

Drugs & Blood

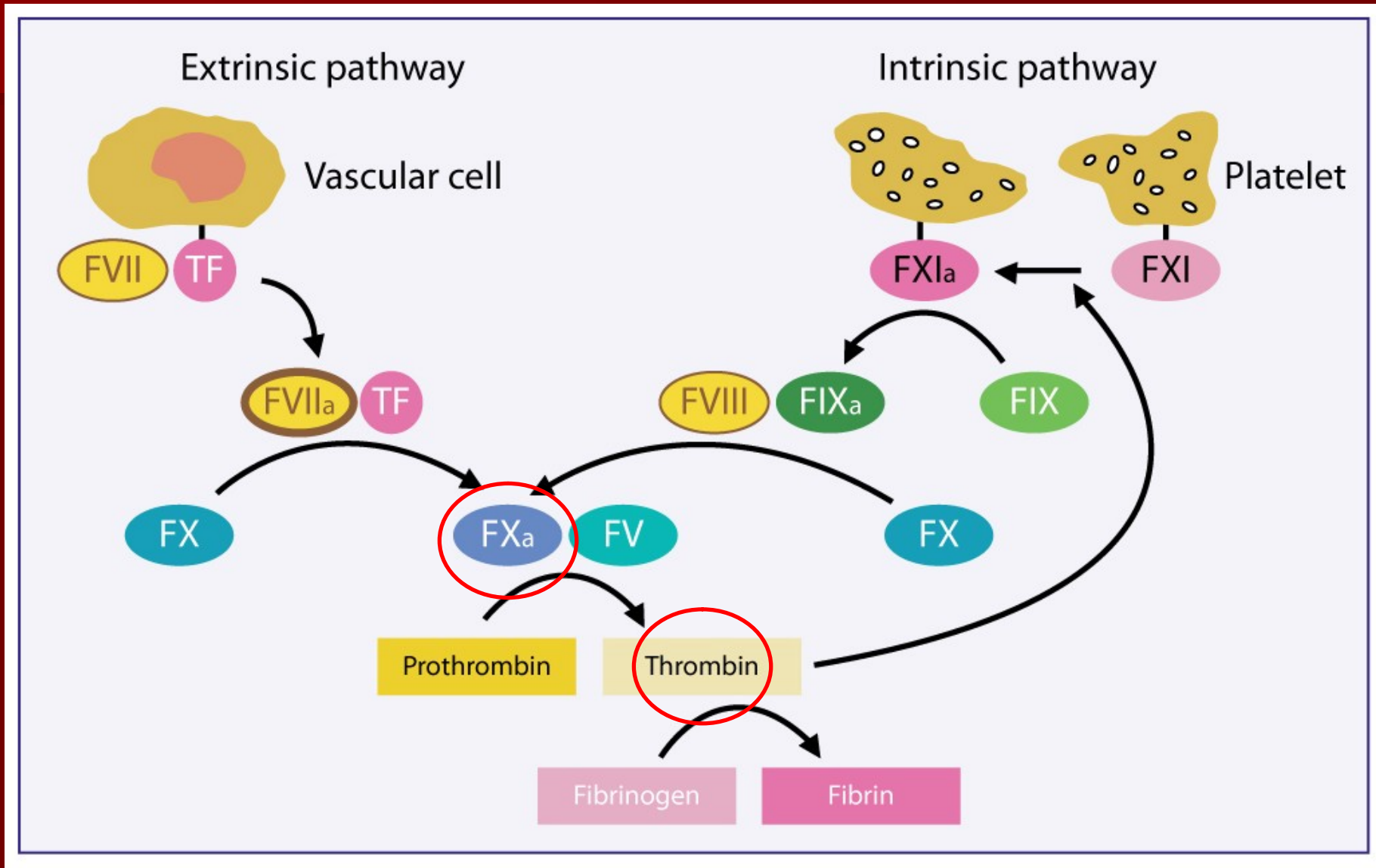
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Aim

