

1.3.11 PERITONITIS

K65

DESCRIPTION

Infection of the peritoneum, usually secondary to a surgical cause such as perforated bowel. In this setting polymicrobial infection with anaerobes and Enterobacteriaceae is usually found.

Primary or spontaneous bacterial peritonitis is much less common and usually complicates ascites in patients with portal hypertension. This is **not** usually polymicrobial but due generally to Enterobacteriaceae such as *E. coli*. Spontaneous bacterial peritonitis is often culture-negative but is diagnosed by ascitic neutrophil count $> 0.25 \times 10^9/L$ (250 cells/ mm³).

NON-DRUG TREATMENT**SECONDARY PERITONITIS**

Intravenous fluids and nasogastric suction.

Prompt surgical intervention is essential.

DRUG TREATMENT**Empiric antibiotic therapy**

For surgical causes of peritonitis:

- benzylpenicillin (Penicillin G), IV, 2 million units every 6 hours

PLUS

- gentamicin, IV, 5 mg/kg/day

PLUS

- metronidazole, IV, 500 mg 8 hourly

As soon as patient can tolerate oral medication:

- metronidazole, oral, 400 mg 8 hourly

For spontaneous bacterial peritonitis:

- ceftriaxone, IV, 1 g daily

Switch to oral therapy when clinically appropriate according to culture or treat with:

- ciprofloxacin, oral, 500 mg 12 hourly

Total duration of therapy: 14 days.



CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

2.1 ANAEMIA, APLASTIC

D61.9

DESCRIPTION

Anaemia caused by bone marrow failure.

DIAGNOSTIC CRITERIA

Clinical

- pallor
- petechiae
- purpura
- bleeding

with frequent or severe infections.

Investigations

Pancytopenia, with anaemia, leucopenia and thrombocytopenia.

Hypoplastic bone marrow on trephine biopsy.

NON-DRUG TREATMENT

All blood products should be used sparingly and all patients should be discussed urgently with a regional haematology centre.

Limit the use of blood and blood products as the patient may be sensitised for future bone marrow transplant.

Blood products as needed, i.e. leucodepleted packed red cells and/or single donor leucodepleted platelets.

DRUG TREATMENT

If neutropenic and febrile, see Section 2.2: Febrile Neutropenia.

REFERRAL

- all cases of suspected aplastic anaemia for consideration such as bone marrow transplants or ATG and ciclosporin

Stabilise patient, if necessary with blood products before transport, but after consultation with an expert.

2.2 FEBRILE NEUTROPENIA

D70

DESCRIPTION

Documented fever 38°C **plus** absolute neutrophil count $0.5 \times 10^9/\text{L}$ from any cause.

This is a **medical emergency** as these patients can rapidly develop features of severe sepsis (multi-organ failure and/or hypotension).

CHAPTER 2

BLOOD AND BLOOD FORMING ORGANS

NON-DRUG TREATMENT

Treat the underlying cause of neutropenia, if applicable.

Withdraw any drug that may cause neutropenia.

Blood cultures must be taken prior to antimicrobial therapy.

DRUG TREATMENT

For patients with febrile neutropenia within 48 hours of admission:

3rd generation cephalosporin, e.g.:

- ceftriaxone, IV, 1 g daily

PLUS

- gentamicin, IV, 5 mg/kg daily

Duration of therapy:

- If neutrophil count increases to $> 0.5 \times 10^9/L$, continue for 2 days after fever has settled.
- If neutrophil count remains $\leq 0.5 \times 10^9/L$, continue for 7 days after fever has settled.

If fever develops after 48 hours of admission:

- piperacillin/tazobactam, IV, 4.5 g 8 hourly

OR

cefepime, IV, 1 g 12 hourly

OR

A carbapenem, e.g.:

meropenem, IV, 1 g 8 hourly

REFERRAL

- persistent fever for 5 days, despite above measures
- for further investigation and management of the underlying cause

2.3 ANAEMIA, HAEMOLYTIC

D59

DESCRIPTION

Anaemia due to destruction of red blood cells. Destruction may be due to:

- extracellular factors such as auto-immunity or mechanical factors, e.g. DIC, hypersplenism, medications
- abnormalities of the cell membrane, e.g. hereditary spherocytosis
- enzymes, e.g. G6PD deficiency
- haemoglobin, e.g. sickle cell anaemia, thalassaemia

Investigations

Evidence of haemolysis: anaemia, reticulocytosis, decreased haptoglobin, increased lactate dehydrogenase (LDH) and unconjugated hyperbilirubinaemia.

Coombs' test (direct antiglobin) is usually positive with autoimmune haemolysis.



CHAPTER 2 **BLOOD AND BLOOD FORMING ORGANS**

Investigate for auto-immune disease or malignancy, such as lymphoma.

NON-DRUG TREATMENT

Do not transfuse prior to appropriate investigations, unless anaemia is life threatening. Coombs-positive haemolytic anaemia may require expert blood cross matching.

In G6PD deficiency, avoid drugs known to cause haemolysis, including aspirin, sulfonamides (including trimethoprim/sulfamethoxazole), dapsone and primaquine. In patients with cold agglutinin all transfusions need to be given through a blood warmer to avoid cold induced haemolysis.

DRUG TREATMENT

AUTOIMMUNE HAEMOLYTIC ANAEMIA

Treat under specialist supervision.

- prednisone, oral, 1–2 mg/kg daily, initial dose
When a satisfactory response is obtained with recovery of the haemoglobin level and lactic dehydrogenase serum values, taper dose over a period of 2–4 weeks to 30 mg daily.
Thereafter further reduction should be slower to prevent disease recurrence. Prednisone treatment can be stopped when the Coomb's reaction becomes negative.

If inadequate response:

ADD

- azathioprine, oral, 2.5 mg/kg daily may be required for several months
Titrate to Hb response.
Monitor for neutropenia.

Patients who fail drug treatment should be considered for splenectomy.

REFERRAL

In consultation with a specialist:

- no response to drug treatment
- other causes of haemolytic anaemia

2.4 ANAEMIA, IRON DEFICIENCY

D50.9

DESCRIPTION

Anaemia due to iron deficiency. Common causes of iron deficiency are poor nutritional intake and blood loss.



CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

HYPOCHROMIC MICROCYTIC ANAEMIA

Investigations

Iron studies are necessary to confirm the iron deficiency.
Document a haematological response to iron therapy.

NON-DRUG TREATMENT

Identify and treat the cause.
Dietary adjustment.

DRUG TREATMENT

ORAL IRON SUPPLEMENTATION

If GIT intolerance occurs, this can be obviated by taking the preparation with meals, at the expense of a decrease in absorption.
A reticulocytosis begins on the 3rd or 4th day after therapy, peaks at approximately day ten and lasts between 12 and 21 days.
The haemoglobin rise is ± 0.1 g/dL/day or 2 g/dL every 3 weeks.

Therapeutic

- iron, elemental, oral, 100–200 mg daily, e.g.:
ferrous sulphate compound, oral, 170 mg three times daily
Treat until haemoglobin normalises.
After the haemoglobin has returned to normal, treatment should be continued for 6 months in order to adequately replenish the iron stores.

Prophylaxis

- E.g. during pregnancy.
- ferrous sulphate compound, oral, 170 mg daily

With failure to respond to iron therapy, consider the following:

- non-compliance, i.e. failure to take tablets
- continued blood loss
- wrong diagnosis/another cause of anaemia
- malabsorption
- mixed deficiency concurrent folate or vitamin B₁₂ deficiency
- use of slow release preparations

PARENTERAL IRON

Intravenous iron is seldom required.
The use of parenteral iron may be associated with anaphylaxis, which may be fatal.
Parenteral iron is **only** indicated where oral iron is:

- ineffective, e.g. malabsorption
- impractical, e.g. active Crohn's disease
- where there is a need to replenish body iron rapidly e.g. late pregnancy or patients on haemodialysis and erythropoietin therapy



CHAPTER 2

BLOOD AND BLOOD FORMING ORGANS

BLOOD TRANSFUSION

Indicated in patients with:

- anaemia leading to cardiac failure or severe dyspnoea
- active, ongoing bleeding
- where rapid correction of anaemia is required prior to performing an invasive procedure or surgery

2.5 ANAEMIA, MEGALOBLASTIC

D53.1

DESCRIPTION

Anaemia caused by a deficiency of folate and/or vitamin B₁₂.

