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Chapter 1 : Hematology and Coagulation Essentials | Medmastery

The intrinsic cascade which has less in vivo significance in normal physiological circumstances than the extrinsic cascade is initiated when contact is made between blood and exposed negatively charged surfaces. The extrinsic pathway is initiated upon vascular injury which leads to exposure of tissue factor, TF also identified as factor III , a subendothelial cell-surface glycoprotein that binds phospholipid. The green dotted arrow represents a point of cross-over between the extrinsic and intrinsic pathways. The two pathways converge at the activation of factor X to Xa. Active factor Xa hydrolyzes and activates prothrombin to thrombin. Factor XIIIa also termed transglutaminase cross-links fibrin polymers solidifying the clot. The kinins are released from both high molecular weight kininogen HMWK and low molecular weight kininogen LMWK as a result of activation of either tissue kallikrein or plasma kallikrein. The kallekreins themselves exist in inactive pre-forms. The kinins are involved in many physiological and pathological processes including regulation of blood pressure and flow via modulation of the renin-angiotensin pathway , blood coagulation, cellular proliferation and growth, angiogenesis, apoptosis , and inflammation. Kinin action on endothelial cells leads to vasodilation, increased vascular permeability, release of tissue plasminogen activator tPA , production of nitric oxide NO , and the mobilization of arachidonic acid, primarily resulting in prostacyclin PGI2 production by endothelial cells. Although the activities of the kallikrein-kinin system are involved in numerous processes, this section will deal only with their function in blood coagulation. With respect to hemostasis the most important kinin is bradykinin which is released from HMWK. The two forms of prekallikrein, plasma and tissue, are derived from distinct genes on different chromosomes. The plasma kallikrein gene symbol KLKB1 is on chromosome 4q34â€”q35 and the tissue kallikrein gene symbol KLK1 located on chromosome 19q When plasma prekallikrein is activated to kallikrein it cleaves HMWK in a two-step process that ultimately releases bradykinin. Bradykinin is a 9-amino acid vasoactive peptide that induces vasodilation and increases vascular permeability. Activated tissue kallikrein cleaves lysyl-bradykinin also called kallidin from LMWK. Lysyl-bradykinin is bradykinin with a lysine residue at the N-terminus making it a amino acid vasoactive peptide. Its activities are essentially identical to those of bradykinin. Exons 1 to 9 encode the heavy chain of both kininogens. Exon 10 encodes bradykinin as well as the light chain of HMWK. Exon 11 encodes the light chain of LMWK. The heavy and light chain nomenclature refers to the disulfide-bonded structure of each kininogen after their activation, which results from kallikrein cleavage. The protein circulates in the plasma as single-chain polypeptide with a molecular weight of 88â€” kDa dependent upon the level of glycosylation. The heavy chain is 64 kDa and contains domains 1, 2, and 3 whereas the light chain is 45â€”56 kDa and comprises domains 5 and 6. The heavy and light chains are linked together through domain 4 which also contains the bradykinin sequence. Domain 1 contains a low affinity calcium-binding site. Domain 3 also has platelet and endothelial cell-binding activity. Domain 5 has sequences for heparin binding, cell-binding sites, and antiangiogenic properties. The binding of HMWK to negatively charged surfaces occurs through a histidine region of the light chain which is in domain 5. Domain 6 contains the prekallikrein and factor XI-binding sites. By being able to bind to charged surfaces via domain 5 and simultaneously bind factor XI and prekallikrein via domain 6, HMWK can serve as the cofactor in contact activation of plasma. Factor XII, prekallikrein, and HMWK saturably and reversibly bind to endothelial cells, platelets, and granulocytes in a zinc-dependent reaction. When plasma makes contact with a negatively charged surface factor XII binds and is autoactivated to factor XIIa the "a" signifies the activated factor. There is also reciprocal activation of factor XII by kallikrein resulting in amplification of the system. The actual surface that leads to factor XII autoactivation is unknown however, several physiologic substances support the process. Once the contact system is activated the intrinsic pathway described below is initiated. However, abnormal physiology such as hyperlipidemic states or bacterial infiltration can lead to activation of thrombosis via the intrinsic clotting cascade. Also required are the proteins prekallikrein PK and high-molecular-weight kininogen HK or HMWK