- To gain a greater understanding of how drugs affect the blood, including drugs which:
 - Affect clotting
 - May be used to stimulate red blood cell production
 - Cause blood dyscrasias as side effects

Clotting Cascade



Clotting Cascade Inhibitors

- **Indirect thrombin inhibitors:**
 - Heparin
 - Low molecular weight heparins (LMWH)
 - Fondaparinux, danaparoid
- **Direct thrombin inhibitors:**
 - Hirudins: bivalirudin
 - Dabigatran, argatroban
- **Vitamin K antagonists:**
 - Warfarin

Indirect Thrombin Inhibitors

- E.g. heparin, tinzaparin, fondaparinux, rivaroxaban
- Affect intrinsic pathway of clotting cascade
- Monitor APTT for heparin or anti-Xa for LMWH
- Care with epidurals – Trust guidance for LMWH:
 - Remove at least 12 hours post-dose
 - Wait until at least 4 hours post-removal for next dose
- Reverse heparins/LMWH with protamine
- Danaparoid may be used in HIT

Direct Thrombin Inhibitors

- **Dabigatran, argatroban, bivalirudin**
- **Used for different indications:**
 - **Dabigatran – post-orthopaedic surgery, AF**
 - **Argatroban – used for HIT**
 - **Bivalirudin – used for PCI**