Investigations

Elevated MCV (mean corpuscular volume) and MCH (mean corpuscular haemoglobin). Macro-ovalocytes on blood smear; polysegmentation of neutrophils, thrombocytopenia with giant platelets.

Decreased serum vitamin B₁₂ or red blood cell folate.

Pancytopenia in severe cases.

Intrinsic factor antibody test in vitamin B₁₂ deficiency, and anti-parietal cell antibodies to document pernicious anaemia.

NON-DRUG TREATMENT

Dietary modifications to ensure adequate intake of folate and vitamin B₁₂. Food fortification of staple foods such as flour, etc.

Try to avoid blood transfusion. Only transfuse in consultation with a specialist. Identify and treat the underlying cause, e.g. antibiotics for intestinal overgrowth with bacteria.

DRUG TREATMENT

After specimens for folate and B₁₂ levels have been taken, start with folic acid, vitamin B₁₂ and potassium supplementation. Monitor serum potassium. When results are available, adjust management as follows:

Folic acid deficiency

- folic acid, oral, 5 mg daily until haemoglobin returns to normal
- Prolonged treatment may be required for malabsorption states.

Vitamin B₁₂ deficiency

- vitamin B₁₂, IM, 1 mg (1 ampoule) daily for 3–5 days, then weekly for a further 1–3 doses (total of 6 mg) or 1 g given on alternate days 3 times a week for 2 weeks, then two monthly for life, except in clear nutritional deficiency where the individual can modify their diet

CHAPTER 2

BLOOD AND BLOOD FORMING ORGANS

Note:

Response to treatment is associated with an increase in strength and improved sense of well-being.

Reticulocytosis begins 3 to 5 days after therapy and peaks at about day 7.

The anaemia is corrected within 1–2 months. The white cell count and platelets normalise in 7–10 days.

Failure to respond, consider the following:

- co-existing folate and/or iron deficiency
- infection
- hypothyroidism
- myelodysplasia
- incorrect diagnosis

Hypokalaemia and salt retention may occur early in course of therapy. **Monitor serum potassium.**

Thrombocytosis may also be seen.

PROPHYLAXIS

Vitamin B₁₂

Indicated for patients after total gastrectomy and ileal resection.

Folic acid

Indications:

- chronic inherited haemolytic anaemias, e.g. sickle cell anaemia, thalassaemia
- myeloproliferative disorders
- exfoliative skin disorders
- increased demands, e.g. pregnancy, chronic haemodialysis

- folic acid, oral, 5 mg daily

2.6 ANAEMIA, SICKLE CELL

D57

DESCRIPTION

Homozygous sickle cell anaemia (HbSS: HbS > 50–100%). Individuals with sickle cell trait have < 50% HbS and are generally asymptomatic.

The disease is characterised by various crises, vaso-occlusive, aplastic, megaloblastic and sequestration crisis, and infection.

THE PAIN CRISIS/VASO-OCCLUSIVE CRISIS

The most common type of crisis is characterised by acute episodes of severe, agonising and relentless pain. The pain may be localised to:

- a single long bone, typically in the juxta-articular area



CHAPTER 2 **BLOOD AND BLOOD FORMING ORGANS**

- symmetrically in several limbs
- involve the axial skeleton, i.e. lumbar spine, ribs or pelvis, abdomen, chest or organ systems

Investigations

The diagnosis is suspected from the history, peripheral blood examination, and/or screening tests for sickling.

Diagnosis is confirmed on haemoglobin electrophoresis.

NON-DRUG TREATMENT

Bed rest and/or hospitalisation.

Give oxygen.

DRUG TREATMENT

Analgesia

For severe pain:

- morphine, IV, 10–15 mg 4 hourly

Fluids

Keep well hydrated with:

- sodium chloride 0.9% or sodium chloride 0.9% with dextrose 5%, IV

All patients:

- folic acid, oral, 5 mg daily

REFERRAL

- all for chronic management in a specialised centre

2.7 MYELODYSPLASTIC SYNDROMES

D46.4

DESCRIPTION

A group of disorders characterised by refractory cytopenia's due to bone marrow failure. Anaemia is very common and patients become easily symptomatic particularly if they have ischaemic heart disease. In some patients these disorders may develop increasing number of blasts and even acute leukaemia.

Investigations

Evidence of cytopenia, with normal B₁₂ and folic levels and substantial morphological dysplasia on the blood smear.

Bone marrow examination confirms dysplasia of the blood elements and the presence of cytogenetic abnormalities.

DRUG TREATMENT

It is advised that transfusion should be with leucodepleted red cells and/or platelets to delay immunisation, as clinically indicated.

CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

Bone marrow transplantation can be curative in younger patients.
If neutropenic and febrile, see Section 2.2: Febrile Neutropenia.

REFERRAL

- all patients for further investigation and management

2.8 BLEEDING DISORDERS

GENERAL PRINCIPLES

A bleeding tendency may result from:

- a coagulation defect (congenital/acquired),
- a vessel wall defect or
- a platelet defect (quantitative/qualitative).

A careful and detailed history, thorough examination and review of relevant laboratory investigations will allow differentiation between these three categories, as the management of each of these groups differ significantly.

Early consultation with a haematologist or a clinician with expertise in the handling of such patients is advisable.

Patients with a chronic bleeding tendency should be advised to wear a medic alert bracelet which clearly mentions the type of disorder he/she suffers from, e.g. Severe Haemophilia A, Factor VIII < 1%, no inhibitors.

2.8.1 HAEMOPHILIA A AND B, VON WILLEBRAND'S DISEASE

D66/7

DESCRIPTION

Haemophilia A, haemophilia B and von Willebrand's disease are chronic bleeding disorders caused, respectively, by a lack of clotting factor VIII, clotting factor IX and von Willebrand factor (VWF, a carrier protein for factor VIII).

Sub classification (factor VIII and IX deficiency):

Class	Clotting factor	% of normal	Signs
Mild	VIII or IX	5–25%	Occasional bleeds
Moderate	VIII or IX	2–5%	Less frequent bleeds post trauma/dental extraction
Severe	VIII or IX	<1–2%	Trauma/spontaneous bleeds



CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

Complications include haemarthrosis with later chronic arthropathy; intracranial haemorrhage, soft tissue and muscle haematomas.

DIAGNOSTIC CRITERIA

Clinical

Major bleeds:

- CNS
- gastrointestinal
- neck and throat
- severe injury
- advanced joint and soft tissue
- hip and iliopsoas
- forearm compartments

Minor bleeds:

- early joint bleed
- muscle
- soft tissue
- mouth and gum
- epistaxis
- haematuria

Pain/tingling in the joints suggests bleeding into the joint in a known haemophiliac complaining of pain.

Investigations

Prolonged partial thromboplastin time (PTT).

Factor VIII or factor IX concentration < 25% of normal activity.

Prolonged bleeding time (Von Willebrand's).

Patient with factor VIII deficiency should be tested annually for factor VIII inhibitor.

NON-DRUG TREATMENT

Haemophilia register.

Ideally, patients should attend a specialised haemophilia centre with a dedicated multi-disciplinary health care team.

Medic alert bracelet.

Dental care (see below for management of tooth extraction)

ACUTE BLEEDS INTO JOINTS

Apply ice packs.

Bed rest and rest of affected joint/limb until pain free and no further bleeding.

No weight bearing.

Splint (no circumferential casting).

DRUG TREATMENT

Avoid IM injections.
Exercise great caution when taking blood specimens.
Avoid aspirin and NSAIDs.
Taking blood from femoral veins is absolutely contra-indicated.



CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

HAEMOPHILIA

Bleeding episodes are treated with factor replacement therapy and spontaneous bleeding is usually controlled if the patient's factor level is raised above 20% of normal. For major surgery, serious post-traumatic bleeding or when haemorrhage is occurring at a dangerous site (such as the CNS), however, the factor level should be elevated to 100% and then maintained above 50% when acute bleeding has stopped, until healing has occurred.

For pain, give analgesia at appropriate doses.

HAEMOPHILIA WITH NO INHIBITORS

Factor VIII deficiency (with no inhibitor present)

Bleeding episodes are treated with factor replacement therapy and spontaneous bleeding is usually controlled if the patient's factor level is raised above 20% of normal. For major surgery, serious post-traumatic bleeding or when haemorrhage is occurring at a dangerous site, such as the CNS, however, the factor level should be elevated to 100% and then maintained above 50% when acute bleeding has stopped, until healing has occurred.

