:

- Blood pressure in glomerular capillaries rises
- Filtration rate rises

The filter:

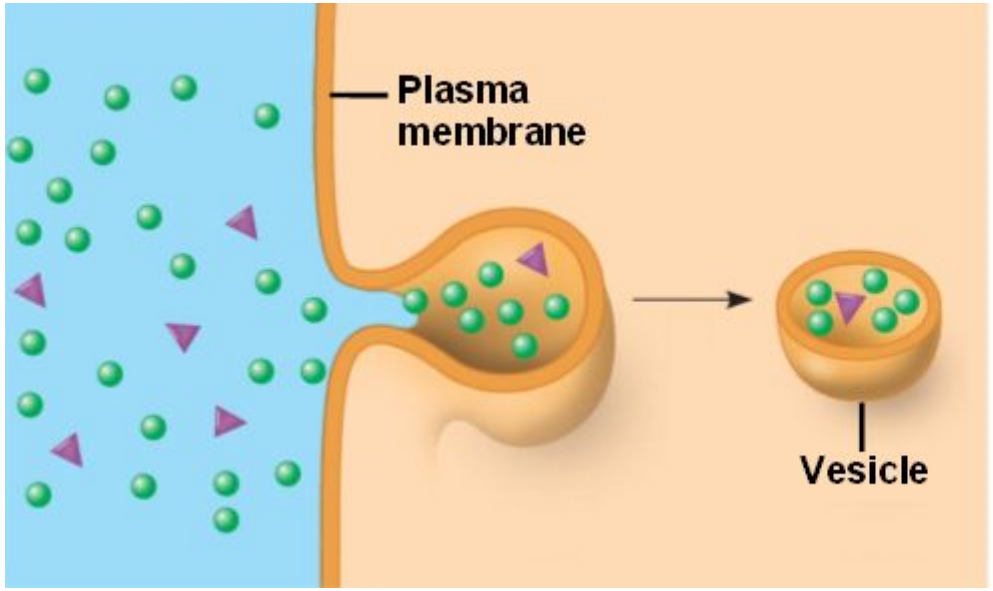
"Design" problems:

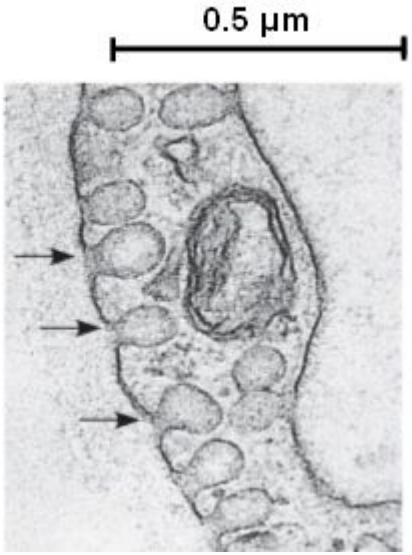
We need to make a very fine filter (cut off c. 4nm = 40Å, free flow below 18Å) ✓

We need the filter not to clog.

