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Angiogenesis 2010-2

<p>Question 3.2</p> <p>Angiogenesis</p>	<p>1. What is angiogenesis?</p> <p>2. Please give some examples?</p> <p>3. What steps are involved in angiogenesis from pre existing vessels?</p>	<p>1. The process of blood vessel formation in the adult. 2 methods</p> <p>1.1. Branching and extension of existing vessels</p> <p>1.2. Recruitment of endothelial progenitor cells (EPCs)</p> <p>2. Wound healing, chronic inflammation, proliferating endometrium, tumours, etc</p> <p>3. Steps in angiogenesis</p> <p>3.1. Vasodilation</p> <p>3.2. Proteolytic degradation of basement membrane</p> <p>3.3. Endothelial cells migrate to angiogenic stimuli</p> <p>3.4. Maturation</p> <p>3.5. Capillary formation</p> <p>3.6. Recruitment of periendothelial cells for support structure formation</p> <p>4. Inhibitors such as endostatin are released by proteinases (This is a small fragment of collagen that inhibits endothelial proliferation and also angiogenesis)</p>	<p>1. Bold and one other</p> <p>2. Any 2</p> <p>3. Any 3</p>
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Angiogenesis 2008-1

Q2. Angiogenesis	Describe how angiogenesis occurs.	<p>1) <u>Mobilisation of Endothelial precursor cells (EPC) from the bone marrow & from pre-existing vessels.</u></p> <p>2) EPC migrate to a site of injury or tumour growth.</p> <p>3) EPC differentiate & form a mature network by linking with existing vessels.</p> <p>4) Stabilisation: Endothelial cells from pre-existing vessels become motile & proliferate to form capillary sprouts.</p> <p>5) Vessels mature involving pericytes & smooth muscle cells to form periendothelial layer.</p>	Pass criteria: underlined
	<p>Factors: VEGF Angioproteins 1 and 2 PDGF TGFB</p> <p>Receptors: VEGFR⁻² FGF⁻² EC receptor Tie 2</p>	<p>1. Haemangioblast generates haemopoietic stem cells and angioblasts. Angioblasts like EPC are stored in adult bone marrow initiate angiogenesis. Participate in replacing lost endothelial cells, in vascular impant endothelization and in neovascularising ischaemic organs, cutaneous wounds and tumours.</p> <p>2. Vasodilatation of pre-existing vessels, increased permeability, degradation of basement membrane, disruption of endothelial cell to cell contact, proliferation and migration towards angiogenic stimulus, and endothelial cell maturation/growth inhibition/remodelling capillary beds.</p>	

Angiogenesis 2004-2

TOPIC: Angiogenesis **NUMBER:** 2

OPENING QUESTION		COMMENTS
	Describe the steps involved in angiogenesis.	
POINTS REQUIRED	1 Proteolysis of basement membrane of parent vessel – allows formation of capillary sprout and subsequent cell migration	Need 2 to pass
	2 Migration and chemotaxis of endothelial cells – towards angiogenic stimulus	
	3 Proliferation of endothelial cells	
	4 Lumen formation, maturation, inhibition of growth/remodelling – of endothelial cells, remodelling into capillary tubes	
	5 Increased permeability through gaps and transcytosis – recruitment of periendothelial cells to support endothelial tubes, providing maintenance and accessory cell function	

Fibrosis and Scar Formation 2008-1

Q1. Scar formation	What are the phases involved in scar formation?	<ol style="list-style-type: none"> 1. Fibroblast migration and proliferation 2. Extracellular matrix (ECM) deposition 3. Tissue remodelling 	Prompt: "One phase is fibroblast migration and proliferation. Can you name another phase" ? Pass criteria 2/3
	What are the local triggers of fibroblast migration and proliferation (at the site of an injury)?	<ol style="list-style-type: none"> 1. Growth Factors- TGF-β; PDGF; EGF; FGF Cytokines – IL-1; TNF	Prompt: "Can you name a growth factor / cytokine involved" ? Pass criteria: 2 to pass
	What are the sources of these local triggers?	<ol style="list-style-type: none"> 1. Platelets 2. Macrophages and other inflamm cells such as mast cells, eosinophils, lymphocytes 3. Endothelium 	Prompt: "Which blood cells or constituents are involved. Platelets are one example. Can you give another" ? Pass criteria: 2 to pass.