- lyophilised factor VIII concentrate, IV, administered 12 hourly for 1–3 days until pain free and full movement of joint/limb is restored

Dose:

Desired % increase in factor x body weight x 0.5

e.g. 50% x 60 kg x 0.5 = 1 500 units

Factor IX deficiency (with no inhibitor present)

- lyophilised factor IX concentrate, IV, administered once daily for 1–3 days

Dose:

Desired % increase in factor x body weight x 1

e.g. 50% x 60 kg x 1 = 1 300 units

HAEMOPHILIA WITH INHIBITORS

Refer for assessment and planning with a haematologist.

- factor VIII inhibitor-bypassing activity (FEIBA) under haematologist supervision only

Dental extraction

Check that inhibitors are absent.

In haemophilia A:

- lyophilised factor VIII concentrate, IV, 40 units/kg immediately before extraction

In haemophilia B:

- lyophilised factor IX concentrate, IV, 40 units/kg immediately before extraction

- tranexamic acid, 250 mg dissolved in 10 mL of water
Rinse mouth 4 times daily for two minutes.

CHAPTER 2

BLOOD AND BLOOD FORMING ORGANS

Mucous membrane bleeds

- tranexamic acid, oral, 25 mg/kg 6 hourly
Contraindicated in haematuria, factor IX deficiency, and with prothrombin complex concentrate.

In mild von Willebrand's disease or established responders of mild factor VIII deficiency:

- desmopressin, IV, 0.3 mcg/kg in at least 30 mL sodium chloride 0.9% administered over 30 minutes

OR

desmopressin, intranasal, 10–20 mcg, once or twice daily

Emergency treatment while awaiting transfer, if indicated

If serious bleeding with known haemophilia, and no factor VIII available:

- fresh frozen plasma, IV, 10–20 mL/kg

VON WILLEBRAND'S DISEASE

Mild bleeding

E.g. epistaxis and menorrhagia.

Antifibrinolytics, e.g.:

- tranexamic acid, oral, 1 g 4 times daily

Recurrent menorrhagia can also be treated effectively with oral contraceptives.

More severe mucous membrane bleeding

For mild von Willebrand's Disease, which occurs in 80% of patients:

- desmopressin, intranasal, 10–20 mcg, once or twice daily

Note:

Desmopressin is not effective in type 3 and the majority of type 2 von Willebrand's disease.

Intermediate-purity factor VIII concentrates, which contain both Von Willebrand factor and factor VIII, may be used for patients with very low von Willebrand factor levels.

During surgery or after major trauma, patients should receive:

- cryoprecipitate, IV, 1 unit/10 kg every 12 hours

OR

lyophilised factor VIII concentrate, IV, 30–50 units/kg/day administered twice daily

Continue for 48–72 hours to ensure optimal haemostasis.

For major surgical procedures, use for 7–10 days.

Antifibrinolytic agents may be used in combination with desmospressin or von Willebrand factor containing concentrates (cryoprecipitate or factor VIII) to treat bleeding episodes.



CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

REFERRAL

- all cases with **suspected** haemophilia (prolonged PTT and normal INR) to a haemophilia treatment centre, for assessment, genetic counselling and planning of management
- patients with proven antibodies against factor VIII
- for further replacement, complex situations and complications in consultation with a haematologist

2.9 IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP)

D69.3

DESCRIPTION

A common bleeding disorder due to immune destruction of platelets.

Exclude drug-induced thrombocytopenia, e.g. penicillins, cephalosporins, quinine, rifampicin and heparin.

Investigations

Thrombocytopenia with normal white cell count and red cell series. Anaemia may be present due to blood loss.

Peripheral blood smear to exclude RBC fragments and may show large platelets. Do INR and APTT, which should be normal in ITP.

Bone marrow aspirate and trephine bone marrow biopsy prior to starting steroids. Patients with suspected ITP should be tested for SLE and for HIV infection, as ITP frequently is a precursor of SLE and may also be associated with HIV infection.

NON-DRUG TREATMENT

Avoid:

- medication that affects platelet function, e.g. NSAIDs and aspirin
- platelet transfusions unless life-threatening bleeds
- contact sport, injury and trauma
- dental procedures in acute phase
- IM injections

Reassure the patient that that resolution usually occurs in acute ITP.

Medic alert bracelet.

Platelet transfusions may be given if surgery is required or in life threatening bleeding.

DRUG TREATMENT

ACUTE ITP

- prednisone, oral, 2 mg/kg daily
Taper dose once response is achieved, usually within 10–14 days.
It may take a few months before prednisone is eventually discontinued.

Platelet transfusions

Platelet transfusions are indicated in acute active bleeding or before procedures. In an adult, 1 mega-unit of single donor, leucocyte depleted platelets is usually



CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

sufficient to control the bleeding initially. Platelet transfusions have very short benefit in this condition as platelets are rapidly destroyed by the immune system.

HIV associated immune thrombocytopenia is an indication for antiretroviral therapy, regardless of CD4 counts.

REFERRAL

- local incapacity to manage the condition
- surgical treatment
 - Splenectomy should be considered in poor responders to oral corticosteroids, after consultation with haematologist.
 - Splenectomy is recommended in patients who still have platelet counts $< 30 \times 10^9/L$ after 3 months of steroid therapy or who require unacceptably high doses of corticosteroids (which are likely to produce adverse effects) to maintain a platelet count $> 30 \times 10^9/L$.
 - Before splenectomy: pneumococcal (polysaccharide) vaccine.
 - After splenectomy: prophylactic penicillin should be used for 2 years.
- for consideration of gammaglobulin or pulse steroids
- ITP complicated by severe haemorrhage, bleeding into vital organs or an intracranial haemorrhage
- ITP that fails to resolve in 6–12 months on adequate treatment, i.e. chronic ITP

2.10 THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

D69

DESCRIPTION

A fulminating, generally lethal disorder characterised by:

- a Coombs'-negative haemolytic anaemia with severely fragmented red blood cells, i.e. microangiopathic haemolytic anaemia
- thrombocytopenic purpura
- fever
- renal failure
- and fluctuating, often bizarre neurologic manifestations.

Thrombocytopenia and haemolysis with fragmented red blood cells may also occur in HIV infection, neoplasms with widespread metastases and in toxæmia of pregnancy.

NON-DRUG TREATMENT

Patients often respond to infusions of fresh frozen plasma if the required volume can be tolerated. Doses of 30 mL/kg are useful until response obtained and then tapered slowly to prevent recurrence of haemolysis. If there is no clinical improvement or patients are unable to tolerate plasma volume, and the equipment is available, plasmapheresis can induce rapid remissions.

DRUG TREATMENT

While the patient is receiving plasma therapy, give:

- prednisone, oral, 1–2 mg/kg daily
Taper dose once response is achieved.

2.11 THROMBOCYTOSIS/THROMBOCYTHEMIA

D75.2/D47.3

DESCRIPTION

Thrombocytosis refers to a platelet count $> 600 \times 10^9/L$. The three most common causes of reactive thrombocytosis include:

- bleeding
- infection
- iron deficiency, where the thrombocytosis responds to treatment of the underlying cause.

Thrombocythemia refers to a platelet count $> 1\,000 \times 10^9/L$.

Thrombocytosis/thrombocythemia may manifest clinically with either thrombosis or bleeding.

Bleeding is more likely to occur with higher platelet counts.

Investigate the underlying cause of:

- thrombocytosis, usually reactive or secondary cause
- thrombocythemia, usually underlying myeloproliferative disorder, including essential thrombocythemia

and manage accordingly.

DRUG TREATMENT

Aspirin and NSAIDs are contraindicated if the platelet count is $> 1\,000 \times 10^9/L$.

To reduce the thrombotic risk, especially in patients younger than 60 years with no previous thrombosis or haemorrhage and platelets $< 1\,000 \times 10^9/L$:

- aspirin, soluble, oral, 150 mg daily

REFER

- all patients

2.12 ACQUIRED COAGULATION DEFECTS**2.12.1 DISSEMINATED INTRAVASCULAR COAGULATION (DIC)****MANAGEMENT**

Identify and treat the underlying cause.

If bleeding, platelet concentrates, cryoprecipitate, and fresh frozen plasma contain the haemostatic factors and inhibitors of blood coagulation commonly depleted in patients with DIC.

SUPPORTIVE THERAPY

In general, patients should be transfused with blood components when they have bleeding and depleted haemostatic factors.