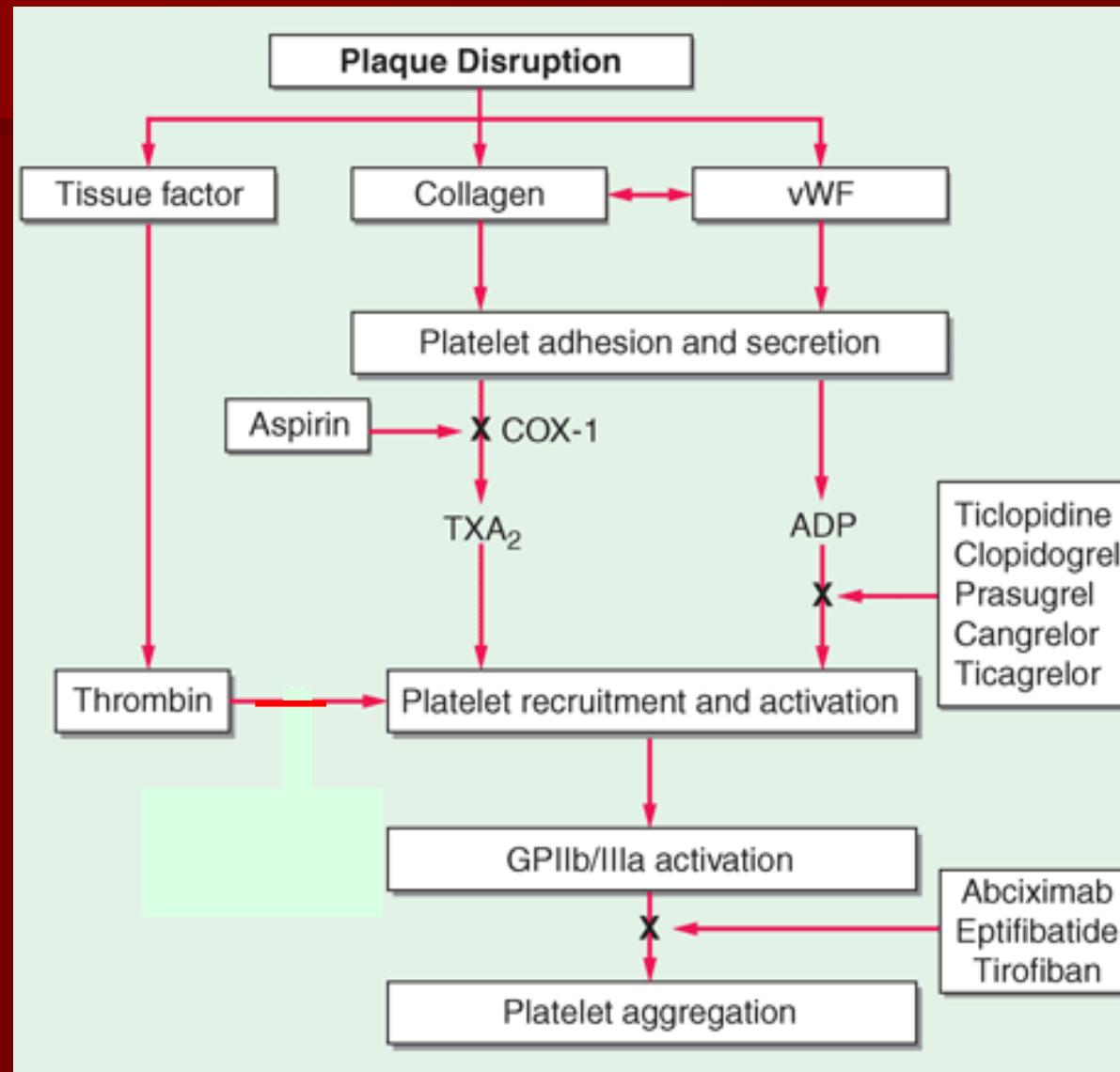
Vitamin K Antagonists

- E.g. warfarin
- Affects extrinsic pathway of clotting cascade
- Monitor with PT (or INR)
- Reverse with vitamin K

Platelet Aggregation Inhibitors

- **Antiplatelets:**
 - Aspirin, clopidogrel, prasugrel, dipyridamole
- **Glycoprotein IIb/IIIa inhibitors:**
 - Abciximab
 - Tirofiban
- **All increase bleeding risk including GI bleeds**

COX Pathway



Epoprostenol

- **Synthetic prostacyclin**
- **Used as alternative to heparin in renal replacement therapy**
- **Inhibits platelet aggregation and can de-clump platelet clumps**
- **Very short half life so given as IV infusion**

Fibrinolytics

- E.g. alteplase, streptokinase
- Used immediately post-stroke, PE, (MI)
- Activate plasminogen to form plasmin, leading to fibrin degradation and thrombus break up
- Given soon after symptom onset
- Many contraindications

Haemostatic Drugs

- **Phytomenadione**
- **Tranexamic acid**
- **Aprotinin**

Phytomenadione

- **AKA vitamin K (fat soluble)**
- **Vitamin K also available orally as fat soluble or water soluble (menadiol)**

Tranexamic Acid

- Inhibits plasminogen activation which inhibits fibrinolysis
- Can treat or prevent bleeding
- CRASH-2 evidence suggests it should be given early to bleeding trauma patients to prevent deaths due to bleeding

Aprotinin

- **Unlicensed**
- **Used in bypass surgery**
- **Inhibits proteolytic enzymes**
- **Short term use only**

Haemopoietic Growth Factors

■ Erythropoietin:

- May be used instead of blood transfusion in Jehovah's Witnesses
- Stimulates red blood cell production