, as well as calcium ions and phospholipids secreted from platelets. Each of these pathway constituents leads to the conversion of factor X inactive to factor Xa. Initiation of the intrinsic pathway occurs when prekallikrein, high-molecular-weight kininogen, factor XI and factor XII are exposed to a negatively charged surface. This is termed the contact phase and can occur as a result of interaction with the phospholipids primarily phosphatidylethanolamine, PE of circulating lipoprotein particles such as chylomicrons, VLDLs, and oxidized LDLs. This is the basis of the role of hyperlipidemia in the promotion of a pro-thrombotic state and the development of atherosclerosis. Indeed, elevated levels of homocysteine in the blood have been shown to correlate with cardiovascular dysfunction. Therefore, it is important to ensure that proper function of the methionine synthase reaction is maintained. Although it would be assumed that increased intake of vitamin B12 should lead to increased conversion of homocysteine to methionine, and thus reduced levels of circulating homocysteine, controlled studies have shown that this does not occur. The assemblage of contact phase components results in conversion of prekallikrein to kallikrein, which in turn activates factor XII to factor XIIa. Factor XIIa will also hydrolyze more prekallikrein to kallikrein, establishing a reciprocal activation cascade. Kallikrein acts upon HMWK leading to the release of bradykinin, a potent vasodilator. One of the responses of platelets to activation is the presentation of phosphatidylserine PS and phosphatidylinositol PI on their surfaces. The exposure of these phospholipids allows the tenase complex to form. Factor VIIIa is termed a cofactor in the clotting cascade. As the concentration of thrombin increases, factor VIIIa is ultimately cleaved by thrombin and inactivated. This dual action of thrombin, upon factor VIII, acts to limit the extent of tenase complex formation and thus the extent of the coagulation cascade. The extrinsic pathway is initiated at the site of injury in response to the release of tissue factor factor III and thus, is also known as the tissue factor pathway. Tissue factor is a cofactor in the factor VIIa-catalyzed activation of factor X. Factor VIIa, a gla residue containing serine protease, cleaves factor X to factor Xa in a manner identical to that of factor IXa of the intrinsic pathway. The activation of factor VII occurs through the action of thrombin or factor Xa. The ability of factor Xa to activate factor VII creates a link between the intrinsic and extrinsic pathways. An additional link between the two pathways exists through the ability of tissue factor and factor VIIa to activate factor IX. The formation of complex between factor VIIa and tissue factor is believed to be a principal step in the overall clotting cascade. Evidence for this stems from the fact that persons with hereditary deficiencies in the components of the contact phase of the intrinsic pathway do not exhibit clotting problems. The protein, lipoprotein-associated coagulation inhibitor, LACI specifically binds to this complex. LACI is composed of 3 tandem protease inhibitor domains. Thrombin, in turn, converts fibrinogen to fibrin. The activation of thrombin occurs on the surface of activated platelets and requires formation of a prothrombinase complex. Factor V is a cofactor in the formation of the prothrombinase complex, similar to the role of factor VIII in tenase complex formation. Like factor VIII activation, factor V is activated to factor Va by means of minute amounts and is inactivated by increased levels of thrombin. Factor Va binds to specific receptors on the surfaces of activated platelets and forms a complex with prothrombin and factor Xa. Prothrombin is a 72 kDa, single-chain protein containing ten gla residues in its N-terminal region. Within the prothrombinase complex, prothrombin is cleaved at 2 sites by factor Xa. This cleavage generates a 2-chain active thrombin molecule containing an A and a B chain which are held together by a single disulfide bond. In addition to its role in activation of fibrin clot formation, thrombin plays an important regulatory role in coagulation. Thrombin combines with thrombomodulin present on endothelial cell surfaces forming a complex that converts protein C to protein Ca. The cofactor protein S and protein Ca degrade factors Va and VIIIa, thereby limiting the activity of these 2 factors in the coagulation cascade see details below. PARs utilize a unique mechanism to convert the result of extracellular proteolytic cleavage into an intracellular signaling event. PARs carry their own ligand which remains inactive until protease cleavage, such as by thrombin, "unmasks" the ligand. Following thrombin cleavage the unmasked ligand is still a part of the intact PAR but is now capable of interacting with the ligand-binding domain of the PAR resulting in the activation of numerous signaling cascades. Because the activation of PARs requires proteolytic cleavage the activation process is irreversible. The thrombin-induced signaling also leads to increased platelet activation and leukocyte adhesion. Thrombin-mediated activation of PAR On the surface of platelets thrombin binds to PAR-1 resulting in release of the ligand portion of the