Cryoprecipitate provides a more concentrated source of fibrinogen (150–200 mg/unit) and red cell transfusions may be required.

The use of heparin or antiplatelet drugs to inhibit the coagulation process is usually not indicated because bleeding may, in some cases, be aggravated.

Replacement therapy for thrombocytopenia should consist of 1 apheresis single donor unit/megaunit (expected platelet count increment $30\text{--}50 \times 10^9/\text{L}$) or 6 random donor units (expected increment $50\text{--}60 \times 10^9/\text{L}$), ideally aiming to raise the platelet count $> 50 \times 10^9/\text{L}$.

In chronic DIC, or in the absence of bleeding, platelet transfusions should not be given merely to correct the thrombocytopenia.

Fibrinolytic inhibitors should not be considered because failure to lyse thrombi in organs such as the kidney may have adverse effects.

For hypofibrinogenaemia:

- cryoprecipitate, 8–10 units

For depletion of other coagulation factors:

- fresh frozen plasma, 2–4 units, i.e. 15–20 mL/kg as initial dose
Volume: ± 280 mL/unit.

Repeat replacement therapy every 8 hours or less frequently, with adjustment according to the clinical picture and laboratory parameters.

Perform frequent estimation of the platelet count and coagulation screening tests.



CHAPTER 3 CARDIOVASCULAR SYSTEM

3.1 ACUTE CORONARY SYNDROMES

3.1.1 ST ELEVATION MYOCARDIAL INFARCTION (STEMI)

I21

DESCRIPTION

Chest pain that is associated with elevated cardiac markers and ECG changes either ST elevation or new LBBB.

NON-DRUG TREATMENT

Rest, reassurance.

Oxygen 40% if clinically hypoxic.

Early ambulation.

DRUG TREATMENT

Inhibit platelet thrombi or aggregation:

- aspirin, soluble, oral, 300 mg immediately, followed by 150 mg daily

PLUS

To relieve spasm and pain, and to reduce preload:

- isosorbide dinitrate, SL, 5 mg immediately

May be repeated at 5-minute intervals for 3 or 4 doses.

PLUS

Thrombolysis

Streptokinase should be used for acute myocardial infarction with ST elevation if history of onset is less than 6 hours. Beyond 6 hours treat as NSTEMI (see below).

For new left bundle branch block:

- streptokinase, IV, 1.5 million units diluted in 200 mL sodium chloride 0.9%, infused over 30–45 minutes

Do not use heparin if streptokinase is given.

Contraindications:

- absolute
 - streptokinase used within the last year
 - CVA within the last 3 months
 - history of recent major trauma
 - previous allergy
 - bleeding within the last month
 - aneurysms
 - surgery or head injury within the preceding month
 - active bleeding or known bleeding disorder



CHAPTER 3

CARDIOVASCULAR SYSTEM

- relative
 - refractory hypertension
 - warfarin therapy
 - pregnancy
 - traumatic resuscitation
 - recent retinal laser treatment
 - subclavian central venous catheter
 - TIA in the preceding 6 months

For persistent pain and if oral therapy is insufficient:

- glyceryl trinitrate, IV, 1–2 mcg/kg/minute titrated over 8 hours
In exceptional cases, may be repeated for a total duration of 24 hours.
No survival benefit with the use of this agent.

PLUS

To relieve pain:

- morphine, IV, 1–2 mg/minute
Dilute 10 mg up to 10 mL with sodium chloride solution 0.9%.
Total maximum dose: 10 mg.
Repeat after 4 hours if necessary.
Pain not responsive to this dose may suggest ongoing unresolved ischaemia.

If there is cardiac failure or LV dysfunction, ACE-inhibitor is indicated.

3.1.2 NON-ST ELEVATION MYOCARDIAL INFARCTION (NSTEMI) AND UNSTABLE ANGINA (UA) (NSTEMI/UA)

I21

DESCRIPTION

Non-ST Elevation MI

Chest pain that is increasing in frequency and/or severity, or occurring at rest. The chest pain is associated with elevated cardiac enzymes and ST segment depression or T wave inversion on ECG.

UNSTABLE ANGINA PECTORIS

Angina that is increasing in frequency and or severity, or occurring at rest. It also encompasses post-infarct angina. The chest pain may be associated with ST segment depression or T wave inversion on ECG. There is no rise in cardiac enzymes.

NON-DRUG TREATMENT

Rest, reassurance.

Oxygen 40% if clinically hypoxic.

Early ambulation.

DRUG TREATMENT

Inhibit platelet thrombi or aggregation:

- aspirin, soluble, oral, 300 mg immediately, followed by 150 mg daily

PLUS

To relieve spasm and pain and to reduce preload:

- isosorbide dinitrate, SL, 5 mg immediately
May be repeated at 5-minute intervals for 3 or 4 doses.

PLUS

Thrombolysis is not indicated except if new left bundle branch block – see above.

For acute myocardial infarction with no ST elevation:

- heparin, IV bolus, 5 000 units, follow with 1 000–1 200 units hourly
Continue infusion for 3–5 days.

OR

Low molecular weight heparin (LMWH), e.g.:
enoxaparin, IV, 1 mg/kg 12 hourly for two days. Specialist initiated.

For persistent pain and if oral therapy is insufficient:

- glyceryl trinitrate, IV, 1–2 mcg/kg/minute titrated over 8 hours
In exceptional cases, may be repeated for a total duration of 24 hours.
No survival benefit with the use of this agent.

PLUS

To relieve pain:

- morphine, IV, 1–2 mg/minute
Dilute 10 mg up to 10 mL with sodium chloride solution 0.9%.
Total maximum dose: 10 mg.
Repeat after 4 hours if necessary.
Pain not responsive to this dose may suggest ongoing unresolved ischaemia.

If there is cardiac failure or LV dysfunction, ACE-inhibitor is indicated.

3.1.3 CHRONIC MANAGEMENT OF STEMI / NSTEMI / UA

T25

NON-DRUG TREATMENT

Stop smoking.

Appropriate risk reduction diet.

Rehabilitation programme.

Risk stratification and modification, including attention to smoking and lipid lowering strategies.

DRUG TREATMENT

Continue medical management.

This is a high-risk condition for CVD and is an indication for a statin for patients with proven lesions.

HMGCoA reductase inhibitors, e.g.:

- simvastatin, oral, 10 mg/day. Specialist initiated.
This therapy requires good initial evaluation, ongoing support for patients and continuous evaluation to ensure compliance.
Random cholesterol should be measured at baseline.
If < 7.5 mmol/L – initiate therapy.
If > 7.5 mmol/L – initiate therapy and refer for further assessment.
Therapy should be initiated together with appropriate lifestyle modification and adherence monitoring.

β-blocker:

- atenolol, oral, 50 mg/day

CARDIAC FAILURE

If heart failure develops, replace atenolol with:

- carvedilol, oral. Specialist initiated.

See Section 3.3: Congestive Cardiac Failure.

REFERRAL

- myocardial infarction related mitral regurgitation or VSD
- ongoing chest pain or post-infarct angina
- refractory ventricular tachyarrhythmias

3.1.4 ANGINA PECTORIS, STABLE

120

DESCRIPTION

Characteristic chest pain due to myocardial ischaemia usually occurring on exercise and relieved by rest.

NON-DRUG TREATMENT

Lifestyle modification.

Intensive health education.

Modify reversible risk factors.

DRUG TREATMENT

Long-term prophylaxis for thrombosis:

- aspirin, soluble, oral, 150 mg daily

PLUS

Nitrates, short acting e.g.:

- isosorbide dinitrate, SL, 5 mg
May be repeated if required at 5-minute intervals for 3 or 4 doses.

PLUS**Step 1**

- atenolol, oral, 50–100 mg daily
Titrate to resting heart rate of approximately 60 beats per minute.

If β -blocker cannot be tolerated or is contraindicated, consider long acting calcium channel blocker.

Step 2**ADD**

Long acting calcium channel blocker e.g.:

- amlodipine, oral, 5 mg
OR
nifedipine slow release, oral, 30 mg daily

Step 3**ADD**

- isosorbide mononitrate, oral, 10–20 mg twice daily
OR
isosorbide dinitrate, oral, 20–40 mg, twice daily
At 8:00 and 14:00 for both drugs in order to provide a nitrate free period to prevent tolerance.
Modify for night shift workers.

