Subcutaneous Abscess

Detailed History of Presenting Illness (HPI)

- Pt presents with infected wound;
  - **Red**
  - **Hot**
  - **Swollen**
  - **Painful**
- History of penetrating trauma at the site; foreign object possibly still present
- Discharge of pus

List of Differential Diagnoses (DDx)

- Subcutaneous Abscess as result of infection
- Local cellulitis
- Allergic reaction (contact dermatitis)
- Skin cancer

List Pertinent Findings on History (Hx)

Need To Know:

- Allergies (ESPECIALLY TO ANTIBIOTICS)
- Tetanus shots? **Should be every 10 years**
- Other vaccinations?
- Diabetes? Lesion may be due to *diabetic neuropathy*
- Previous infectious disease?
- History of the lesion:
  - How did this happen (eg. gomer fell down)
  - immediate management (antiseptic)?
  - Attempt to remove foreign matter?
  - Cleaned / dressed wound?

UNDERLYING CAUSE OF FALL: may be functional impairment; gomer assessment:

- Glasses: short or long sighted? Used continuously?
- Use of **alcohol**?
- Support network, i.e. who would come if the pt. yelled for help- (lives alone?)
- Previous falls requiring hospitalisation? In similar circumstances?..

List pertinent findings on Examination (Ex)

CARDINAL SIGNS OF INFLAMMATION:

1. **PAIN**
2. **HEAT**
3. **SWELLING**
4. **REDNESS**

- **Lymph Nodes** draining the injured site: **enlarged?**
- Temperature: **FEVER?**
- **Range of movement** in affected region: **painful? Limited?**
- **Tenderness localised to lesion or GENERALISED?**

Tests and Investigations: How is this diagnosis made?

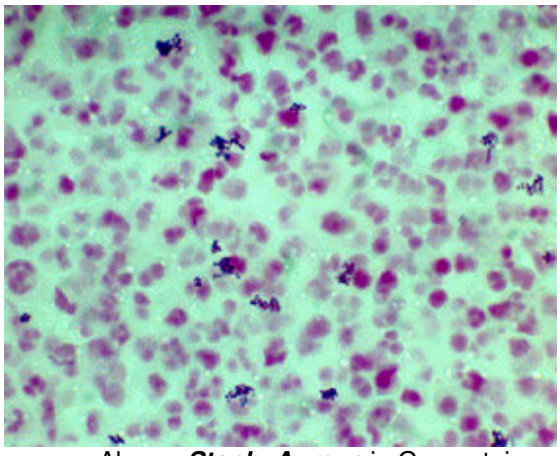
SWAB OF PUS FROM WOUND:

CULTURE: incubation of agar plates; AIM is to separate cultures into easily identifiable clumps (anaerobically or aerobically or 5% CO_2; physiological (37 degrees) or 25 degrees Celsius for **24hrs – 6 weeks**)

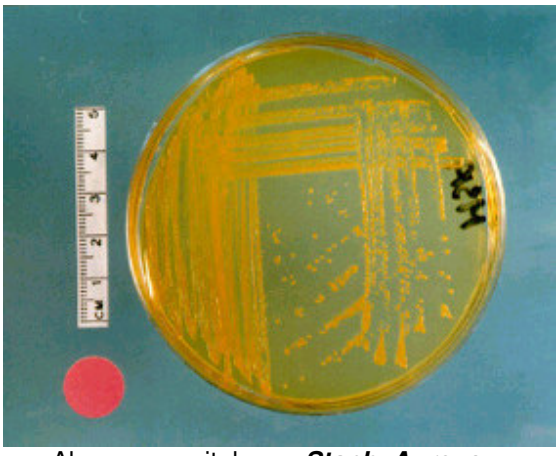
- **Blood Agar (all-purpose)**
- **Selective Medium eg. MANNITOL SALT AGAR for *staph*** *(nothing else lives in that much salt)*

<u>IDENTIFICATION</u>: done for SINGLE COLONIES OF SUSPECTED ORGANISM
through:

- **MORPHOLOGY** i.e. appearance on growth media (eg. golden-yellow = *staph.A*)
- ***<u>mannitol</u>* <u>salt agar</u>** differentiates between ***Staph aureus*** and **Staph *epidermidis*** because
- **S.A** can ferment mannitol, generating acid by-products (detected as yellow colour change)
- **S.E** cannot do this; agar stays same colour



Above: ***Staph. Aureus*** in Gram stain



Above: mannitol agar ***Staph. Aureus***

<u>Or appearance on</u> <u>GRAM STAIN:</u> Rods, cocci, etc.
POSITIVE = BLUE
NEGATIVE = PINK
Staphylococcus organisms are seen as **Gram-Positive** (BLUE) bunches of grapes