receptor. The response to the activated signal transduction cascades includes granule secretion, release of arachidonic acid from membrane phospholipids, and changes in cytoskeletal architecture. All of these effects of thrombin activation of a PAR on platelets leads to further platelet activation and ultimately blood coagulation. Thrombin also activates thrombin-activatable fibrinolysis inhibitor TAFI thus modulating fibrinolysis degradation of fibrin clots. This leads to an impairment of plasminogen activation, thereby reducing the rate of fibrin clot dissolution i. There are 2 principal mechanisms by which thrombin activity is regulated. The predominant form of thrombin in the circulation is the inactive prothrombin, whose activation requires the pathways of proenzyme activation described above for the coagulation cascade. At each step in the cascade, feedback mechanisms regulate the balance between active and inactive enzymes. The activity of antithrombin III is potentiated in the presence of heparin by the following means: This effect of heparin is the basis for its clinical use as an anticoagulant. The naturally occurring heparin activator of antithrombin III is present as heparan and heparan sulfate on the surface of vessel endothelial cells. It is this feature that controls the activation of the intrinsic coagulation cascade. Its physiological significance is demonstrated by the fact that lack of this protein plays a causative role in the development of emphysema. Control of Coagulation and Sepsis Protein C PC is a trypsin-like serine protease that serves as a major regulator of the coagulation process. These gla residues in the amino terminus of PC constitute the "gla domain" of the protein. In addition to the gla domain, PC contains two epidermal growth factor-like regions EGF domains , the serine protease domain, and an activation peptide. Thrombin cleavage of PC removes the activation peptide generating aPC. This results in the termination of the role of VIIIa as the scaffold for the formation of the tenase complex and Va as a co-factor in the conversion of prothrombin to thrombin in the prothrombinase complex.

Chapter 2 : Coagulation, the essentials (edition) | Open Library

Coagulation and assessment of hemostasis In this chapter, you'll learn how to order and interpret tests to assess hemostasis and platelet function, interpret a thromboelastograph, and explain the coagulation pathway.

Search Conventional Coagulation-Flocculation-Sedimentation Conventional coagulationâ€"flocculation-sedimentation practices are essential pretreatments for many water purification systemsâ€"especially filtration treatments. These processes agglomerate suspended solids together into larger bodies so that physical filtration processes can more easily remove them. Particulate removal by these methods makes later filtering processes far more effective. The process is often followed by gravity separation sedimentation or flotation and is always followed by filtration. A chemical coagulant , such as iron salts, aluminum salts, or polymers , is added to source water to facilitate bonding among particulates. Coagulants work by creating a chemical reaction and eliminating the negative charges that cause particles to repel each other. The coagulant-source water mixture is then slowly stirred in a process known as flocculation. Improper coagulants make these treatment methods ineffective. Dissolved Air Flotation Dissolved air flotation is a form of coagulation-flocculation technology that is used as a pretreatment. Employing this technique before water filtration reduces the clogging that causes maintenance problems of downstream filtration. Dissolved air flotation is particularly well-suited for the removal of algae, unwanted coloring, and lighter particles that resist settling out of treated source water. The process does not work well with highly turbid waters because heavier particles, like silt and clay, are not as easily floated to the water surface. To begin the process, a chemical coagulant , such as iron salts, aluminum salts, or polymers , is added to the source water to facilitate bonding among particulates. Coagulants work by creating a chemical reaction, eliminating negative charges that cause particles to repel each other. The action of these bubbles forces clots or flocs of particles to the water surface where they can be skimmed off. Dissolved air flotation is an alternative to sedimentation. It performs a similar task by a diametrically opposed methodâ€"forcing contaminant clumps to the surface rather than allowing them to settle out on the bottom. Flocculation-Chlorination A system that incorporates coagulation-flocculation followed by chlorination has been developed as a point of use technology, especially for developing countries. It uses a small packet of powdered ferrous sulfate a common flocculent and calcium hypochlorite a common disinfectant. A user opens the packet, adds the contents to an open bucket containing about ten liters of water, stirs for five minutes, lets the solids settle to the bottom, strains the water through cotton cloth into another container, and waits 20 minutes for the chlorine to disinfect the water. The combination of particle removal and disinfection appears to produce high removal rates of bacteria , viruses , and protozoa , even in highly turbid waters. There is considerable evidence that the system has reduced diarrheal disease significantly in various locations. There is also evidence that the flocculation process helps remove arsenic ; however, these systems are not an adequate substitute for high-quality centralized treatment when it can be made available. But it also removes harmful toxins like radon and arsenic. Though there is no consensus, some studies have even suggested that lime softening is effective at removal of Giardia. Hard water is a common condition responsible for numerous problems. Users often recognize hard water because it prevents their soap from lathering properly. Because of these inconveniences, many treatment facilities use lime softening to soften hard water for consumer use. Before lime softening can be used, managers must determine the softening chemistry required. This is a relatively easy task for groundwater sources, which remain more constant in their composition. Surface waters , however, fluctuate widely in quality and may require frequent changes to the softening chemical mix. In lime softening, lime and sometimes sodium carbonate are added to the water as it enters a combination solids contact clarifier. This raises the pH i. Later, the pH of the effluent from the clarifier is reduced again, and the water is then filtered through a granular media filter. The water chemistry requirements of these systems require knowledgeable operators, which may make lime softening an economic challenge for some very small systems.