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Fibrosis and Scar Formation 2004-2

TOPIC: Mechanism of fibrosis and scar formation **NUMBER:** 2

OPENING QUESTION	Describe the process of fibrosis and scar formation.	COMMENTS
POINTS REQUIRED	1 Formation of new blood vessels (angiogenesis) – pre-existing vessels send out capillary buds/sprouts	Need 2 points to pass.
	2 Migration and proliferation of fibroblasts – within granulation tissue framework	
	3 Deposition of extracellular matrix (ECM) – fibrillar collagens, spindle shaped fibroblasts, elastic tissue	
	4 Maturation and organisation of fibrous tissue (tissue remodelling) – changes in composition of ECM, degradation of collagen and other ECM proteins by matrix metalloproteinases	

Wound Healing 2015-2-D

Stem: Moving onto Pathology.			
Question 2 Repair by healing, scar formation and fibrosis Subject: Path LOA: 2	What is the sequence of events for tissue healing by scar formation?	1) Blood Clot (stop bleeding, create scaffold) 2) Granulation tissue (angiogenesis, migration and proliferation of fibroblasts) 3) Cell Proliferation and Collagen Deposition (extracellular matrix (ECM) deposition) 4) Scar formation (blanching, increased collagen: type 3 then type 1) 5) Wound contraction (myofibroblasts) 6) Connective tissue remodelling (ECM synthesis and degradation) 7) Recovery of tensile strength	5/7 to pass
	How do skin wounds recover tensile strength?	Increase in collagen synthesis (type 1) and reduction in collagen degradation (first 2/12) then structural modification of collagen with cross linking & increased fibre size	Bold to pass
	What is the approximate time frame for recovery of tensile strength in skin wounds?	Skin wound has 10% tensile strength at 1/52 , and continues to improve over next 3 weeks and plateaus at ~3/12 when tensile strength is 70-80% . May never recover to 100%	Concept that very weak at time of suture removal and months to attain plateau phase
	(prompt : what is the strength of skin wounds when sutures are removed?)		

Wound Healing 2015-1-D

Stem: Once the procedure has finished, his mother asks you about the healing process. We will now move to Pathology.			
Question 4 Cutaneous wound healing (pp102-108) Subject: Path LOA:1	1. Describe the phases of cutaneous wound healing?	1. Inflammation, proliferation, and maturation. Phases overlap, and separation arbitrary. The initial injury -> platelet adhesion and aggregation + formation of clot on wound surface -> inflammation . Proliferative phase -> formation of granulation tissue, proliferation and migration of connective tissue cells, and re-epithelialization of the wound surface. Maturation involves ECM deposition, tissue remodelling + wound contraction.	2 of 3 phases in bold with correct descriptions to pass
	2. What factors influence cutaneous wound healing?	2. Systemic factors: • Nutrition. Protein deficiency and vitamin C deficiency, -> retard healing. • Metabolic status : Diabetes mellitus, -> delayed healing • Circulatory status: Inadequate blood supply or drainage (arteriosclerosis or varicose veins). • Hormones eg. glucocorticoids influence various components of inflammation, also inhibit collagen synthesis. Local factors: • Infection single most important cause of delay in healing, • Mechanical factors , (early motion of wounds). • Foreign bodies impede healing. • Size, location, and type of wound (mechanism of injury).	2 systemic and 2 local factors to pass
	3. What is wound contraction?	3. Wound contraction generally occurs in large surface wounds. The contraction helps to close the wound by decreasing the gap between its dermal edges + reducing the wound surface area. Important feature in healing by secondary union. Initial steps of wound contraction involve formation, at the edge of the wound, of a network of myofibroblasts .	Bold to pass