- **BIOCHEMISTRY** i.e does the microbe **degrade** / **ferment** any different sugars, eg **mannitol?**
- Does the microbe produce **Enzymes** eg coagulase, catalase, DNAase
  - *<u>Staph A. does all of the above</u>*
- **SEROLOGY** : Specific microbial antigens can be detected by using **SPECIFIC ANTIBODIES**
- **MOLECULAR GENETICS: PCR** (Polymerase Chain Reaction) used to multiply microbial nucleic acid sequences; VERY SENSITIVE (no false positives) but EXPENSIVE
- **ANTIBIOTIC SENSITIVITY: 3 major methods**
  - **Disk Diffusion:** small paper disk with incorporated antibiotic is placed in centre of agar dish; should inhibit growth of organisms- degree of inhibition is distance of bacteria from centre of disk.
  - **Enzyme Detection: β-Lactamase** activity can be measured with simple test.
    Most Staph (95%) are resistant to penicillin due to β-Lactamase (enzyme) which breaks down penicillin's β-Lactam ring;
    β-Lactam ring is the basis of its efficacy vs bacteria (ring gets incorporated into bacterial cell wall leading to:
    loss of cell wall integrity, influx of water and cell lysis);
  - **Gene Detection:** genes that cause drug resistance have been identified;
    Detection of these genes is now possible to identify MRSA
    (eg. ***mecA*** gene = methycillin resistance;
    nuc gene = Staph A specific)

- **<u>CULTURE RESULTS</u>** are sent back to clinician **2-4 days following submission**
  for fast growing organisms like *Staph aureus, E. coli*

Disease Definition:

Superficial infection [at location] secondary to foreign body with local cellulitis, by the following pathogen [p]

Management

Immediate:

SURGICAL: Lesion has to be

- incised
- drained
- *Foreign body must be removed*
- cleaned with antiseptic (chlorhexidine gluconate)
- dressed with gauze

PROPHYLAXIS: give TETANUS BOOSTER SHOT

ADVICE: patient has to

- Rest and elevate affected body part
- change dressings daily
- monitor temperature

ANTIBIOTICS: SYSTEMIC with beta-lactamase resistant activity –
amoxycillin/clavulanate 500mg tid **5 days**.
(short course; watch for contraindications)

ANALGESIA: with Paracetamol or NSAIDS

Long Term:

MANAGE THE CAUSES OF FALL: Visit from **occupational therapist to home**;
thus **make living arrangements safe**
ENSURE COMPLIANCE, monitor pain, etc.
ARRANGE SOCIAL SUPPORT eg. meals on wheels, neighbours to help with chores, etc.

Epidemiology

Infection is one of most common causes of death in elderly

Basic Sciences and Comparative Diseases

7 deadly sins' of geriatric rehab; the consequences of immobility:

- ***Pressure sores,***
- ***Venous thrombosis,***
- ***Constipation/UTI's,***
- ***Bronchopneumonia,***
- ***Depression,***
- ***Deconditioning (atrophy)***
- ***Malnutrition***

Pathophysiology

Acute Inflammation:

localised, rapid, short-lived, stereotypic response of vascularised living tissues to injury;
Characterised by influx of FLUID and POLYMPORPHONUCLEAR LEUCOCYTES

AIM:

- to **contain infectious agents**, inanimate foreign particles, damaged or cancerous cells to localised area
- and/or to **eliminate them**
- AND to **initiate healing** (= some combo of **tissue regeneration** and **repair with scar** (fibrotic) tissue

EARLY RESPONSE (minutes-hours):

ENHANCED BLOOD FLOW: (**REDNESS, HEAT**):

- allows fluid and plasma proteins inc. complement to move **from microvessels into interstitial spaces** ie '**exudate' (combo of fluid, salts, complement, Ab, neutrophils etc)**
- **dilutes toxins**
- **increases flow to lymphatics,**
- **delivers Ab, complement, fibrin system components and polymorphonuclear leukocytes**;
- **THUS**: **causes SWELLING and PAIN**
- neutrophils infiltrate and begin phagocytosis if extracellular microbes present,
- eosinophils phagocytose helminth worms if present
- mast cells secrete histamine which increases inflammation

• **neutrophils** are drawn to the scene by **margination** (due to cytokines)

- and **emigration from blood stream;**
  - **attachment by selectins**,
  - **rolling**,
  - **arrest and activation by integrins**,
  - spreading into **flattened form**
  - **diapedesis** (squeezing through endothelial cells)
  - **climbing up chemotactic gradient** in a process called chemotaxis to site of tissue injury/infection

MEDIUM TERM RESPONSE (hours-days):

- if **tissue damage and/or infection still not resolved**,
  circulating **monocytes differentiate into macrophages** and
  move into affected tissue:
  - to **clear debris**,
  - **produce cytokines** that regulate inflamm. and start healing process;