Chapter 3 : Coagulation - Wikipedia

Coagulation, the essentials by David P. Fischbach, , Williams & Wilkins edition, in English.

Download our discussion guide so you ask the right questions and cover the right topics. Allergic reactions may occur. Call your healthcare provider or get emergency treatment right away if you have any of the following symptoms: ALPROLIX may increase the risk of forming abnormal blood clots in your body, especially if you have risk factors for developing blood clots. Call your healthcare provider or seek emergency care if you have symptoms of a possible abnormal blood clot, which may include: Your healthcare provider may need to test your blood for inhibitors from time to time. Talk to your healthcare provider for more information and about any side effect that bothers you or does not go away. Tell your healthcare provider about all your health conditions, including if you: Have or have had any medical problems. Are taking any prescription and non-prescription medicines, such as over-the-counter medicines, supplements, or herbal medicines. Are pregnant or planning to become pregnant. If your bleeding is not controlled and you experience a lack of clinical response to Factor IX therapy, call your healthcare provider right away. Medicines are sometimes prescribed for purposes other than those listed here. Hemophilia B is also called congenital Factor IX deficiency. You should be trained on how to do infusions by your healthcare provider. If you are unsure of the procedure, please ask your healthcare provider. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment. The risk information provided here is not comprehensive. The FDA-approved product labeling can be found at www. You are encouraged to report negative side effects of prescription drugs to the FDA.