This is a high-risk condition for CVD and is an indication for a statin for patients with proven lesions.

HMGCoA reductase inhibitors, e.g.:

- simvastatin, oral, 10 mg/day. Specialist initiated.
This therapy requires good initial evaluation, ongoing support for patients and continuous evaluation to ensure compliance.
Therapy should be initiated together with appropriate lifestyle modification and adherence monitoring.

REFERRAL

- when diagnosis is in doubt
- failed medical therapy



CHAPTER 3

CARDIOVASCULAR SYSTEM

3.1.5 ATHEROSCLEROTIC PERIPHERAL DISEASE

I25.0

DESCRIPTION

History and palpation of pulses confirms diagnosis.

NON-DRUG TREATMENT

Smoking cessation is essential and is the single most important intervention to prevent progression.

Exercise within exercise tolerance and other lifestyle modifications.

DRUG TREATMENT

For prevention of platelet thrombi and aggregation:

- aspirin, soluble, oral, 150 mg daily

This is a high-risk condition for CVD and is an indication for a statin for patients with proven lesions.

HMGCoA reductase inhibitors, e.g.:

- simvastatin, oral, 10 mg/day. Specialist initiated.
This therapy requires good initial evaluation, ongoing support for patients and continuous evaluation to ensure compliance.
Therapy should be initiated together with appropriate lifestyle modification and adherence monitoring.

REFERRAL

- ongoing vascular insufficiency, which may be surgically reversible

3.2 CARDIAC ARRHYTHMIAS/ DYSRHYTHMIAS

Exclude underlying structural cardiac disease in all patients with cardiac dysrhythmias.

3.2.1 NARROW QRS COMPLEX (SUPRAVENTRICULAR) TACHYARRHYTHMIAS

I47.1

DESCRIPTION

Sustained (> 30 seconds) or non-sustained narrow QRS (≤ 0.1 seconds) tachycardias.



CHAPTER 3

CARDIOVASCULAR SYSTEM

ATRIAL FIBRILLATION

Acute onset (< 48 hours)

Assess clinically, e.g. heart failure, mitral stenosis, thyrotoxicosis, hypertension, age and other medical conditions.

Consider anticoagulation with heparin or warfarin

Synchronised DC cardioversion is occasionally necessary in emergency. Consider if first episode.

Non-acute/chronic (> 48 hours)

As above, but not immediate DC cardioversion, unless emergency.

ATRIAL FLUTTER

P waves visible before QRS.

Commonly occurs, usually 2:1. (\pm 150 per minute).

P waves, usually negative in Lead II precede QRS, blocked P in ST segment or hidden by QRS.

Vagal stimulation with ECG may reveal blocked P waves.

AV JUNCTIONAL RE-ENTRY TACHYCARDIAS

Usually paroxysmal.

Often young with normal heart.

AV nodal re-entry or WPW syndrome.

P waves usually not visible (hidden by QRS).

ATRIAL TACHYCARDIAS

Rare.

Often incessant

May cause heart failure (tachycardia cardiomyopathy).

P before QRS (often long PR) or hidden in T.

ATRIAL FIBRILLATION

148

DRUG TREATMENT

INITIAL

Anticoagulate with warfarin.

Control the ventricular rate with **one** of the following:

- digoxin, oral, 0.25 mg daily
Use only in heart failure.

- atenolol, oral, 50–100 mg daily
Contra-indicated in asthmatics; caution in heart failure.
- DC cardioversion in selected cases, after 4 weeks warfarin anticoagulation.

LONG-TERM

Continue warfarin anticoagulation long-term, unless contra-indicated:

- warfarin, oral, 5 mg daily
Control with INR to therapeutic range:
INR between 2–3: patient is stable do 3 monthly monitoring
INR < 1.5 or > 3.5: do monthly monitoring
Use:
 - Prophylaxis in chronic atrial fibrillation
 - Prior to cardioversion to sinus rhythm
 - In lone atrial fibrillation of persons 65 or older.

If the patient has a prosthetic valve,

ADD

- aspirin, soluble, oral, 150 mg daily

CAUTION
Use warfarin only if INR can be monitored regularly.
If not, consider aspirin.

Rate control

Continue as above.

Digoxin only controls rate at rest and is insufficient on its own.

If used long-term, combine with a β -blocker.

In the elderly and patients with renal impairment:

- digoxin, oral, 0.125 mg initial dose
Adjust dosages according to trough levels within the therapeutic range.
Do levels only if the patient has been on the drug for at least 10 days.
- atenolol, oral, 50–100 mg daily

Prevention of recurrent paroxysmal atrial fibrillation

Only in patients with severe symptoms despite the above measures:

- amiodarone, oral, 200 mg three times daily for 1 week, followed 200 mg twice daily for one week and thereafter 200 mg daily. Specialist initiated.
Precautions:
 - halve dosage of warfarin and monitor INR closely, until stable
 - avoid concomitant digoxin
 - monitor thyroid function every 6–12 months as thyroid abnormalities may develop



CHAPTER 3

CARDIOVASCULAR SYSTEM

ATRIAL FLUTTER

148

NON-DRUG TREATMENT

Synchronised DC cardioversion, 200 J, after sedation with:

- diazepam, IV, 10–20 mg

If flutter has been present longer than 48 hours, defer cardioversion for 4 weeks after anticoagulation with warfarin, unless severe symptoms or heart failure require urgent conversion.

DRUG TREATMENT

None is nearly as effective as DC cardioversion.

Most drugs have serious side effects. Do not use verapamil as it will **not** convert flutter to sinus rhythm and may cause serious hypotension.

Anticoagulants if sustained.

LONG-TERM TREATMENT

Recurrent atrial flutter is an indication for referral. Many can be cured by radiofrequency catheter ablation.

AV JUNCTIONAL RE-ENTRY TACHYCARDIAS

NON-DRUG TREATMENT

Vagal manoeuvres: Valsalva or carotid sinus massage. The patient should be supine and as relaxed as possible, to avoid competing sympathetic reflexes.

DRUG TREATMENT

If vagal manoeuvres fail:

- adenosine, rapid IV bolus, 6 mg through a good IV line, followed by a bolus of 10 mL sodium chloride 0.9% to ensure that it reaches the heart before it is broken down. Half life: \pm 10 seconds.
Run the ECG for 1 minute after the injection.
If 6 mg fails, repeat with 12 mg.
If the drug reaches the central circulation before it is broken down the patient will experience flushing, sometimes chest pain and anxiety.
If the tachycardia fails to terminate without these symptoms, the drug did not reach the heart.

If none of the above is effective, or if the patient is hypotensive, consider DC shock.

Verapamil and digoxin are contraindicated in WPW syndrome.



CHAPTER 3

CARDIOVASCULAR SYSTEM

LONG-TERM TREATMENT

Teach the patient to perform vagal manoeuvres, Valsalva is the most effective.

For infrequent, non-incapacitating symptoms:

β -blocker, e.g.:

- atenolol, oral, 50–100 mg daily

If asthmatic, but normal heart:

- verapamil, oral, 80–120 mg three times daily

REFERRAL

NARROW QRS COMPLEX (SUPRAVENTRICULAR) TACHYARRHYTHMIAS

- poor rate control
- severe persistent symptoms
- patients with severe symptoms

REGULAR NARROW QRS (SUPRAVENTRICULAR) TACHYCARDIAS

- frequent or severe symptoms for curative radiofrequency catheter ablation
- all WPW syndrome (sinus rhythm ECG shows delta waves) for radiofrequency catheter ablation

3.2.2 WIDE QRS (VENTRICULAR) TACHYARRHYTHMIAS

I47.1

DESCRIPTION

Sustained (> 30 seconds) or non-sustained wide QRS (> 0.12 seconds) tachycardias

A REGULAR WIDE QRS TACHYCARDIAS

are **ventricular** until proved otherwise.

Regular wide QRS supraventricular tachycardias are uncommon.

B SUSTAINED (> 30 SEC) IRREGULAR WIDE QRS TACHYCARDIAS

are usually due to atrial fibrillation with bundle branch block, or pre-excitation (WPW syndrome).

C NON-SUSTAINED (< 30 SEC) IRREGULAR WIDE QRS TACHYCARDIAS

are usually ventricular.

They are common in acute myocardial infarction.

D TORSADES DE POINTES VENTRICULAR TACHYCARDIA (VT)

has a twisting pattern to the QRS complexes and a prolonged QT interval in sinus rhythm.