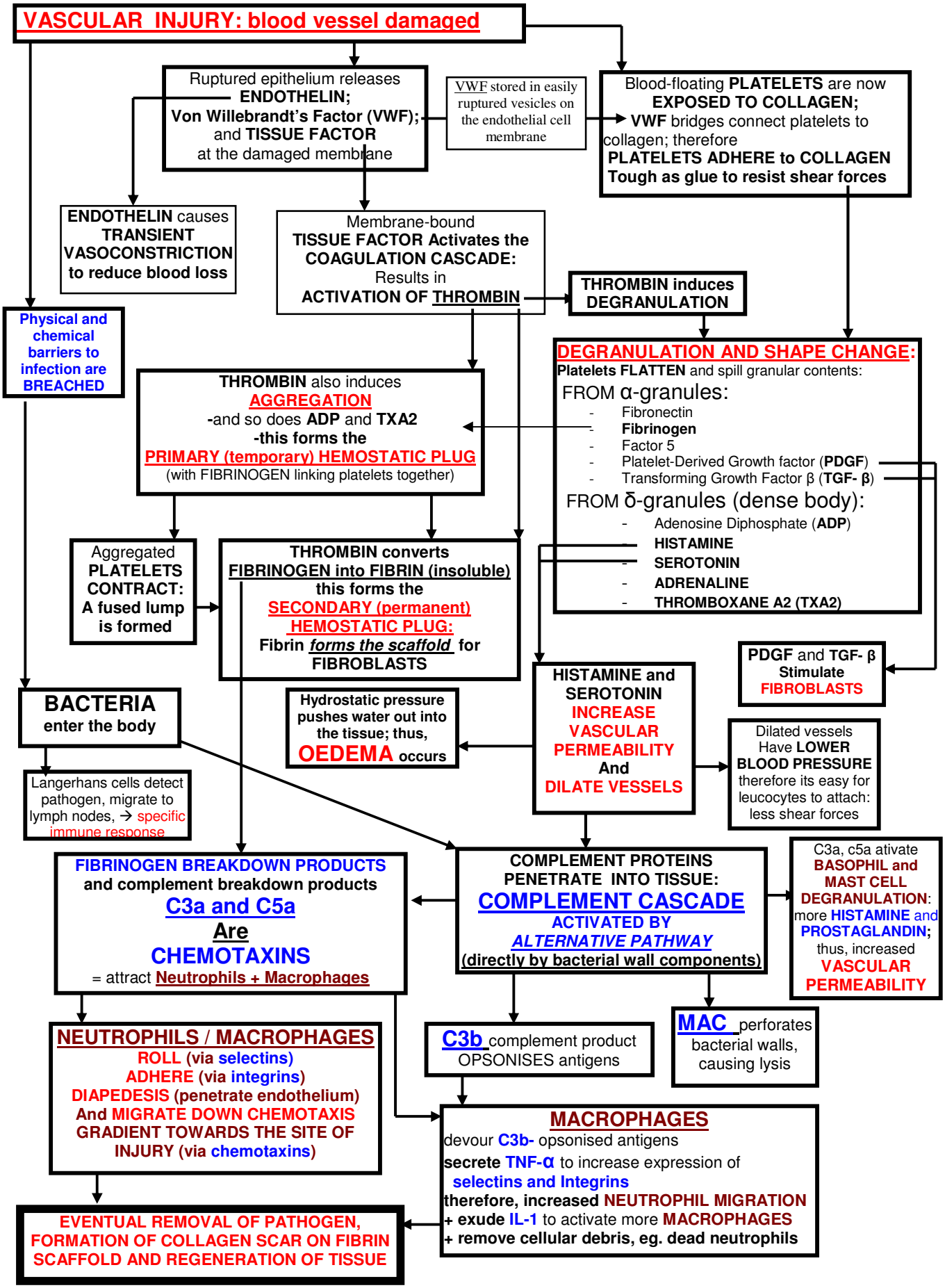
  systemic manifestations (**fever and lymphatic involvement) may occur at this stage**
  due to **IL-1 and TNF-α**

LONG-TERM RESPONSE (days-months):