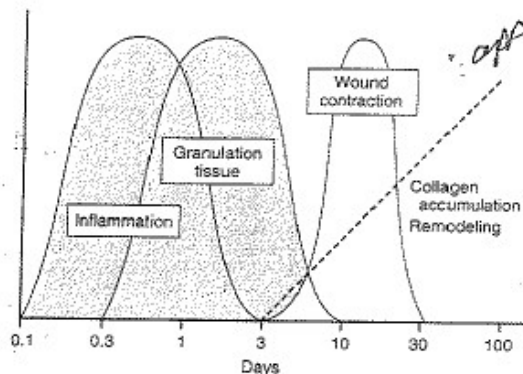
Wound Healing 2012-1

<p>Question 2</p> <p>Wound Healing</p> <p>LOA: 1</p>	<p>Describe the process of healing of an incised skin wound?</p> <p>(Prompt: include the timing of these processes.)</p> <p>What factors influence wound healing?</p>	<ul style="list-style-type: none"> a) Formation of a blood clot – immediate b) Neutrophil migration at wound margins – within 24 hours c) Formation of granulation tissue (fibroblasts and vascular endothelial tissue). Blood vessels are leaky and proteins and fluid pass into the extravascular space leading to oedema– 24-72 hours d) Cell proliferation and Collagen deposition – neutrophils are replaced by macrophages between 48 and 96 hours e) Scar formation – leucocytic infiltrate, oedema and increased vascularity disappear; increased accumulation of collagen – second week f) Wound Contraction – formation of myofibroblasts at the wound edges that contract. g) Connective tissue remodelling h) Recovery of Tensile strength – 10% at 1 week to a peak of 70-80% at 3 months <ul style="list-style-type: none"> a) Local (infection / mechanical eg motion of wound / FB / size, location, type eg incised vs blunt trauma) b) Systemic (nutrition / metabolic status / circulatory status / hormones) 	<p>Bold 3 and 2 others = 5</p> <p>To pass: 2 local & 2 systemic</p>
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Wound Healing 2010-1

a) What systemic factors affect wound healing? (50%)	1) Nutrition- (protein/ Vit C/ zinc/debilitation) 2) Metabolic- partic diabetes/ hypermetabolic/ unwell/ sepsis 3) Hormonal (steroids? effect of other hormone deficiencies/ XS catechols) 4) Circulatory status (e.g shocked/ hypotensive PVD/ venous ob, lymphatic obstruction)/ 5) age 6) drugs	Need 3 factors + 3 examples
b) What local factors impede wound healing (50%)	a) Infection b) Type/ / size of wound/not opposed c) Position- eg vasc/mvt/ pressure d) foreign bodies e) Wound vascularity/ local pressure excess f) Movement- excess g) Genetic features h) Excessive granulation " proud wounds" i) Neuropathic wounds	Bold plus At least 3 local factors- some
1. What is the coagulation cascade?	"The coagulation cascade is essentially a series of conversions of inactive pro-	Series of reactions

Wound Healing 2009-2

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Question 1	<p>Describe the process of skin wound healing by first intention.</p> <p>Prompt: Describe the timeline of these steps.</p>  <p>FIGURE 3-20 Phases of wound healing. (Modified from Clark RAF: Wound repair. In Clark RAF (ed): The molecular and cellular biology of wound repair, 2nd ed, New York, Plenum Press, 1996, p. 3.)</p>	<ul style="list-style-type: none"> • 24 hours: Scab; Neutrophils; Clot • 3 to 7 days: Mitoses; Granulation tissue; Macrophage; Fibroblast; New capillary • Weeks: Fibrous union <p><24 hours: neutrophils at the margins of the incision., 24 to 48 hours: epithelial cells move from the wound edges and fuse in the midline beneath the surface scab, producing a continuous but thin epithelial layer that closes the wound.</p> <p>By day 3, neutrophils replaced by macrophages. Granulation tissue progressively invades the incision space. Collagen fibres in the margins of incision. Epithelial cell proliferation thickens the epidermal layer.</p> <p>By day 5, the incisional filled with granulation tissue. Neovascularization is maximal. Collagen bridges the incision. The epidermis recovers its normal thickness.</p> <p>During the second week, continued accumulation of collagen and proliferation of fibroblasts. The leukocytic infiltrate, oedema, and increased vascularity have largely disappeared.</p> <p>By the end of the first month, the scar is made up of a cellular connective tissue devoid of inflammatory infiltrate, covered now by intact epidermis.</p>	<p>Timeline +</p> <ul style="list-style-type: none"> • Clot • Inflammation (neutrophils + macrophages) • Granulation • Remodelling