Chapter 4 : Essential Guide to Blood Coagulation - Google Books

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Selected general articles Fibrinolysis simplified. Blue arrows denote stimulation, and red arrows inhibition. Plasmin is an important enzyme that participates in fibrinolysis and degradation of various other proteins. Elevated PAI-1 is a risk factor for thrombosis and atherosclerosis PAI-1 is a serine protease inhibitor serpin that functions as the principal inhibitor of tissue plasminogen activator tPA and urokinase uPA , the activators of plasminogen and hence fibrinolysis the physiological breakdown of blood clots. APC is classified as a serine protease as it contains a residue of serine in its active site. The zymogenic form of protein C is a vitamin K -dependent glycoprotein that circulates in blood plasma. Its structure is that of a two-chain polypeptide consisting of a light chain and a heavy chain connected by a disulfide bond. Because of the crucial role that protein C plays as an anticoagulant , those with deficiencies in protein C, or some kind of resistance to APC, suffer from a significantly increased risk of forming dangerous blood clots thrombosis. Plasmin is an important enzyme EC 3. The degradation of fibrin is termed fibrinolysis. In humans, the plasmin protein is encoded by the PLG gene. It is an enzyme of the serine protease class. Food and Drug Administration approval for uncontrolled bleeding in hemophilia patients. It is sometimes used unlicensed in severe uncontrollable bleeding, although there have been safety concerns. A biosimilar form of recombinant activated factor VII AryoSeven is also available, but does not play any considerable role in the market. Deficiency of this protein causes haemophilia B. It was discovered in after a young boy named Stephen Christmas was found to be lacking this exact factor, leading to haemophilia. It is a serine endopeptidase protease group S1, PA clan. Factor X is synthesized in the liver and requires vitamin K for its synthesis. It is therefore the first member of the final common pathway or thrombin pathway. Protein Z-dependent protease inhibitor is a protein circulating in the blood which inhibits factors Xa and XIa of the coagulation cascade. It is a member of the class of the serine protease inhibitors serpins. Its name implies that it requires protein Z , another circulating protein, to function properly, but this only applies to its inhibition of factor X. It is about 72 kDa heavy and amino acids large. It is produced by the liver. Factor V pronounced factor five is a protein of the coagulation system, rarely referred to as proaccelerin or labile factor. In contrast to most other coagulation factors, it is not enzymatically active but functions as a cofactor. Deficiency leads to predisposition for hemorrhage , while some mutations most notably factor V Leiden predispose for thrombosis. Protein Z is a member of the coagulation cascade , the group of blood proteins that leads to the formation of blood clots. It is a gla domain protein and thus vitamin K -dependent, and its functionality is therefore impaired in warfarin therapy. It is a glycoprotein. Micrograph showing fibrin dark pink amorphous material in a blocked vein surrounded by extravasated red blood cells right of image. An artery left of image and the amnion far left of image is also seen. Placenta in a case of fetal thrombotic vasculopathy. Fibrin also called Factor Ia is a fibrous , non-globular protein involved in the clotting of blood. It is formed by the action of the protease thrombin on fibrinogen which causes it to polymerize. The polymerized fibrin together with platelets forms a hemostatic plug or clot over a wound site. When the lining of a blood vessel is broken, platelets are attracted forming a platelet plug. These platelets have thrombin receptors on their surfaces that bind serum thrombin molecules which in turn convert soluble fibrinogen in the serum into fibrin at the wound site. Fibrin forms long strands of tough insoluble protein that are bound to the platelets. Factor XIII completes the cross-linking of fibrin so that it hardens and contracts. The cross-linked fibrin forms a mesh atop the platelet plug that completes the clot. Tissue factor , also called platelet tissue factor, factor III, or CD is a protein encoded by the F3 gene , present in subendothelial tissue and leukocytes. Its role in the clotting process is the initiation of thrombin formation from the zymogen prothrombin. Thromboplastin defines the cascade that leads to the activation of factor X - the tissue factor pathway. In doing so it has replaced the previously named extrinsic pathway in order to eliminate ambiguity. It is a serine protease EC 3. As an enzyme , it catalyzes the conversion of plasminogen to