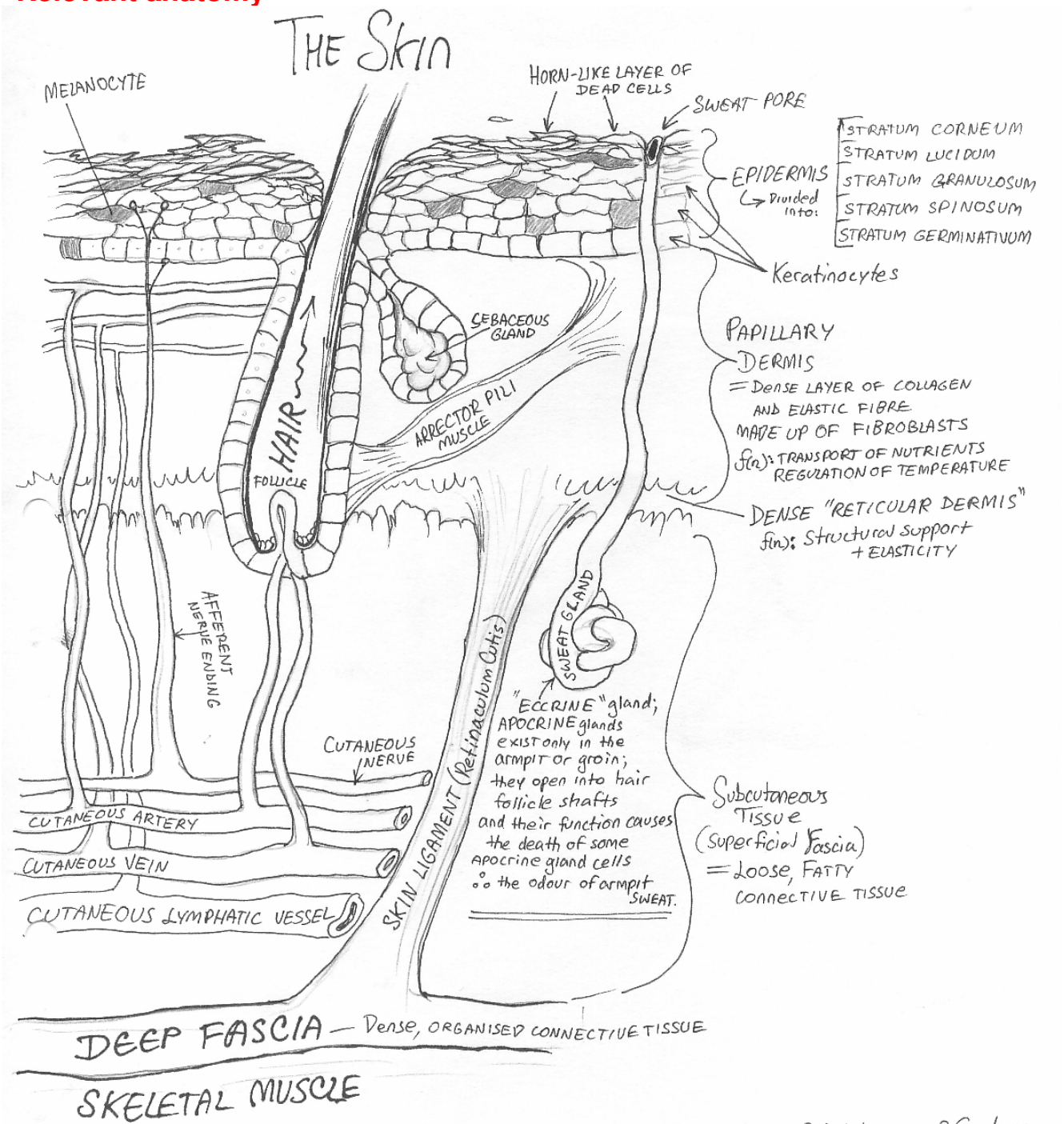
- even if acute inflamm persists, healing will start to occur;
- some microbes provoke excess exudate ie pus formation (esp. Staph and Strep infex)
  - either diffusely or in discrete tissue foci:
    - '**abscess' (enclosed)** or
    - '**ulcer' if open** (where necrotic inflamm tissues have been sloughed off)
    - pus contributes to tissue damage (contains lots of oxygen species and inflamm. chemicals)
- necrotic tissue contains, in this case, pus, plus neutrophils and oedema
- **fibrous tissue contains lots fibroblasts which produce lots collagen**
- **hyperaemia** is increased blood flow to an area of tissue causes **REDNESS and HEAT**
- **oedema** is consequence of increased fluid movement across microvascular bed (**SWELLING**)
- **vasoactive mediators** (inc**. histamine, prostaglandins, certain kinins and leukotrienes**) cause **PAIN**

- scurvy is due to **severe Vit C deficiency in which collagen can't be formed properly** so there is
  - reduced strength of healed wounds,
  - increased bruising and
  - microhaemorrhages

FLOWCHART OF INFLAMMATORY MECHANISM:



Relevant anatomy



*KERATINISATION: Continuous movement of Keratinocytes into Superficial layers of Epidermus

1) ORIGINATE in Stratum GERMINATIVUM
2) BECOME DENSE in Stratum Spinosum
3) ACCUMULATE LIPID in Stratum GRANULOSUM (to assist in maintenance of WATER BARRIER)
4) FLATTEN into DISCS, LOSE NUCLEI & ACQUIRE MELANIN GRANULES in Stratum Lucidum
5) APOPTOSE AND DRY OUT in the OUTERMOST STRATUM CORNEUM

This Journey may take 6 to 10 weeks

RELEVANT LT KEYWORDS FOR SKIN ANATOMY:

Rete ridges: The dermal-epidermal junction interlocks forming **fingerlike projections** called rete ridges
Merkel cell: MECHANORECEPTOR, **detect pain, itch and temperature**
Pacinian Corpuscles: MECAHNORECEPTOR **FOR PRESSURE**
Meissener Corpuscles: MECHANORECEPTOR **FOR TOUCH**
skin is largest organ of body: protective barrier, regulates body temp and H20 loss, sensory and excretory (sweat contains urea), produces Vit D from precursors, post-puberty apocrine glands release pheromones

Behavioural science

Aging and Mental Acuity:

- **Ability to pursue activities of daily living is** affected by
  extrinsic factors (eg **finances, living situation**)
  intrinsic factors (eg **physical health and mobility, mental health, cognition**)
- **Cognitive functioning** = capacity to attend to stimuli, process info, learn, make decisions
  - Memory types:
    - **sensory memory** (brief, immediate),
    - **short-term memory** STM (temporary storage of info for processing),
    - **long-term memory** (parts of STM that are rehearsed and/or categorized and 'filed'
      - **Active processes** (learning intentionally)
      - vs **Passive** (learning incidentally)
    - **Episodic** (memory of things done)
    - vs **semantic memory** (generalisations, abstract knowledge)
    - **Declarative** (factual)
    - vs **procedural knowledge** (skills, rules, algorithms to process facts)