We need to be able to filter a lot of fluid in a small-ish space

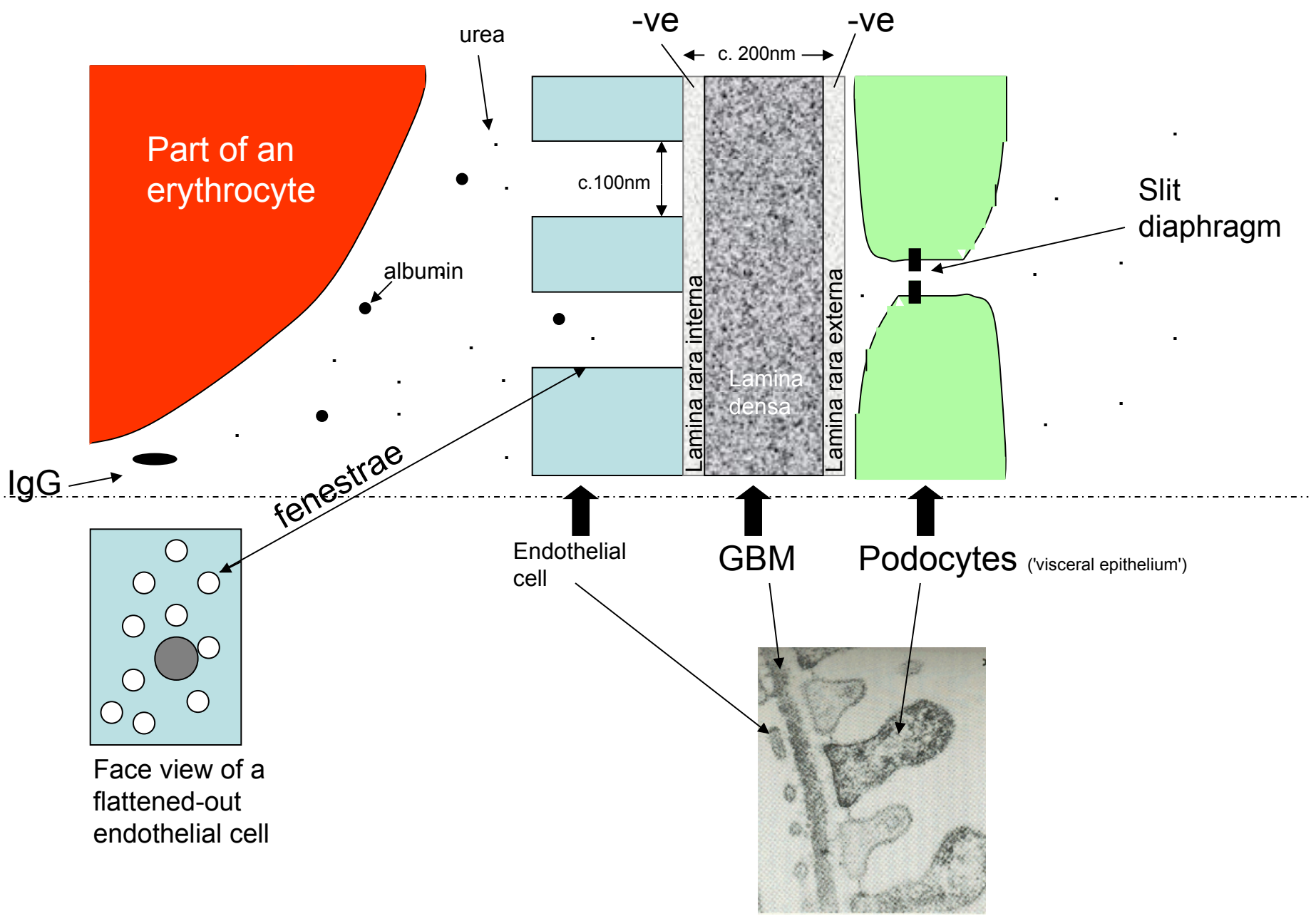
Anti-clogging: pinocytosis of trapped proteins