Wound Healing 2008-2

2. Local and Systemic influences on wound healing	1. Describe the factors that affect wound healing Prompt: Outline how they affect the healing process	(Table 3-5) Local: blood supply, denervation, local infection, FB, haematoma, mechanical stress, necrotic tissue, protection, surgical technique, tissue type Systemic: Age, anaemia, drugs, genetic disorders, hormones, diabetes, malignant disease, malnutrition, obesity, systemic infection, temperature, trauma, hypovolaemia, hypoxia, uraemia, vitamin deficiency (C), trace metal deficiency (Cu, Zn)	At least 3 local and 3 systemic. Must describe effect to pass.
	2. Describe the effect of an additional local/systemic factor.		If < 3 factors described in a group.

Wound Healing 2007-1

2. Cutaneous wound healing 1 st intent	1. Describe the order of events involved in healing by first intention Prompt: "Healing by first intention occurs in incised wounds"	1. (Day 1): Neutrophils appear, then spurs of epithelial cells from wound edges, that eventually fuse in midline 2. (Day 3): Macrophages replace neutrophils. Granulation tissue progressively invades 3. (Day 5): Incision filled with granulation tissue. Neovasc minimal. 4. (Week 2): Fibroblasts / collagen proliferate. Blanching 5. (Month 1): All inflamm infiltrate gone.	2 + 1 other
	2. What important effects does platelet-derived growth factor (PDGF) have in relation to wound healing?	1. Monocyte chemotaxis 2. Fibroblast migration and proliferation 3. Collagen synthesis 4. Collagenase secretion	2/4

Wound Healing 2005-1

Primary wound repair	Describe the process of "Primary Wound Repair" (5/8 to pass)	<ol style="list-style-type: none"> 1. <i>Immediate</i>: Blood clot (dehydration of the surface clot forms the "scab") 2. <i>Within 24 hours</i>: neutrophils move towards the fibrin clot 3. <i>24 - 48 hours</i>: wound closure by spurs of epithelial cells 4. <i>By Day 3</i>: neutrophils replaced by macrophages, granulation tissue, collagen fibres 5. <i>By Day 5</i>: Incisional space filled with granulation tissue, neovascularization maximal, bridging collagen fibres. Epidermis normal thickness, surface keratinization 6. <i>During second week</i>: continued accumulation of collagen & proliferation of fibroblasts. Blanching.10% strength 7. <i>By the end of the first month</i>: cellular connective tissue devoid of inflammatory infiltrate 8. <i>Ensuing months</i>: full tensile strength takes many months 70-80% strength 	
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Wound Healing 2004-2

TOPIC: Healing by first intention

NUMBER: 2

OPENING QUESTION	Describe the processes involved in healing by first intention.	COMMENTS
POINTS REQUIRED	1. Within 48 hrs: space filled by clotted blood/fibrin, neutrophils at margins, epidermis thickens at cut edges due to mitotic activity of basal cells, dehydration of surface clot forms scab, spurs of epithelial cells from edges migrate and grow along cut margins of dermis and deposit BM components, epithelial cells fuse in midline producing continuous thin epithelial layer	Get candidate to say in chronological order
	2. 3-7 days: neutrophils replaced by macrophages, granulation tissue invades incision space, collagen fibrils at margins then bridge incision, neovascularisation, differentiation of surface cells produces mature epidermal architecture	
	3. weeks: proliferation of fibroblasts and collagen, regression of vascular channels, disappearance of leukocytic infiltrate and oedema and loss of increased vascularity	