- **Sensory, short term and long term episodic memory are STABLE WITH AGE**;
- **manipulation of material in short term memory adversely affected by age**
- **Intelligence = relatively enduring ability** to respond successfully to perceptual/cognitive/verbal problems;
- 50% of IQ can be attributed to inheritance(?)
- **Binet's intelligence test by performance of tasks**
- **Spearman's intelligence test of general vs specific intelligence**
- Catell's 2 intellectual factors:
  - **fluid** intelligence (inherited thinking and reasoning),
  - **crystallised** intelligence (learned skills);
  - **fluid sets limit on crystallised ability**
- Sternberg's 3 types intelligence highest to lowest:
  - **analytical**/componential (break problem into step by step),
  - **creative**/experienced (extrapolate),
  - **contextual**/street smarts
- **Decline in fluid intelligence with age vs crystallised intelligence endures**
- <10% ppl aged 65-80 have dementia; 20% 80+ year olds have it

FUNCTIONAL STATUS IN THE ELDERLY

NB 50% hospital bed occupied by persons 60+ years old!

- **continuum from partial loss of ability through threshold for clinical diagnosis**
- one presentation in elderly (eg a fall) has many causes (eg Alzheimer's, cardiac arrhythmia, UTI)
- multifactorial aetiology: **no single disease process for syndromes in elderly**
- **definition of disability = reduction/loss of ability within a person's environment**
- **personal activities of daily living (PADLs) =**
  - bathing,
  - dressing,
  - grooming,
  - toilet,
  - getting out of bed/chair,
  - eating,
  - continence,

- mobility
- **instrumental activities of daily living (IADLs) (manipulation of environment, interaction):**
  - cooking,
  - shopping,
  - finances,
  - housework,
  - telephone,
  - managing medications

  always take complete medication hx,
- ASK ABOUT:
  - activities of daily living,
  - nutritional hx,
  - immunisations;
  - beware deafness impeding communication;
  - assess pain by effect on ADLs;
  - neurological and cognitive functioning exams essential
- **Geriatric giants (NB probable exam question!):**
  - **falls (fractures/injury)#####################################**
    - **FALLS:** = one of most common/ serious problems in elderly:
    - 30% people aged 65+ fall each yr; **3 times more common in nursing homes/hospitals**
    - **many more institutional falls require hospitalisation** than home falls
    - consequences of falls more serious in elderly due to high prevalence of co-morbid disease
    - ***risk factors for falls:***
      - **intrinsic**
        - lower limb weakness,
        - poor grip strength,
        - balance disorders,
        - functional and cognitive impairment,
        - vision
      - **extrinsic**
        - (polypharmacy (>4 meds esp. psychotropic),
        - loose carpets,
        - poor lighting,
        - lack of bathroom safety equipment)
    - **Hx of fall**: loss of consciousness? (beware of amnesia about this);

      ASSESS the FOLLOWING:
      - **postural hypotension,**
      - **gait** : get up and go test:

        get up from chair and walk around, difficulties require further investigation), balance,
      - **cardiac arrythmias**,
      - **medications,**
      - **neuro function**
    - **FOLLOW UP OF FALL:**
      - OT assessment of home environment;
      - review meds esp. if taking >4;
      - consider walking aids, hip protectors,
      - vision assessment,
      - muscle strengthening/balance training (Tai Chi)

OTHER GERIATRIC GIANTS:

- confusion (delirium, dementia),
- incontinence,
- functional decline/not coping

- Drug efficacy decreases in elderly and risks may outweigh benefits;
- **randomized trials rarely look at adverse effects and only study homogeneous younger people**

- **When considering treatment,**
  - **life expectancy for men is 77-78 years**
    women is 81-82 years

BUT at 60, expect another 20 yrs life, at 70 expect 10 yrs, at 80 expect 5 yrs , at 90 expect 2.5 years

Immunology

Immunity is

- **humoral (eg complement, Ab's)**

or

- **cellular (B and T cells, macrophages)**

antigen is a substance that can stimulate Immune Response (IR) ie it's immunogenic

- **leucocytes (white blood cells):** derived from haemopoietic stem cell in bone marrow
  - **Neutrophils** (phagocytic, bacteriocidal, shortlived, terminally differentiated),
  - **eosinophils** (anti-parasitic, allergies),
  - **mast cells** (local inflamm, allergies, anti-parasitic, in tissues),
  - **basophils** (same as mast cells but in blood), dendritic cells (trap and present antigen),
  - **macrophages** (phagocytosis, in tissues, long lived),
  - **monocytes** (macrophage precursors in blood) – all derived from myeloid

  - **Natural Killer** cells,
  - **T helper** lymphocytes,
  - **T cytotoxic** lymphocytes,
  - **B lymphocytes** –all derived from lymphoid, **all specific except NK cells**

- **PROTECTION VS. INFECTION:**
  1. **Physical barriers** eg intact skin, secretions (eg lysozome in tears/saliva), natural flora
  2. **Innate immunity** vs everyday microbial assaults: cells and molecules
  3. **Acquired immunity** for better efficiency of innate immunity