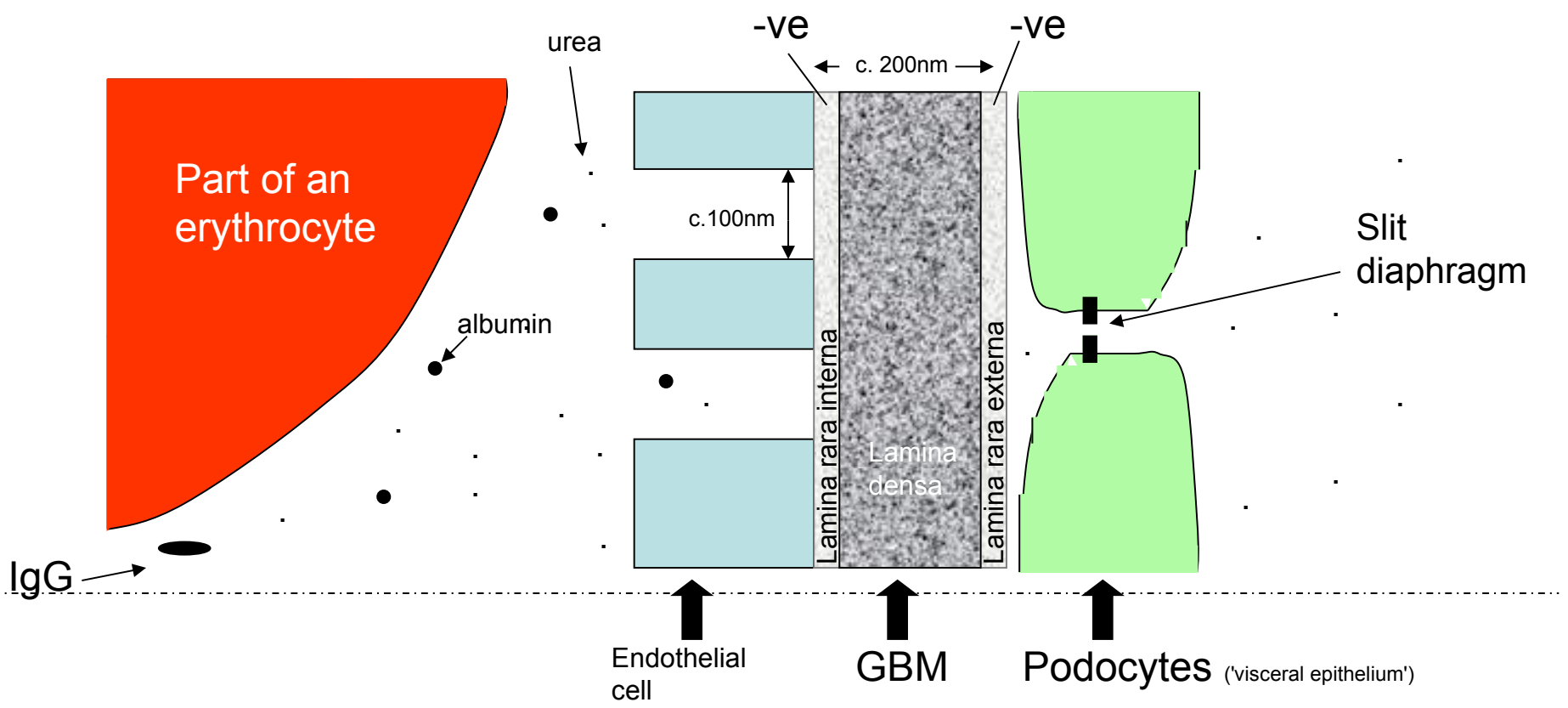


BUT – this kind of thing only works for proteins small enough to pinocytose. If big protein aggregates, bacteria, platelets etc got jammed against the slit membrane, there would be a problem…

Additional filters are needed to keep these out.



NB – in this diagram, everything has been 'flattened out' for clarity.


Part of an erythrocyte
urea
albumin
IgG
-ve
-ve
c. 200nm
c.100nm
Lamina rara interna
Lamina densa
Lamina rara externa
Slit diaphragm
Endothelial cell
GBM
Podocytes ('visceral epithelium')
Cleaned by blood flow and phagocytes
Renewed by mesangial cells
Cleaned by pinocytosis by podocytes

The filter:

"Design" problems:

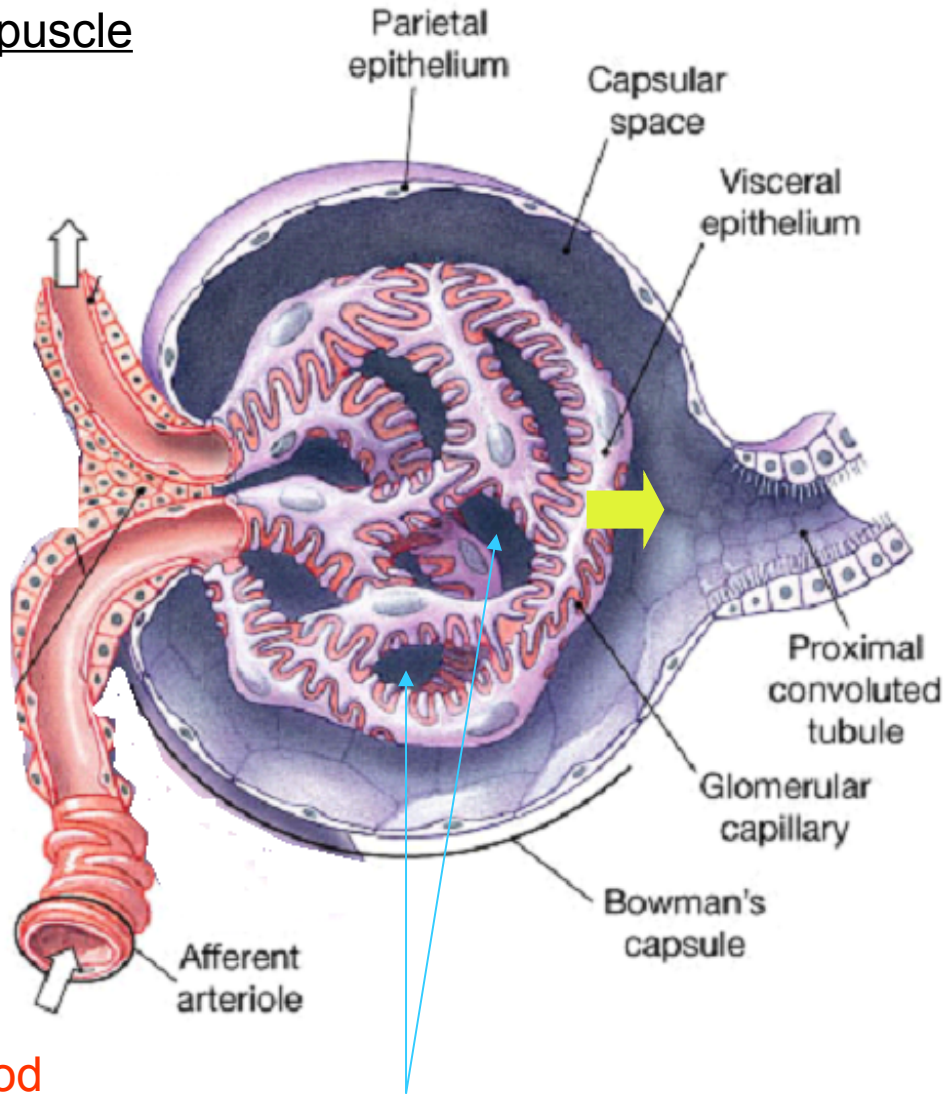
We need to make a very fine filter (cut off c. 4nm = 40Å, free flow below 18Å)

We need the filter not to clog.

We need to be able to filter a lot of fluid in a small-ish space

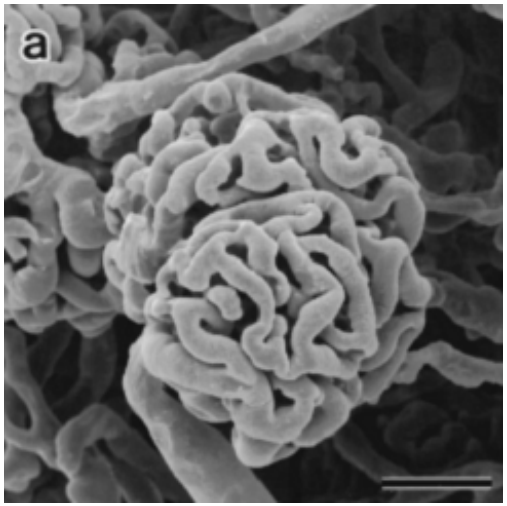
Solution number 1: bundle lots of this up in one place:

Renal corpuscle

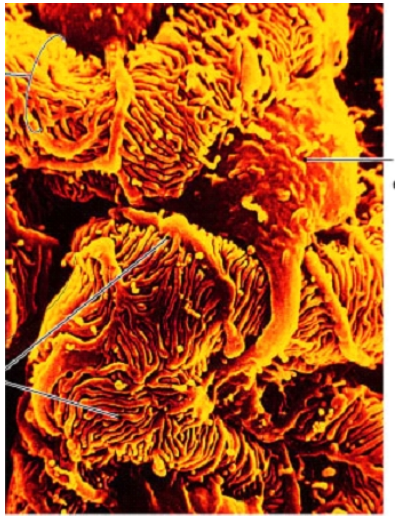


blood

Mesangial cells fill these spaces

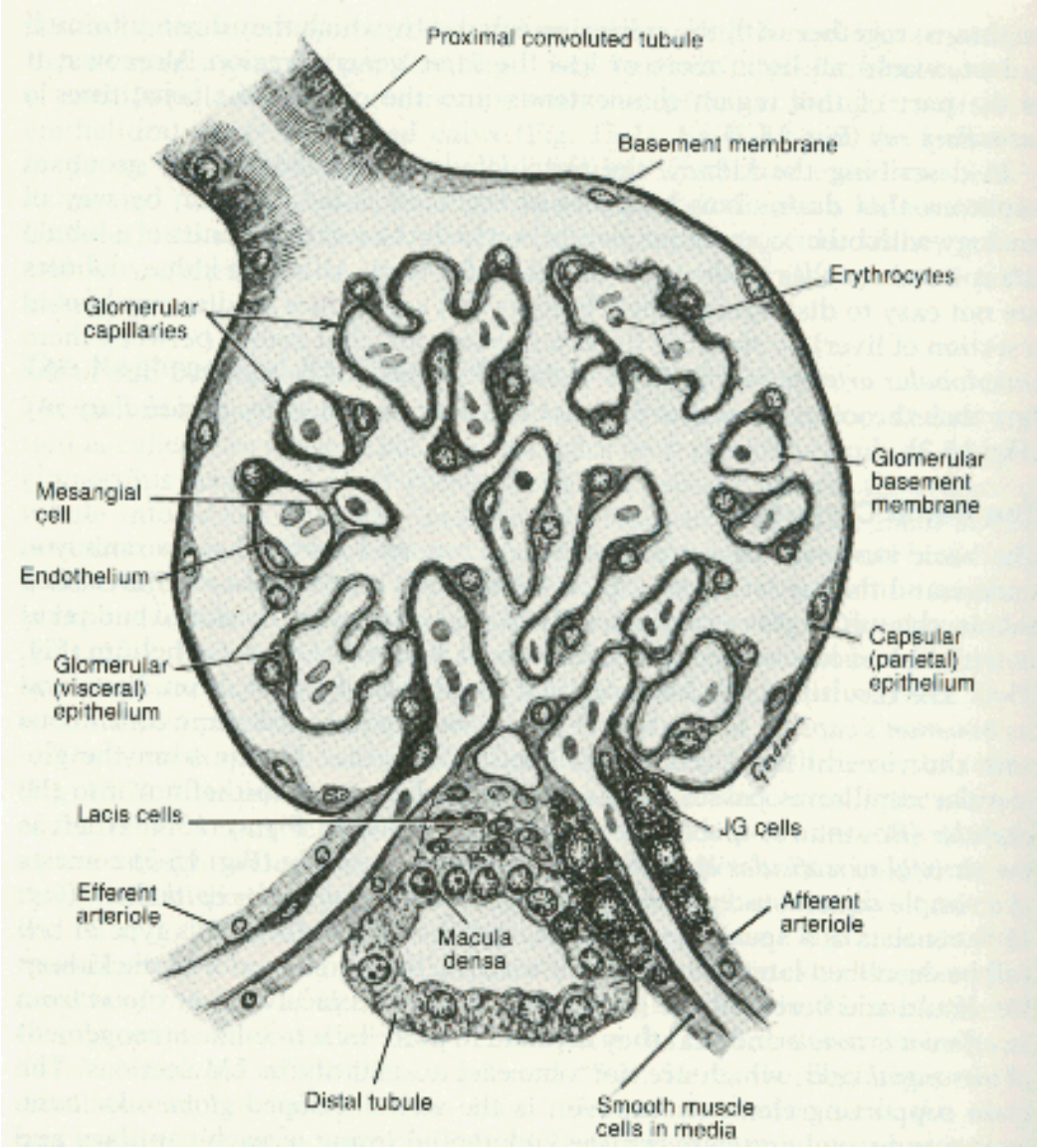


Real vascular cast



Real SEM

The renal corpuscle

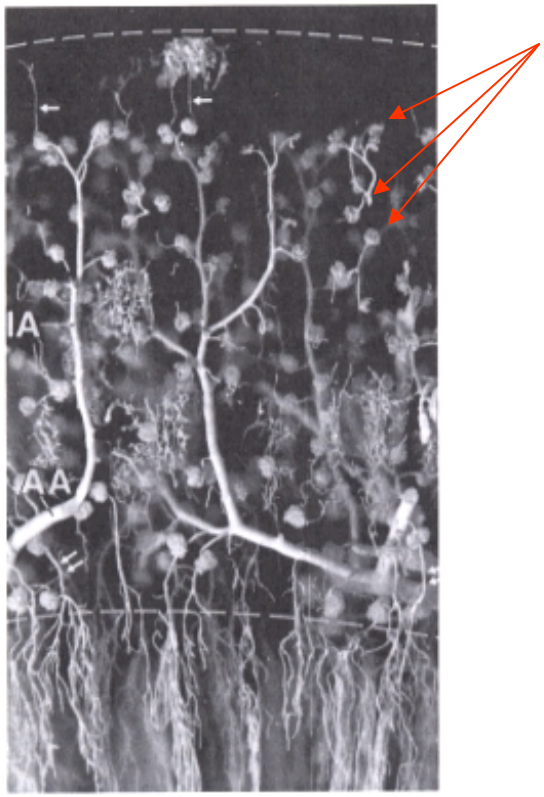


Sorry – I have permission to show you the medical art that appeared at this point in the lecture in the live presentation, but I do not have permission to include it in a slide set on the web. You can, however, use this link to see it on the artist's own website (or you can scan the QR code below with your phone/ pad to see it that way).