It is usually due to a QT-prolonging drug, \pm hypokalaemia.

A REGULAR WIDE QRS TACHYCARDIAS

Refer all cases after resuscitation and stabilisation.

Emergency DC cardioversion is mandatory with a full protocol of CPR.

NON-DRUG TREATMENT

Cardio-pulmonary resuscitation (CPR).

If no cardiac arrest:

DC cardioversion, 200 J, after sedation with:

- diazepam, IV, 10–20 mg
If 200 J fails, use 360 J.

If cardiac arrest:

Defibrillate (not synchronised).

DRUG TREATMENT**CAUTION**

Never give verapamil IV to patients with a wide QRS tachycardia.

DC cardioversion is first line therapy for regular wide QRS tachycardias. Drugs are needed if VT recurs after cardioversion, or if spontaneous termination/recurrence.

- amiodarone, IV, 5 mg/kg infused over 30 minutes

Follow with:

- amiodarone, oral, 800 mg/day for 7 days
then 600 mg/day for 3 days
followed by a maintenance dose of 200–400 mg/day, depending upon clinical judgement.

Also the drug of choice in acute arrhythmia with myocardial infarction, CCF and other conditions with VT.

Also benefits Supraventricular tachycardia (SVT).

Disadvantage: serious long-term side effects and long half-life.

Patients require regular monitoring by specialist for complications – See Section 3.2.1.

OR

Only in a haemodynamically stable patient:

- lidocaine, IV, 50–100 mg (1–2 mg/kg) initially and at 5 minute intervals if required to a total of 200–300 mg

Thereafter, for recurrent ventricular tachycardia only:

- lidocaine, IV infusion, 1–3 mg/minute for 24–30 hours
Lidocaine will only terminate \pm 30% of sustained ventricular tachycardias, and may cause hypotension, heart block or convulsions.

For emergency treatment of ventricular tachycardia, DC cardioversion is first-line therapy, even if stable.

B SUSTAINED (> 30 SECONDS) IRREGULAR WIDE QRS TACHYCARDIAS

If the QRS complexes have a pattern of typical right or left bundle branch block, with a rate < less than 170/minute, treat as for atrial fibrillation. See Section 3.2.1

If the rate is > 170 per minute, and/or the complexes are atypical or variable, the likely diagnosis is WPW syndrome with atrial fibrillation, conducting via the bypass tract, DC conversion.

Do not treat with drugs.

Verapamil and digoxin may precipitate ventricular fibrillation by increasing the ventricular rate.

C NON-SUSTAINED (< 30 SECONDS) IRREGULAR WIDE QRS TACHYCARDIAS

Most are ventricular.

In acute myocardial infarction, only treat non-sustained ventricular tachycardia if it causes significant haemodynamic compromise. Ensure the serum potassium level is above 4 mmol/L.

DRUG TREATMENT

- amiodarone, IV, 5 mg/kg infused over 30 minutes. Specialist initiated.

Follow with:

- amiodarone, oral, 800 mg/day for 7 days
then 600 mg/day for 3 days,
followed by a maintenance dose of 200–400 mg/day, depending upon clinical judgement.

Also the drug of choice in acute arrhythmia with myocardial infarction, CCF and other conditions with ventricular tachycardia.

Also benefits Supraventricular tachycardia (SVT).

Disadvantage: serious long-term side effects and long half-life.

Patients require regular monitoring by specialist for complications – See Section 3.2.1.

OR

Only in a haemodynamically stable patient:

- lidocaine, IV, 50–100 mg (1–2 mg/kg) initially and at 5 minute intervals if required to a total of 200–300 mg.

Thereafter, for recurrent ventricular tachycardia only:

- lidocaine, IV infusion, 1–3 mg/minute for 24–30 hours
Lidocaine will only terminate \pm 30% of sustained ventricular tachycardias, and may cause hypotension, heart block or convulsions.

In the absence of acute ischaemia or infarction, consider torsades de pointes, due to QT prolonging drugs.

D TORSADES DE POINTES VENTRICULAR TACHYCARDIA (VT)**NON-DRUG TREATMENT**

Cardioversion/defibrillation, as necessary.

Torsades complicating bradycardia: temporary pacing.

DRUG TREATMENT

Stop all QT-prolonging drugs.

Correct serum potassium.

- magnesium sulphate, IV, 2 g over 5–10 minutes
- If recurrent episodes after initial dose of magnesium sulphate:
- magnesium sulphate, IV, 2 g over 24 hours

Torsades complicating bradycardia:

- adrenaline infusion to raise heart rate to > 100 per minute (if temporary pacing unavailable).

REFERRAL

- all cases of wide QRS tachycardia, after resuscitation and stabilisation

3.2.3 HEART BLOCK (SECOND OR THIRD DEGREE)

I44.2

DESCRIPTION

The majority of cases occur in patients over 60 years and are idiopathic, with an excellent long-term prognosis, provided a permanent pacemaker is implanted. Acute, reversible AV block commonly complicates inferior myocardial infarction. The condition may also be induced by metabolic and electrolyte disturbances, as well as by certain medicines.

NON-DRUG TREATMENT

Emergency cardio-pulmonary resuscitation.

External pacemaker should be available in all secondary hospitals and must be preceded by appropriate analgesia.

DRUG TREATMENT

Analgesia if external pacemaker:

- morphine, IM, 10–15 mg 3–6 hourly

AV nodal block with narrow QRS complex escape rhythm only:

- atropine, IV bolus, 0.6–1.2 mg
May be repeated until a pacemaker is inserted.
Use in a patient with inferior myocardial infarct and hypotension and second degree AV block.
It is temporary treatment of complete AV block before referral (urgently) for pacemaker.

OR

For resuscitation of asystole:

- adrenaline 1:10 000, slow IV, 5 mL (0.5 mg)
Used as temporary treatment of complete heart block when other drugs are not effective.

REFERRAL

**HEART BLOCK IS A MEDICAL EMERGENCY.
REFER URGENTLY!**

- all cases with a heart rate below 40 beats/minute after resuscitation and stabilisation
- all cases of second or third degree AV block, whether or not myocardial infarct or other reversible cause is suspected, and whether or not the patient is thought to be symptomatic
- a permanent pacemaker is the definitive form of treatment. These are only available in tertiary institutions.

3.2.4 SINUS BRADYCARDIA

I49.8

DESCRIPTION

This rhythm does not require treatment, unless they are causing symptoms, i.e. syncope, dizziness, tiredness and poor effort tolerance.

Sinus bradycardia < 50/minute or sinus arrest with slow escape rhythm, accompanied by hypotension, strongly suggest a treatable underlying cause:

- acute inferior myocardial infarct
- hyperkalaemia, especially if wide QRS and/or peaked T waves
- drugs, especially combination of verapamil and β -blocker or digoxin
- hypothermia
- hypoxia

Treat the cause. Consider atropine if inferior infarct.

3.2.5 SINUS ARREST

I45.5

Refer all to a cardiologist.

3.3 CONGESTIVE CARDIAC FAILURE (CCF)

I50.0

DESCRIPTION

CCF is a clinical syndrome and has several causes. The cause and immediate precipitating factor(s) of the CCF must be identified and treated to prevent further damage to the heart.

Potentially reversible causes include:

- anaemia
- thyroid disease
- valvular heart disease
- constrictive pericarditis
- thiamine deficiency
- ischaemic heart disease

NON-DRUG TREATMENT

Patient and family education.

Monitor body weight to assess changes in fluid balance.

Limit fluid intake to 1–1.5 L/day if fluid overloaded despite diuretic therapy.

Salt restriction.

Regular exercise within limits of symptoms.

Avoid NSAIDs as these may exacerbate fluid retention.

Counsel regarding the risk of pregnancy and the use of oral contraceptives.

DRUG TREATMENT

Mortality is significantly reduced by the use of ACE-inhibitors, β -blockers and spironolactone in heart failure.

Digoxin has only been shown to reduce hospitalisation.

1. Diuretics

Mild volume overload (mild CCF) and normal renal function, thiazide diuretic:

- hydrochlorothiazide, oral, 25–50 mg daily
Caution in patients with gout.
Contraindicated in impaired renal function.

Significant volume overload or abnormal renal or hepatic function, loop diuretic:

- furosemide, oral, daily
Initial dose: 40 mg/day.
Higher dosages may be needed if also renal failure.