plasmin , the major enzyme responsible for clot breakdown. Specific rtPAs include alteplase , reteplase , and tenecteplase. They are used in clinical medicine to treat embolic or thrombotic stroke. The use of this protein is contraindicated in hemorrhagic stroke and head trauma. The antidote for tPA in case of toxicity is aminocaproic acid. Antithrombin AT is a small protein molecule that inactivates several enzymes of the coagulation system. Antithrombin is a glycoprotein produced by the liver and consists of amino acids. It contains three disulfide bonds and a total of four possible glycosylation sites. Its activity is increased manyfold by the anticoagulant drug heparin , which enhances the binding of antithrombin to factor IIa Thrombin and factor Xa. Increased plasma levels in a large number of cardiovascular, neoplastic, and connective tissue diseases are presumed to arise from adverse changes to the endothelium , and may contribute to an increased risk of thrombosis. Prekallikrein PK , also known as Fletcher factor, is an 85, Mr serine protease that complexes with high-molecular-weight kininogen. PK is the precursor of plasma kallikrein , which is a serine protease that activates kinins. Platelet membrane glycoproteins are surface glycoproteins found on platelets thrombocytes which play a key role in hemostasis. When the blood vessel wall is damaged, platelet membrane glycoproteins interact with the extracellular matrix. Factor XI or plasma thromboplastin antecedent is the zymogen form of factor XIa, one of the enzymes of the coagulation cascade. Like many other coagulation factors, it is a serine protease. In humans, Factor XI is encoded by the F11 gene. High-molecular-weight kininogen HMWK or HK is a circulating plasma protein which participates in the initiation of blood coagulation , and in the generation of the vasodilator bradykinin via the kallikrein-kinin system. HMWK is inactive until it either adheres to binding proteins beneath an endothelium disrupted by injury, thereby initiating coagulation; or it binds to intact endothelial cells or platelets for functions other than coagulation. It is mainly produced by the liver , and also locally synthesized by macrophages , fibroblasts , and adrenocortical cells. In humans it is encoded by the A2M gene. Alpha 2 macroglobulin acts as an antiprotease and is able to inactivate an enormous variety of proteinases. It functions as an inhibitor of fibrinolysis by inhibiting plasmin and kallikrein. It functions as an inhibitor of coagulation by inhibiting thrombin. Coagulation factor XII , also known as Hageman factor, is a plasma protein. In humans, factor XII is encoded by the F12 gene. FXIIID, while generally rare, does occur, with Iran having the highest global incidence of the disorder with cases. The city of Khash , located in Sistan and Balochistan provinces, has the highest incidence in Iran, with a high rate of consanguineous marriage. Fibrinogen factor I is a glycoprotein that in vertebrates circulates in the blood. During tissue and vascular injury it is converted enzymatically by thrombin to fibrin and subsequently to a fibrin-based blood clot. Fibrinogen functions primarily to occlude blood vessels and thereby stop excessive bleeding. This activity, sometimes referred to as antithrombin I, serves to limit blood clotting. Loss or reduction in this antithrombin 1 activity due to mutations in fibrinogen genes or hypo-fibrinogen conditions can lead to excessive blood clotting and thrombosis. Fibrin also mediates blood platelet and endothelial cell spreading, tissue fibroblast proliferation, capillary tube formation , and angiogenesis and thereby functions to promote tissue revascularization, wound healing, and tissue repair. These disorders represent a clinically important group of rare conditions in which individuals may present with severe episodes of pathological bleeding and thrombosis; these conditions are treated by supplementing blood fibrinogen levels and inhibiting blood clotting, respectively. Certain of these disorders may also be the cause of liver and kidney diseases. Defects in this gene result in hemophilia A , a recessive X-linked coagulation disorder. Factor VIII is produced in liver sinusoidal cells and endothelial cells outside the liver throughout the body. This protein circulates in the bloodstream in an inactive form, bound to another molecule called von Willebrand factor , until an injury that damages blood vessels occurs. In response to injury, coagulation factor VIII is activated and separates from von Willebrand factor. The active protein sometimes written as coagulation factor VIIIa interacts with another coagulation factor called factor IX. This interaction sets off a chain of additional chemical reactions that form a blood clot. The factor VIII gene produces two alternatively spliced transcripts. Transcript variant 1 encodes a large glycoprotein , isoform a, which circulates in plasma and associates with von Willebrand factor in a noncovalent complex. This protein undergoes multiple cleavage events. Transcript variant 2 encodes a putative small protein, isoform b, which consists primarily of the phospholipid binding domain of factor VIIIc. This binding domain is essential for coagulant activity. Role of thrombin in the blood coagulation cascade

Thrombin EC 3. Prothrombin coagulation factor II is proteolytically cleaved to form thrombin in the clotting process. Thrombin in turn acts as a serine protease that converts soluble fibrinogen into insoluble strands of fibrin , as well as catalyzing many other coagulation-related reactions. Consider asking it at the Wikipedia reference desk. Selected images The classical blood coagulation pathway Blood coagulation pathways in vivo showing the central role played by thrombin Modern coagulation pathway.

Chapter 5 : Stago - Coagulation: an Essential Choice

*Coagulation the Essentials [P. David and Fogdall, P. Richard Fischbach, Illustrated by Barbara Haynes] on calendrierdelascience.com *FREE* shipping on qualifying offers.*

Laboratoire Stago Paris, France founded Development of the first Haemostasis reagents Laboratoire Stago becomes Diagnostica Stago: The business becomes wholly devoted to Haemostasis US subsidiary opened Instrumentation activity launched First automated coagulation analyser patented STA released worldwide BioCytex joins the Stago Group STA-R released worldwide New reagents production unit Taverny â€" France China subsidiary opened United Kingdom subsidiary opened Distribution office in Hong Kong Distribution office in Gurgaon India Carefully controlled growth Stago, an unlisted independent family group, is seeking long-term development. All strategic decisions related to the organization, investment, acquisitions, partnerships, product development and new subsidiaries are carefully taken by the executive board and the president with a view to ensuring that the group endures. Strength in specialisation Since , Stago has dedicated its entire resources to developing the single field of coagulation. Permanently attuned to the medical and scientific communities, Stago is actively interested in all advances in this domain and in all the implications of such progress. Through this strategic approach, the company now has many major patents and innovations. With more than coagulation products, Stago offers a wide product portfolio through its highly effective commercial network subsidiaries and distributors and is a market leader in its field. From routine tests to investigation of highly specialised parameters, some of which have been developed solely for specific studies throughout the world.