NB – size of dissolved molecules is hugely exaggerated.

Solution number 2: have lots of renal corpuscles in one kidney.

Humans: 50,000 – 1,000,000 (some variation is due to foetal programming – Barker hypothesis – nephron number follows mother's amino acid nutrition).



Resin fill of the blood vessels of a piece of rabbit kidney: each of these 'balls' is a glomerulus.

(never mind the rest of the complex blood system – we'll meet that in a few lectures' time).

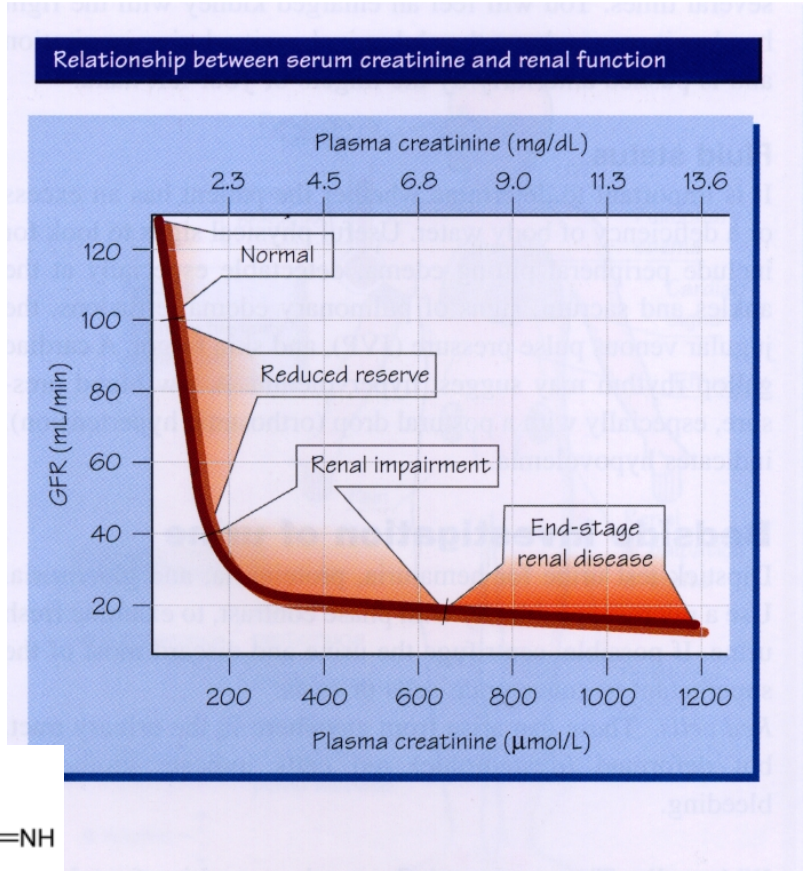
Typical values:

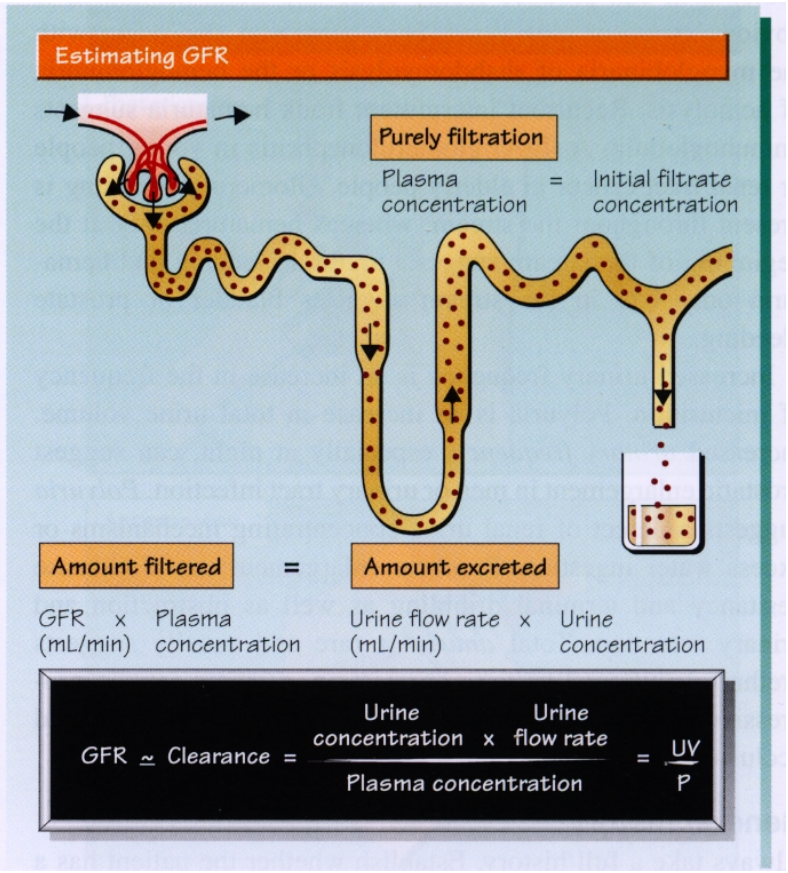
Blood flow to kidneys - 1.2L / min

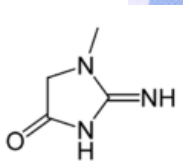
Plasma flow to kidneys – 0.66L /min (assuming normal haematocrit of 0.45)

Rate of filtration through glomerulus = 0.13L /min

-> 20% of plasma is removed as filtrate.







creatinine

From: the renal system at a glance

The filter:

"Design" problems:

We need to make a very fine filter (cut off c. 4nm = 40Å, free flow below 18Å)

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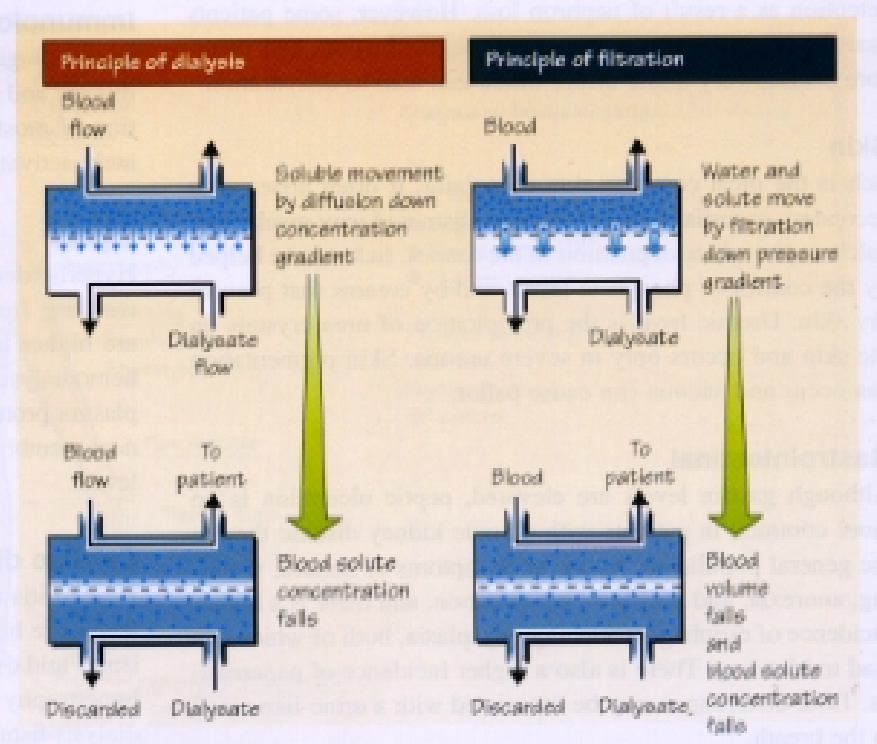
An artificial glomerulus – the dialysis machine.