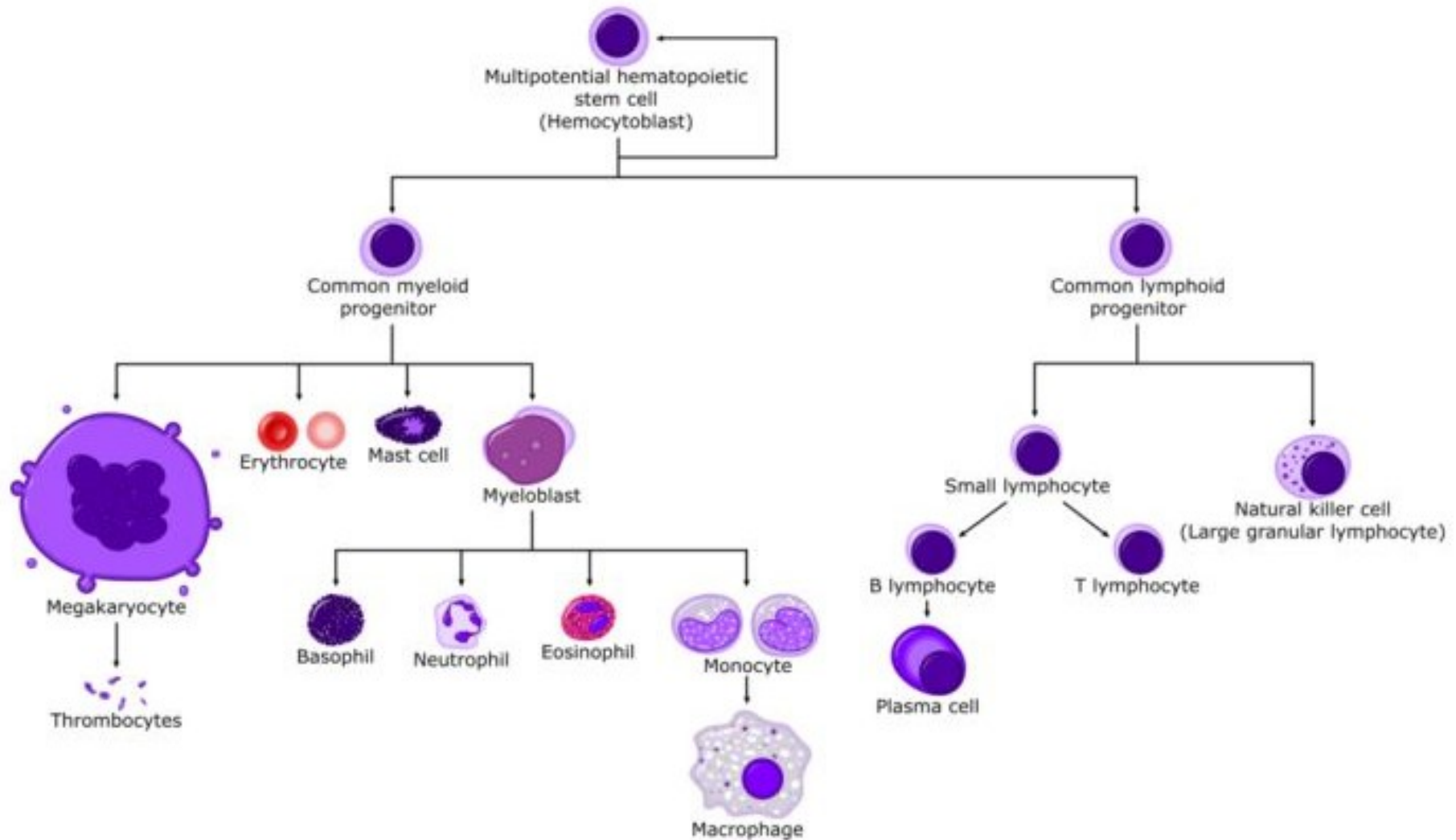
■ Granulocyte Colony Stimulating Factors:

- Controls development of neutrophils
- Used in neutropenia and post-BMT

Blood Dyscrasias as Side Effects

- Often serious reactions
- Type A:
 - Predictable due to pharmacology of drug
- Type B:
 - Unpredictable
- Signs and symptoms:
 - Cytopenias, bleeding, anaemia, bruising, fever, sore throat, mouth ulcers

Haemopoiesis



Genetics

- May affect how we handle certain drugs
- Can increase likelihood of type B blood dyscrasias (and other effects)
- Drugs include chloramphenicol, azathioprine and clozapine

Thrombocytopenia

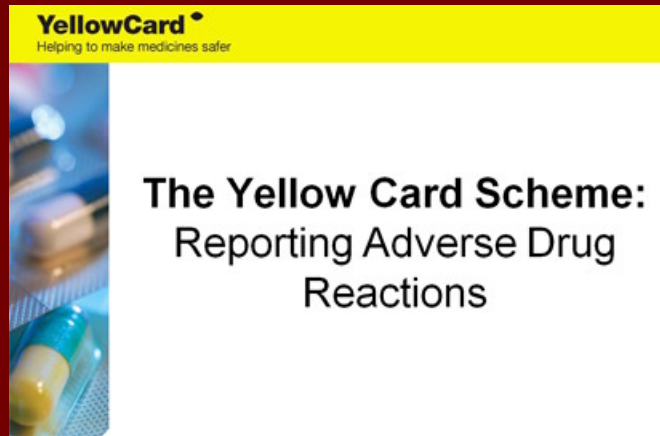
- Due to suppression or failure of bone marrow or may be auto-immune
- Occurs 7-10 days after starting drug
- Heparin:
 - Heparin associated
 - Heparin induced