Chapter 6 : Coagulation:The Essential | Anesthesiology | ASA Publications

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Essential notes on the clotting or coagulation of blood Ashiya Advertisements: When there is an injury and blood flows, a mechanism is provided within the body whereby blood loss is prevented. This is termed as the coagulation or clotting of blood. The actual mechanism of blood coagulation is a complicated one, but the general principles are simple and important. Before clotting, there are some substances which must be present in the blood. They are prothrombin, calcium, fibrinogen and thromboplastin. Prothrombin, calcium and fibrinogen are all normal constituents of blood. But thromboplastin is released only when there is a damage in a blood vessel or tissue cell the release of thromboplastin from thrombocytes or blood platelets brings about a series of changes or events which finally produces a blood clot. Normally, prothrombin protein present in the plasma as such is inactive, but when acted upon thromboplastin in the presence of calcium is converted to an active substance thrombin. Thrombin in turn acts on fibrinogen, another plasma protein, to produce an in soluble thread-like substance called fibrin. The fibrin threads entrap blood cells to form a solid mass, the clot. The mechanism of clotting can be expressed in a simple formula: Calcium salts acts as good coagulants. Vitamin K has a coagulant action because it helps in the formation of prothrombin, which is necessary for blood clotting. Injury to the tissues or vessel wall helps in coagulation, so that a clean cut with a sharp knife bleeds more freely than a crushed wound in which there is bruising and damage to the surrounding tissues. Contact with a foreign body as the application of surgical dressings help in the speedy formation of a clot and arrest of hemorrhage. Slightly higher temperature than that of the body helps clotting and hence the use of hot swabs to stop surgical bleeding. Heparin is a protein normally present in the blood is formed in the liver and prevents blood clotting in the vessels. Addition of sodium citrate and potassium Oxalate to the blood will combine with calcium and form insoluble salts, thereby make it inactive. In this method, blood is preserved in the blood banks without coagulation. Contact with oil, grease or paraffin wax, would retard clotting. Snake venom is another anticoagulant.

Chapter 7 : Blood Coagulation: Hemostasis

Coagulation is the name for the process the body uses to form a blood clot. This can be a wanted process, where the clot is formed to stop bleeding; such as when you cut yourself or after you've had a tooth out.