Innate system of immunity:

ancient, responds rapidly (minutes), stereotypical response to every situation, non-specific, no memory;

- exocytes release mediators (eosinphils and mast cells) vs phagocytes ingest and destroy diseased cells

PHAGOCYTOSIS:

1. **Foreign particle adheres to phagocytic cell membrane**
2. **Cell membrane invaginates and forms a phagosome** trapped inside cell
3. **Phagosome fuses with lysosome** and toxins/enzymes/oxygen species kill and degrade bacterium and phagocyte digests remnants

- Phagocytes recognise invaders using **pattern recognition receptors (PRR) specific to microrganisms**
  - eg. components of bacterial cell wall receptors such as mannose receptor;
  - lipopolysaccaride (LPS) receptor for gram –ve bacteria);
- **activation of PRR's on leucocytes is danger signal**:
  - LEADS TO
    - increased phagocytic activity,
    - increased cytokine secretion :
      - IL1 recruits more cells, causes monocytes to become macrophages,
      - TNF raises body temp → fever; increases selctin + integrin expression
- **Soluble mediators of innate immunity** =
  1. **complement system**
     (serum proteins activated in cascade in response to tissue injury +/- bacterial invasion (latter recognised by PRR): end result of cascade: increased phagocytosis, bacterial cell lysis by Membrane Attack Complex (MAC) and inflammation;
  2. **Acute phase reactants eg C-reactive proteins** which reinforce innate immunity (thus, CRP test for inflam)
- **Innate response vs virus**: virus infected fibroblasts in tissues secrete type 1 interferons (IFN alpha and beta) –these act on surrounding host cells and prevent them being infected by stopping all protein synthesis (ANTI-VIRAL STATE)

NK cells recognise and kill virus infected host cells:

- by checking their MHC class 1 molecules for signs of presented viral antigen

Specific (adaptive) immunity: 'specialised' immune response to **target a certain pathogen**

KEY CONCEPT: 1 lymphocyte for 1 antigen; 1 kind of receptor x10^5 all over the surface.

There are 10^{10} antigen types;

There are 10^{12} Lymphocytes.

THUS: 1 in 10,000 chance of a lymphocyte meeting its antigen

THUS: Lymphocytes must CIRCULATE to inrease chances of this meeting, and

PROLIFERATE to increase their fighting numbers

CLONAL SELECTION:

PRIMARY RESPONSE

Lymphocyte + its antigen = Rapidly Dividing Lymphocyte

= Divides into 2 sets of CLONES:

the EFFECTOR clones (activated, to fight with cytokines and antibodies)- live for days/hours

the MEMORY clones (inactive, to float around and express the receptors for this antigen)-live for YEARS

SECONDARY RESPONSE:

Memory cells become effectors, activate and begin dividing

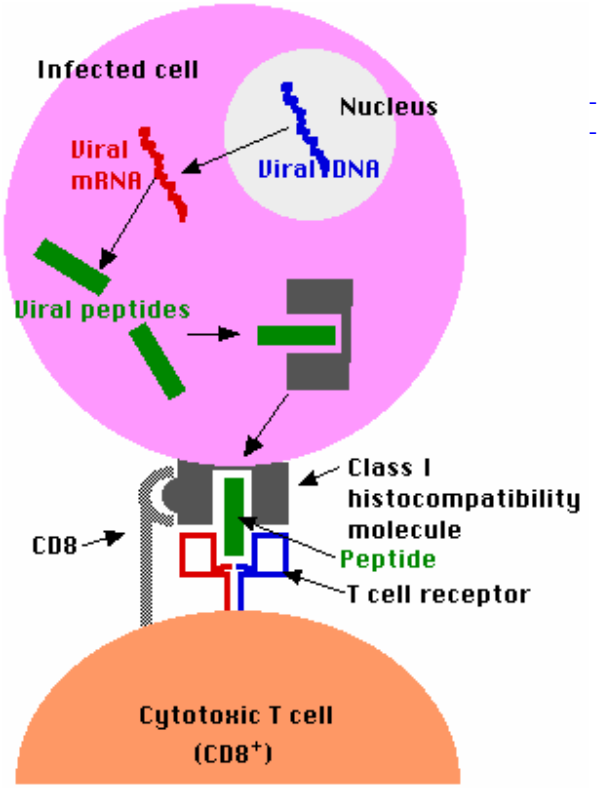
THEREFORE suddenly there are numerous cells specific for the stimulating antigen

THREFORE THE RESPONSE IS SWIFT AND BRUTAL- greater chance of meeting antigen

TYPES OF LYMPHOCYTES:

B CELLS:

- originate in bone marrow
- Migrate into secondary lymphoid tissue (lymph nodes, spleen, MALT)
- Ingest antigens and present them on MHC class 2 molecules to Helper T Cells
- When stimulated by Helper T Cells , they differentiate into Memory cells and **Plasma cells (which produce antibodies)**



T CELLS:

- Originate in thymus

2 major subtypes:

- **CD 4 T-HELPER** CELLS- **regulate immune response**
- AIDS patients lose their CD4+ T cells
- CD4+ T cells bind an antigen epitope lying in the groove of a **class II MHC molecule**
  - **TH1** participate in **cell-mediated immunity**, eg. TUBERCULOSIS MANTOUX TEST-
  - THESE RESPOND TO MHC CLASS 2 presented by APC
    - then release lymphokines that attract other leucocytes
  - **TH2** provide help for B cells and, in so doing, are **essential** for antibody-mediated immunity.
  - **bind to antigen when it is presented by B cells**
  - **-THIS CAUSES THE B CELLS TO…**
    - **Replicate like mad**
    - **Switch from synthesizing their antibodies as integral membrane proteins to a soluble version**

The result is the development **of a population of Plasma cells** secreting antibodies against the antigenic material.