Aplastic Anaemia

- **Persists and worsens despite drug withdrawal**
- **Anaemia, infection, bleeding**
- **May be acute or chronic**
- **May occur after drug has been stopped**
- **More likely to occur after second or subsequent course of drug**
- **Associated with a variety of drugs**

Yellow Card

- If the side effect has harmed your patient, prolonged their stay or they have died as a result of it, yellow card it (or ask the pharmacist to)
- <http://yellowcard.mhra.gov.uk>



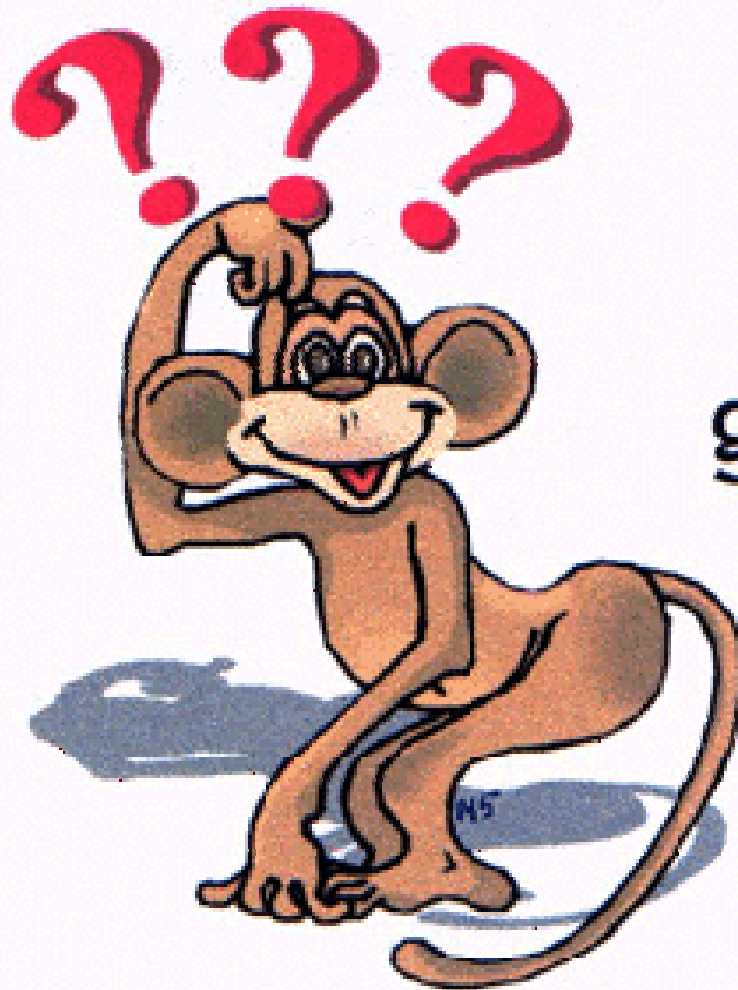
Safety Guidance

- Heparin: standard strength 1000 units/ml
- LMWH: ensure correct dosing
- Warfarin: ensure appropriate follow up
- Erythropoietin: ensure correct brand (and ensure doses aren't inadvertently missed)
- See NPSA / DoH Never Events

Summary

- **Drugs that affecting clotting, including antiplatelets, anticoagulants and haemostatic agents**
- **Blood dyscrasias and their relationship to drugs**

Any Questions...?



Questions
are
guaranteed in
life;
Answers
aren't.