Plasmin [edit] Plasmin is generated by proteolytic cleavage of plasminogen, a plasma protein synthesized in the liver. This cleavage is catalyzed by tissue plasminogen activator t-PA , which is synthesized and secreted by endothelium. Plasmin proteolytically cleaves fibrin into fibrin degradation products that inhibit excessive fibrin formation. Prostacyclin [edit] Prostacyclin PGI2 is released by endothelium and activates platelet Gs protein-linked receptors. This, in turn, activates adenylyl cyclase , which synthesizes cAMP. Fibrinolysis Eventually, blood clots are reorganised and resorbed by a process termed fibrinolysis. The main enzyme responsible for this process plasmin is regulated by various activators and inhibitors. Coagulation can physically trap invading microbes in blood clots. Also, some products of the coagulation system can contribute to the innate immune system by their ability to increase vascular permeability and act as chemotactic agents for phagocytic cells. In addition, some of the products of the coagulation system are directly antimicrobial. For example, beta-lysine , an amino acid produced by platelets during coagulation, can cause lysis of many Gram-positive bacteria by acting as a cationic detergent. In addition, pathogenic bacteria may secrete agents that alter the coagulation system, e. Assessment[edit] Numerous tests are used to assess the function of the coagulation system: The contact activation intrinsic pathway is initiated by activation of the "contact factors" of plasma, and can be measured by the activated partial thromboplastin time aPTT test. The tissue factor extrinsic pathway is initiated by release of tissue factor a specific cellular lipoprotein , and can be measured by the prothrombin time PT test. PT results are often reported as ratio INR value to monitor dosing of oral anticoagulants such as warfarin. The quantitative and qualitative screening of fibrinogen is measured by the thrombin clotting time TCT. Measurement of the exact amount of fibrinogen present in the blood is generally done using the Clauss method for fibrinogen testing. Many analysers are capable of measuring a "derived fibrinogen" level from the graph of the Prothrombin time clot. If a coagulation factor is part of the contact activation or tissue factor pathway, a deficiency of that factor will affect only one of the tests: If an abnormal PT or aPTT is present, additional testing will occur to determine which if any factor is present as aberrant concentrations. Deficiencies of fibrinogen quantitative or qualitative will affect all screening tests. Role in disease[edit] Coagulation defects may cause hemorrhage or thrombosis, and occasionally both, depending on the nature of the defect. This protein receptor complex is found on the surface of platelets, and in conjunction with GPV allows for platelets to adhere to the site of injury. Mutations in the genes associated with the glycoprotein Ib-IX-V complex are characteristic of Bernard-Soulier syndrome Platelet conditions may be congenital or acquired. Most are rare conditions. Most inborn platelet pathologies predispose to hemorrhage. Von Willebrand disease is due to deficiency or abnormal function of von Willebrand factor , and leads to a similar bleeding pattern; its milder forms are relatively common. Decreased platelet numbers may be due to various causes, including insufficient production e. Most consumptive conditions lead to platelet activation, and some are associated with thrombosis. Disease and clinical significance of thrombosis[edit] The best-known coagulation factor disorders are the hemophilias. Hemophilia A and B are X-linked recessive disorders, whereas Hemophilia C is a much more rare autosomal recessive disorder most commonly seen in Ashkenazi Jews. Von Willebrand disease which behaves more like a platelet disorder except in severe cases , is the most common hereditary bleeding disorder and is characterized as being inherited autosomal recessive or dominant. This binding helps mediate the activation of platelets and formation of primary hemostasis. Bernard-Soulier syndrome is a defect or deficiency in GPIb. GPIb, the receptor for vWF, can be defective and lead to lack of primary clot formation primary hemostasis and increased bleeding tendency. This is an autosomal recessive inherited disorder. Thrombasthenia of Glanzmann and Naegeli Glanzmann thrombasthenia is extremely rare. In liver failure acute and chronic forms , there is insufficient production of coagulation factors by the liver; this may increase bleeding risk. Deficiency of Vitamin K may also contribute to bleeding disorders because clotting factor maturation depends on Vitamin K. Thrombosis is the

pathological development of blood clots. These clots may break free and become mobile, forming an embolus or grow to such a size that occludes the vessel in which it developed. An embolism is said to occur when the thrombus blood clot becomes a mobile embolus and migrates to another part of the body, interfering with blood circulation and hence impairing organ function downstream of the occlusion. This causes ischemia and often leads to ischemic necrosis of tissue. Most cases of venous thrombosis are due to acquired states older age, surgery, cancer, immobility or inherited thrombophilias e. Mutations in factor XII have been associated with an asymptomatic prolongation in the clotting time and possibly a tendency toward thrombophlebitis. Other mutations have been linked with a rare form of hereditary angioedema type III essentialism. Procoagulants[edit] The use of adsorbent chemicals, such as zeolites , and other hemostatic agents are also used for sealing severe injuries quickly such as in traumatic bleeding secondary to gunshot wounds. Thrombin and fibrin glue are used surgically to treat bleeding and to thrombose aneurysms. Desmopressin is used to improve platelet function by activating arginine vasopressin receptor 1A. Coagulation factor concentrates are used to treat hemophilia , to reverse the effects of anticoagulants, and to treat bleeding in patients with impaired coagulation factor synthesis or increased consumption. Prothrombin complex concentrate , cryoprecipitate and fresh frozen plasma are commonly used coagulation factor products. Recombinant activated human factor VII is increasingly popular in the treatment of major bleeding. Tranexamic acid and aminocaproic acid inhibit fibrinolysis, and lead to a de facto reduced bleeding rate. Before its withdrawal, aprotinin was used in some forms of major surgery to decrease bleeding risk and need for blood products. Rivaroxaban drug bound to the coagulation factor Xa. The drug prevents this protein from activating the coagulation pathway by inhibiting its enzymatic activity. Antiplatelet drug and Anticoagulant Anticoagulants and anti-platelet agents are amongst the most commonly used medications. Of the anticoagulants, warfarin and related coumarins and heparin are the most commonly used. A newer class of drugs, the direct thrombin inhibitors , is under development; some members are already in clinical use such as lepirudin. Also under development are other small molecular compounds that interfere directly with the enzymatic action of particular coagulation factors e.

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