CD 8 T-CYTOTOXIC CELLS

- secrete molecules that destroy the cell to which they have bound.
- The CD8 molecule, together with the MHC 1 receptor, signals that the cell to which the T cell has bound is virus-infected and needs to be destroyed

Lymphocyte Development: SELF vs NON-SELF PARADIGM

GROW IN PRIMARY LYMPHOID ORGANS: bone marrow and thymus
Need RECEPTORS FOR 10^{10} antigens; THUS: SPECIFICITY OF RECEPTORS IS ARRANGED BY
RANDOM DNA SHUFFLING: "SOMATIC RECOMBINATION" of 200 genes-
THIS IS THE **G**ENERATION **O**F **D**IVERSITY, or G.O.D. of immunology
…Thus; numerous RANDOM receptors are generated;
THEREFORE some lymphocytes end up with SELF-TARGETTING RECEPTORS! This is no good; thus:
THE LYMPHOCYTES ARE TESTED in primary lymphoid tissues to see if they react to self-antigens;
IF THEY ARE SELF-TARGETTING, THEY ARE DESTROYED (commanded to apoptose)
THUS: all "graduating" lymphocytes have SELF-TOLERANCE; the rest (90%) are disqualified and killed.
BREAKDOWN OF THIS MECHANISM LEADS TO **AUTOIMMUNE DISEASE**

Microbiology

- normal flora of gut, skin etc **essential for health**: **more microbial cells than human ones in our body**!
- Human host acquires flora just after birth and flora changes continuously thereafter;
- **COMMENSALISM** – organism acquires nutrients without being harmful to host eg *Staph epidermidis*
- BUT: commensals can become pathogens if environment or balance changes or host immunity impaired **(opportunism);**
- **PARASITISM** is ability to attach, enter, adapt, multiply and persist **without benefit to host**
- Disease results from:
  - imbalance in normal flora;
  - establishment of microbe with pathogenic potential;
  - any bacteria in normally 'aseptic tissues'
    (eg blood, bladder, eye, testis – NB not strictly sterile as viruses and prions may be present);
  - host response to infection (inflammation is damaging to human cells too!)

Koch's postulates: to attribute a disease to a specific organism

- 1. The organism must always be present in cases of disease,
- 2. It must be cultivated in pure culture (on non-living substrate),
- 3. Inoculation of susceptible hosts must reproduce disease,
- 4. Organism must be detected in inoculated hosts –
- (some problems (eg can't always cultivated in pure culture notably viruses!) but still a useful paradigm)

- **PRIONS: infectious single (sialoglyco)protein, no nucleic acid**,
  - long incubation period (years),
  - loss muscle coordination, dementia and insomnia (think: mad cow syndrome),
  - standard autoclaving does not eliminate!
- **VIROIDS:** 'viruses that infect viruses', circular single-stranded RNA with some double stranded bits,
  - only relevant eg: delta agent that infects Hep B virus
  - → additional Hep D virus in humans, hepatotoxic
- **VIRUSES:** either RNA or DNA; single stranded (ss) or double stranded (ds);
  - icosahedral, helical or complex morphology;
  - replication by adsorption, penetration, uncoating, replication of nucleic acid, assembly & accumulation
  - (inclusion body) and release- HIJACK CELLULAR PROTEIN SYNTHESIS MECHANISM;
- **RICKETTSIA:** gm negative bacteria which are obligate intracellular parasites (need cell cultures),
  - spread by arthropod vectors (lice, fleas, etc) – spotted fevers and typhus
- **CHLAMYDIA**: gm negative bacteria which are obligate intracellular parasites of mammals and birds,
  - *C. trachomatis* infects mucous membrane of eye/genital tract,
  - *C. psittaci* transmitted from birds to immunodeficient humans (lung infection);
  - elementary body is infectious, extracellular and induces endocytosis
  - reticulate body is not infectious, it is intracellular and replicating
- **MYCOPLASMA:** free-living bacteria lacking rigid cell wall,
  cause atypical pneumonia and non-gonococcal urethritis;
  - L-forms: formed from certain bacteria when cell-wall synthesis is impaired eg by antibiotics
- **SPIROCHAETES:**) – all small, gm neg; usually thin and corkscrew-shaped
  - *Treponema pallidum* (syphilis)
  - *,Borrelia recurrentis* (relapsing fever –tick borne),
  - *Leptospira interrogans* (leptospirosis – rodent borne)
- **BACTERIA**(procaryotic cells): no nucleus, cell wall present, plasma membrane +/-: flagella, spores, fibriae or pili, capsule, plasmids (DNA) – all of these add virulence