Note:

Unless patient is clinically fluid overloaded, reduce the dose of diuretics before adding an ACE-inhibitor.

After introduction of an ACE-inhibitor, try to reduce diuretic dose and consider a change to hydrochlorothiazide.

Routine use of potassium supplements with diuretics is not recommended. They should only be used short term to correct documented low serum potassium level.

2. ACE-inhibitor, e.g.:

- enalapril, oral, 2.5 mg 12 hourly up to 10 mg 12 hourly

If ACE-inhibitor intolerant:

- hydralazine, oral
Initial dose: 25 mg 4 times a day.
Maximum dose: 200 mg/day.

PLUS

- isosorbide dinitrate, oral
Initial dose: 20 mg 3 or 4 times a day.
Maximum dose: 160 mg/day.

3. Spironolactone

Use with an ACE-inhibitor in patients presenting with Class III or IV heart failure.

Do not use if GFR < 30 mL/minute.

Monitoring of potassium levels is essential if spironolactone is used with an ACE-inhibitor or other potassium sparing agent or in the elderly.

- spironolactone, oral, 25 mg once daily

4. β -blockers

For all stable patients with heart failure who tolerate it.

Patients should not be fluid overloaded or have low blood pressure prior to initiation of therapy.

- carvedilol, oral. Specialist initiated.
Initial dose: 3.125 mg/day.
Increase after two weeks to 3.125 mg twice daily, if tolerated.
Increase at two-weekly intervals by doubling the daily dose until a maximum of 25 mg twice daily, if tolerated.
If not tolerated, i.e. worsening of cardiac failure manifestations, reduce the dose to the previously tolerated dose.
Up-titration can take several months.

5. Digoxin

Symptomatic CCF due to systolic dysfunction.

- digoxin, oral, 0.125 mg daily
- Patients at high risk of digoxin toxicity are:
- the elderly
 - patients with poor renal function
 - hypokalaemia
 - low body weight

Digoxin trough blood levels (before the morning dose) should be maintained between 0.65 and 1.5 nmol/L.

6. Anticoagulants

Heparin for DVT prophylaxis.

For patients admitted to hospital, unless contraindicated:

- heparin, SC, 5 000 units 8 hourly

Warfarin: See Section 3.2.1

- warfarin, oral, 5 mg daily
Control with INR to therapeutic range, i.e. between 2.0 and 2.5.

7. Anti-arrhythmic drugs

See Section 3.2: Cardiac Arrhythmias.

Only for potentially life-threatening ventricular dysrhythmias.

Always exclude electrolyte abnormalities and drug toxicity first.

8. Thiamine

Consider in all unexplained heart failure.

REFERRAL

- where specialised treatment and diagnostic work-up is needed and to identify treatable and reversible causes

3.4 ENDOCARDITIS, INFECTIVE

109.1

NON-DRUG TREATMENT

Bed rest.

Early surgical intervention in acute fulminant and prosthetic valve endocarditis is often indicated.

DRUG TREATMENT

Treat accompanying complications, e.g. cardiac failure.

Antibiotic therapy

It is essential to do at least three and no more than six blood cultures before starting antibiotics.

In patients with subacute presentation and no haemodynamic compromise wait for the results before starting antibiotics.

Empiric treatment is indicated in patients with a rapidly fulminant course or with severe disease only.

Aminoglycoside therapy should be monitored with trough levels for safety.

Duration of therapy given is the minimum and may be extended based on the response (clinical and laboratory).

In **penicillin-allergic patients** vancomycin is the antibiotic of choice.

EMPIRIC THERAPY

Native valve	<ul style="list-style-type: none"> benzylpenicillin (Penicillin G), IV, for 4 weeks 4 million units 4 hourly OR 5 million units 6 hourly* PLUS <ul style="list-style-type: none"> gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks If staphylococcal infection is suspected (acute onset): ADD <ul style="list-style-type: none"> cloxacillin, IV, 3 g 6 hourly
Prosthetic valve	<ul style="list-style-type: none"> vancomycin, IV, 15 mg/kg 12 hourly PLUS <ul style="list-style-type: none"> rifampicin, oral, 7.5 mg/kg 12 hourly for 6 weeks PLUS <ul style="list-style-type: none"> gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks

*For the administration of penicillin a 4-hourly regimen or constant infusion regimen is preferable. Six hourly dosing should only be used when dictated by staffing realities.

DIRECTED THERAPY (NATIVE VALVE)

Streptococcal	
Fully susceptible to penicillin MIC < 0.2 mg/L	<ul style="list-style-type: none"> benzylpenicillin (Penicillin G), IV, for 4 weeks 4 million units 4 hourly OR 5 million units 6 hourly*
Moderately susceptible MIC 0.2–0.5 mg/L	<ul style="list-style-type: none"> benzylpenicillin (Penicillin G), IV, for 4 weeks 4 million units 4 hourly OR 5 million units 6 hourly* PLUS <ul style="list-style-type: none"> gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks
Moderately resistant MIC 0.5–2 mg/L Enterococci and Abiotrophia spp. (nutritionally variant streptococci)	<ul style="list-style-type: none"> benzylpenicillin (Penicillin G), IV, for 4 weeks 4 million units 4 hourly OR 5 million units 6 hourly* PLUS <ul style="list-style-type: none"> gentamicin, IV, 1.5 mg/kg 12 hourly for 4 weeks Six weeks of therapy may be required in cases with a history of > 3 months, or mitral or prosthetic valve involvement.
Fully resistant MIC > 2 mg/L	<ul style="list-style-type: none"> vancomycin, IV, 15 mg/kg 12 hourly PLUS <ul style="list-style-type: none"> gentamicin, IV, 1.5 mg/kg 12 hourly for 4 weeks

Staphylococcal (cloxacillin/methicillin sensitive)	
<i>S. aureus</i>	<ul style="list-style-type: none"> • cloxacillin, IV, 3 g 6 hourly for 4 weeks With optional addition: <ul style="list-style-type: none"> • gentamicin, IV, 5 mg/kg/day for the first 3–5 days The benefit of adding an aminoglycoside has not been established.
coagulase-negative staphylococci	<ul style="list-style-type: none"> • cloxacillin, IV, 3 g 6 hourly for 4 weeks PLUS <ul style="list-style-type: none"> • gentamicin, IV, 2.5 mg/kg 12 hourly for 2 weeks
In the rare occurrence of a penicillin sensitive staphylococcus, penicillin should be used in preference to cloxacillin.	
Staphylococcal (cloxacillin/methicillin resistant)	
<i>S. aureus</i>	<ul style="list-style-type: none"> • vancomycin, IV, 15 mg/kg 12 hourly for 4 weeks
coagulase-negative staphylococci	<ul style="list-style-type: none"> • vancomycin, IV, 15 mg/kg 12 hourly for 4 weeks PLUS <ul style="list-style-type: none"> • rifampicin, oral, 7.5 mg/kg 12 hourly for 4 weeks PLUS <ul style="list-style-type: none"> • gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks

ENDOCARDITIS PROPHYLAXIS**Cardiac conditions**

Selected procedures are listed and are not meant to be all-inclusive.

Endocarditis prophylaxis is recommended for:

- patients with prosthetic valves or with surgically constructed cardiac shunts
- patients who have had endocarditis previously
- all patients with congenital cardiac disease other than those with an isolated secundum atrial septal defect
- patients with valvular dysfunction, including those with mitral valve regurgitation due to prolapse
- patients with hypertrophic cardiomyopathy

Endocarditis prophylaxis is **not** recommended for:

- patients with surgically repaired secundum atrial septal defect, ventricular septal defect, or patent ductus arteriosus who are more than 6 months post-operative and have no murmur
- patients who have undergone coronary artery bypass grafting
- patients with mitral valve prolapse but no regurgitation
- patients with functional murmurs or who have had rheumatic fever but have no valvular dysfunction
- patients with pacemakers

Dental or surgical procedures

Selected procedures are listed and are not meant to be all-inclusive.