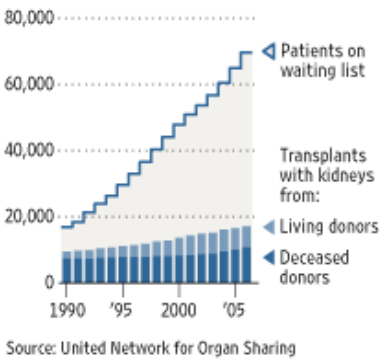
From *The Renal System at a Glance*

Wikipedia commons

NB – the fresh dialysate is full of the 'wanted' small molecules of the blood (glucose etc) so that there is no net loss of these.

Or Transplant – but there are four problems:

Availability



Social

A Manila Slum. Source: writingthirty.blogspot.com/

Rejection

www.pharmaceutical-technology.com

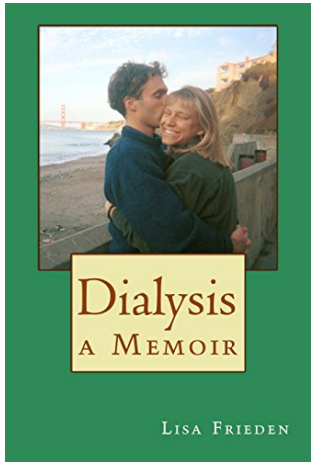
Theft (India)
abcnews.go.com

Tumours

3x⬆ risk.

Wong & Chapman (2008)
Trans Rev 22: 141-149

Tangent (not on syllabus) – books about the patient experience



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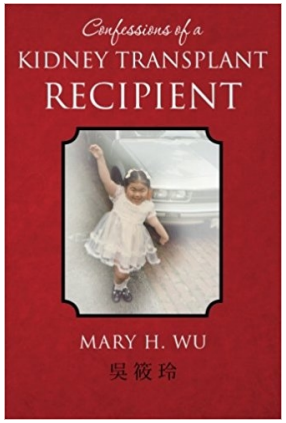

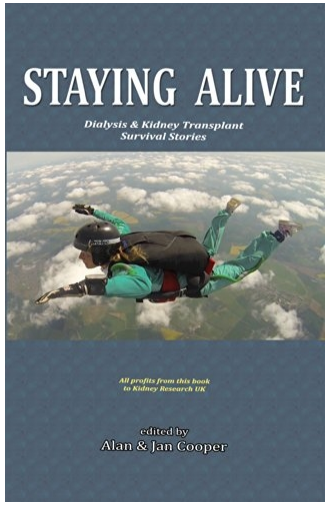

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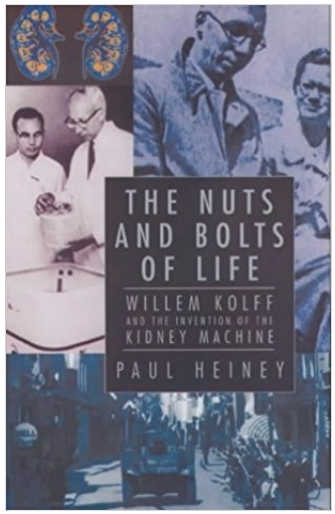
And about
the invention
of dialysis

click



www.kidneyresearchuk.org

Kidney Research UK
Funding research to save lives

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- Our strategy
- Position statements
- Our people
- Our ambassadors
- Work for us
- Fundraising promise
- Reports and accounts
- Accredited membership
- Where we spend our money
- Keep In touch

Who are we?

Kidney Research UK is the leading charity dedicated to research into kidney disease in the UK. We rely almost wholly on the generous donations of the UK public and we believe that everybody deserves a life free of kidney disease.

Our aim

We aim to find better treatments, and ultimately cures for kidney diseases.

Our research saves lives

Kidney disease is a silent killer. There are three million people in the UK with it right now. One million don't even know they have it and there is no cure. For decades our developments in treatment, better information for patients and raising vital public awareness have been saving lives. As the likelihood of kidney disease striking you becomes ever greater, our work is more essential now than ever.

Our supporters are amazing

Thanks to the help from our supporters, we have achieved breakthroughs in the diagnosis, treatment and patient care of those affected by the disease. But much more needs to be done. There are

Related links and resources

- Health equality showcase

Health Information

- Health Information
- Are your kidneys ok leaflet
- Online health check

Choose your challenge

Fundraise for us

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