- **Virulence factors** (increase pathogenicity, also increase bacterial survival):

  (EAT RICE)

  E – enzymes (damage tissue)
  A- adhesion (allows colonisation to occur)
  T- toxin (exotoxins)
  R- resistance (via slime to receptors, or generally to antibiotic therapy)
  I- invasion (of surrounding tissue, or the blood/lymph system)
  C- capsule (slime layers often protect against immune response)
  E- endotoxins

- **How bacteria cause disease:**
- **entry and attachment** (inflammation increases secretions and symptoms facilitate spread eg cough, diarrhoea,; flagella for motility eg up urethra; haematogenous spread by direct inoculation or vector),
- **establishing a niche** (attach to tissues via receptors, compete with other flora and host cells eg iron acquisition), colonisation/adhesion (by pili/fimbriae and/or bacterial surface proteins);
- **local or general spread**,
- **multiplication,**
- **evasion of host defences** (egs capsule that evade phagocytic recognition, antiphagocytic toxins and evasion of Ab's by molecular mimicry and antigenic variation), exotoxins, shedding – transmission;

Tissue/organo tropism: tissue preference or predilection for colonisation due to membrane receptors

Endotoxin:

lipopolysaccharide (LPS) in cell wall of all gram negative bacteria, released when they die, mildly pyrogenic
- LPS causes MACROPHAGES TO GO MAD; begin to issue forth great streams of TNF and IL-1

Exotoxin:

secreted by some gram positive bacteria,
much more toxic than endotoxin!
eg's include the virulence factors above (such as lecithinase); *S aureus* has many!

Bacterial growth:

- **lag phase** (increase in cell size, no cell division),
- **exponential or logarithmic phase** (lots cell division, nutrients and wastes constant),
- **stationary phase** (build up of wastes and or depletion of nutrients and/or host defences lead to decreased growth rate but constant cell count),
- **decline phase** (more bacteria killed than formed)

Genetic exchange between bacteria:

- **transformation** (uptake of extracellular DNA),
- **transduction** (bacteriophage transmits fragment of DNA from one bacterium to other,
- **conjugation** (bacteria transmits DNA to another via sex pilus – more common in gm negative).

All of these allow plasmid to be integrated into bacteria;
plasmids contain genes for virulence, antibiotic resistance, antimicrobial agents and metabolic activities.

- ***Staph aureus*** is only pathogen that is frequently carried on skin and in nose as part of flora in 10-20% healthy adults; wound/foreign body infections include subcutaneous abscesses called 'furuncles' (boils) or if bigger and deeper 'carbuncles', impetigo (localized, superficial, crusty skin lesion esp. in kids);
  other main suspect in a purulent wound is *Step pyogenes*; also consider enteric species and anaerobes
- **Tetanus due to ubiquitous anaerobic pathogen *Clostridium tetani***,
- exotoxin of this bacteria causes spasms,
  - treat in 4 steps:

  1. Supportive care (respiration, cardiac, etc)
  2. Deliver passive immunisation (ie Ab's vs the toxin)

3. Immunise actively (ie with toxoid which is an attenuated toxin that stimulates immune response vs part of toxin molecule not involved in toxicity)
4. Give antibiotics – penicillin D.O.C. (need to arrest *C tetani* infection or it will continue to produce toxin!)

- ***Pasteurella multicida* in cat and dog bites causes local purative inflammation** and progresses to septicaemia due to exotoxins
- **Fungi (eukaryotic cells):** ; **gm positive**; cell wall is chitin
  - –1) yeast (asexual) and 2) hyphae (asexual/sexual);
  - mass of hyphal elements = mycelium;
  - amphotericin B blocks ergosterol synthesis and disrupts plasma membrane;
  - **fungi not inhibited by antibacterial antibiotics**;
  - fungal infections '**mycoses**' –
    - **superficial,** cutaneous (eg ringworm/tinea),
    - **subcutaneous, systemic** (eg candidiasis, cryptococcosis),
    - **opportunistic** (candidiasis, aspergillosis)

Pharmacology (drug names – how they act and where they act)

Antibiotics:

1. **Competitive antagonism** eg isoniazid, suphonamides (inhibit bacterial synthesis of folic acid);
2. **Inhibition of nucleic acid synthesis** eg quinolones, metronidazole;
3. **Inhibition of bacterial protein synthesis** eg rifampicin and actinomycin D inhibit transcription, aminoglycosides, spectinomycin, tetracyclines, macrolides, chloramphenicol, erythromycin, clarithromycin and clindamycin inhibit translation; 4. **Alteration of cell membranes** eg Polymyxin B and Colistin;
5. **Inhibition of cell wall synthesis** eg B-lactam antibiotics (penicillins, cephalosporins, carbanemens), cycloserine, ethionamide, isoniazid, vancomycin, bacitracin, ristocetin

Minimal inhibitory concentration is lowest conc that inhibits multiplication of organism in vitro vs min. bacteriocidal concentration: can use this to predict therapeutic capacity,
other factors to consider are **toxicity, host's immune capacity, ability of antibiotic to reach tissues**