Procedures for which endocarditis prophylaxis should be given include:

- dental procedures known to cause bleeding (but not fillings or adjustment of braces)
- tonsillectomy or adenoidectomy (but not tympanostomy)
- surgical operations that involve intestinal or respiratory mucosal incisions
- rigid, but not flexible, bronchoscopy
- oesophageal dilation, or sclerotherapy for oesophageal varices
- biliary tract surgery, or ERCP in the presence of obstruction
- cystoscopy, urethral dilatation or prostatic surgery
- urethral catheterisation in a patient with a urinary tract infection
- incision and drainage of infected tissue
- vaginal delivery in the presence of suspected infection such as with prolonged rupture of membranes or manipulative vaginal deliveries

Procedures for which endocarditis prophylaxis **not** recommended**

- shedding of primary teeth
- endotracheal intubation
- cardiac catheterisation
- endoscopy with or without gastrointestinal biopsy
- urinary catheterisation in the absence of infection
- if infection is not suspected: Caesarean section or vaginal hysterectomy, dilatation and curettage, uncomplicated vaginal delivery, therapeutic abortion, sterilisation procedures, or insertion or removal of intrauterine devices

**In patients who have prosthetic heart valves, a previous history of endocarditis, or surgically constructed systemic-pulmonary shunts or conduits, physicians may choose to administer prophylactic antibiotics even for low-risk procedures that involve the lower respiratory, genitourinary or gastrointestinal tracts.

Antibiotic Prophylaxis

Oral cavity, respiratory tract or oesophageal procedures:

- amoxicillin, oral, 2 g one hour before the procedure
Repeat dose 6 hours later.
OR
Penicillin allergy:
clindamycin, oral, 600 mg one hour before the procedure

If patient cannot take oral:

- ampicillin, IV/IM, 2 g 30 minutes before the procedure
Repeat dose 6 hours later.
OR
Penicillin allergy:
vancomycin, IV, 1 g

Genitourinary or gastrointestinal procedures:

Also for patients with prosthetic heart valves or previous infective endocarditis.

- ampicillin, IV/IM, 2 g 30 minutes before the procedure
Repeat dose 6 hours later.

OR

Penicillin allergy:
vancomycin, IV, 1 g

PLUS

- gentamicin, IV/IM, 1.5 mg/kg 30 minutes before the procedure
Do not exceed 120 mg.

REFERRAL

- complications such as renal failure and progressive cardiac failure
- for surgical intervention, e.g. emergency valve replacement
- assessment for post treatment valve replacement

3.5 HYPERTENSION

110

KEY POINTS

- Hypertension control has shown to have significant benefit for patients.
- Co-existent risk factors should be detected and treated.
- Assess cardiovascular risk.
- Lifestyle modification and patient education are essential in all patients.
- Drug treatment for SBP >140 mmHg; DBP > 90 mmHg.

First line:

Low dose thiazide diuretic, unless compelling indication for another class.

Second line:

Add one of the following: ACE-inhibitor or calcium channel blocker.

Third line:

Add one of the second line drugs, which has not already been used, or β -blocker

Immediate drug treatment is needed for DBP > 110 mmHg and/or
SBP > 180 mmHg

PATIENT EVALUATION FOR RISK STRATIFICATION (TARGET ORGAN DAMAGE (TOD) AND CLINICAL CARDIOVASCULAR DISEASE (CCD) AND CO-MORBIDITY)

Thorough focused history and clinical examination is complemented by investigations.

MAJOR RISK FACTORS FOR CVD

Treat these risk factors:

- diabetes mellitus
- hypertension
- obesity
- smoking

- dyslipidaemia
- family history of primary hypertension or premature cardiovascular disease in men less than 55 years and in women less than 65 years
- physical inactivity
- pre-existing disease (target organ damage)
- left ventricular hypertrophy
- ischaemic heart disease (angina or prior myocardial infarction)
- heart failure
- transient ischaemic attacks
- stroke
- chronic kidney disease/impairment
- retinopathy
- peripheral arterial disease

INVESTIGATIONS

- if overweight, body weight and waist circumference should be recorded at each visit when BP is measured:
 - Men: 100 cm
 - Women: 88 cm
- do urine test strip analysis for protein, blood and sugar at presentation
 - If normal, repeat urine test strip every 6 months.
 - If abnormal, do spot albumin creatinine ratio. Repeat yearly.
- if haematuria > 1+, investigate further
- if glycosuria, exclude diabetes mellitus
- if known diabetic, HbA_{1c}
- random total cholesterol
- if diabetic, do spot albumin creatinine ratio, which should be repeated yearly
- perform a resting electrocardiogram for left ventricular hypertrophy or ischaemia
- assess renal function by calculating creatinine clearance
GFR calculated using the Cockcroft and Gault formula:

$$\text{CrCl (mL/minute)} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{0.82 * \text{plasma Cr (micromol/L)}}$$

*in males

* In females, multiply plasma Cr by 0.85 instead of 0.82.

GOALS OF TREATMENT

- aim for SBP <140 mmHg and DBP < 90 mmHg
- aim for the blood pressure ¹³⁰/₈₀ mmHg or lower in patients with diabetes, chronic kidney disease with GFR < 60, proteinuria > 1 g/24hours or equivalent albumin creatinine ratio, congestive heart failure
- hypertensive emergency (pulmonary oedema, encephalopathy), reduce mean arterial pressure by 25% in first 2 hours



CHAPTER 3

CARDIOVASCULAR SYSTEM

NON-DRUG TREATMENT LIFESTYLE MODIFICATION

All persons with hypertension should be encouraged to make the following lifestyle changes as appropriate:

- maintain ideal weight, i.e. BMI < 25
weight reduction in the overweight patient, i.e. BMI > 25
- salt restriction (e.g. remove the salt from the table, gradually reduce added salt in food preparation, avoid processed foods), with increased potassium intake from fresh fruits and vegetables
- reduce alcohol intake to no more than 2 standard drinks/day
- follow a prudent eating plan i.e. low fat, high fibre and unrefined carbohydrates, with adequate fresh fruit and vegetables
- regular moderate aerobic exercise, e.g. 30 minutes brisk walking 3–5 times/week
- smoking cessation

DRUG TREATMENT

Initial drug choices in patients qualifying for treatment is dependent on presence of compelling indications.

DRUG TREATMENT CHOICES WITHOUT COMPELLING INDICATIONS

Treat if BP > ¹⁴⁰/₉₀ mmHg

First line

Low dose thiazide diuretic e.g.:

- hydrochlorothiazide, oral, 12.5 mg daily

Second line

If target blood pressure is not reached after two months, add one of the following: ACE-inhibitor or calcium channel blocker

Third line

If target blood pressure is not reached after two months, add one of the second line drugs which has not already been used or a β -blocker.

CHAPTER 3**CARDIOVASCULAR SYSTEM****DRUG TREATMENT CHOICES - WITH COMPELLING INDICATIONS**

COMPELLING INDICATIONS	DRUG CLASS
Angina	<ul style="list-style-type: none"> • β-blocker • calcium channel blocker
Prior myocardial infarct or coronary artery disease	<ul style="list-style-type: none"> • β-blocker • ACE-inhibitor If β -blocker contraindicated: <ul style="list-style-type: none"> • verapamil
Post myocardial infarction	<ul style="list-style-type: none"> • β-blocker • ACE-inhibitor
Heart failure	<ul style="list-style-type: none"> • ACE-inhibitor • carvedilol • spironolactone • furosemide
Left ventricular hypertrophy	<ul style="list-style-type: none"> • ACE-inhibitor
Stroke	<ul style="list-style-type: none"> • hydrochlorothiazide • ACE-inhibitor
Diabetes type 1 or 2 with or without evidence of microalbuminuria or proteinuria	<ul style="list-style-type: none"> • ACE-inhibitor, usually in combination with a diuretic*
Chronic kidney disease	<ul style="list-style-type: none"> • ACE-inhibitor, usually in combination with a diuretic
Isolated systolic hypertension	<ul style="list-style-type: none"> • hydrochlorothiazide • calcium channel blocker
Pregnancy	See Chapter 6
Prostatism	<ul style="list-style-type: none"> • alpha-blocker

* In 60-80% of patients a combination of the drugs above is needed.

RISK STRATIFICATION AND TREATMENT

The criterion for management is that BP has been measured and recorded as elevated over a two-month period for high-normal and stage 1 hypertension.

High normal: SBP 130–139 mmHg and/or DBP 85–89 mmHg

- no risk factor, TOD/CCD:
 - Low risk: lifestyle modification for 6–12 months only.
- ≥ 1 major risk factor; no TOD/CCD:
 - Low risk: lifestyle modification for 6 months only.
- TOD/CCD, diabetes mellitus with or without other risk factors:
 - High risk: lifestyle modification and drug therapy for those with heart failure, diabetes mellitus or chronic kidney disease.