



**Mercy  
Ships®**

Bringing Hope and Healing...

# Formulary 2009-2011



**An Essential Medicines Dosing Guide  
Based on the WHO Model Formulary**

## ENDOCRINE SYSTEM

### 7.01 CORTICOSTEROIDS

#### WHO MODEL FORMULARY 2008 NOTES:

Corticosteroids include hormones secreted by the adrenal cortex and synthetic analogues of these hormones. The adrenal cortex normally secretes **hydrocortisone** which has glucocorticoid activity and weak mineralocorticoid activity. It also secretes the mineralocorticoid aldosterone. Synthetic glucocorticoids include betamethasone, **dexamethasone** and **prednisolone**. Fludrocortisone [not included on WHO Model List] has glucocorticoid properties but it is used for its potent mineralocorticoid effects. In physiological (low) doses, corticosteroids replace deficient endogenous hormones. In pharmacological (high) doses, glucocorticoids decrease inflammation and suppress the immune response. In therapeutic doses glucocorticoids suppress release of corticotrophin (adrenocorticotrophic hormone, ACTH) from the pituitary thus the adrenal cortex ceases secretion of endogenous corticosteroids. If suppressive doses are given for prolonged periods, the adrenal cortex may atrophy; this leads to a deficiency on sudden withdrawal or dosage reduction of the corticosteroid in or situations such as stress or trauma when corticosteroid requirements are increased. After high dosage or prolonged therapy, withdrawal of the corticosteroid should be gradual, see Withdrawal of Systemic Corticosteroids. The suppressive effect of a corticosteroid on cortisol secretion is least when it is given as a single dose in the morning. Because the therapeutic effects of corticosteroids are of longer duration than the metabolic effects, intermittent therapy may allow the therapeutic effects to be maintained while reducing metabolic effects. Alternate-day dosing is, however, suitable only in certain disease states and for corticosteroids with small mineralocorticoid effects and a relatively short duration of action.

**Hydrocortisone** is used in adrenal replacement therapy and on a short-term basis by intravenous injection for the emergency management of some conditions. Its mineralocorticoid activity is too high for it to be used on a long-term basis for disease suppression. The high mineralocorticoid activity of fludrocortisone is used together with glucocorticoids in adrenal insufficiency. **Prednisolone** has predominantly glucocorticoid activity and is the corticosteroid used for long-term disease control. **Dexamethasone** has very high glucocorticoid activity and insignificant mineralocorticoid activity, making it particularly suitable for conditions where water retention would be a disadvantage. It also has a long duration of action and this, together with its lack of mineralocorticoid activity makes it particularly suitable for conditions requiring suppression of corticotrophin secretion such as congenital adrenal hyperplasia.

**DISADVANTAGES.** Overdosage or prolonged use may exaggerate some of the normal physiological actions of corticosteroids leading to mineralocorticoid and glucocorticoid adverse effects.

Mineralocorticoid adverse effects include hypertension, sodium and water retention and potassium loss. These effects are most marked with fludrocortisone but are significant with hydrocortisone, occur slightly with prednisolone and are negligible with dexamethasone.

Glucocorticoid adverse effects include diabetes mellitus and osteoporosis which is of particular importance in the elderly since it may result in osteoporotic fractures of the hip or vertebrae. High doses may also be associated with avascular necrosis of the femoral neck. Muscle wasting may also occur and there is a weak link with peptic ulceration. Mental disturbances can occur, including serious paranoid state or depression with risk of suicide, particularly in patients with a history of mental disorders; euphoria is also common. High doses may cause Cushing syndrome with moon face, striae and acne; it is usually reversible on withdrawal of treatment, but this should always be tapered gradually to avoid symptoms of acute adrenal insufficiency (see also Withdrawal if Systemic Corticosteroids). Corticosteroids may result in suppression of growth in children. Corticosteroids administered during pregnancy can affect adrenal development in the fetus. Any adrenal suppression in the neonate following prenatal exposure usually resolves spontaneously after birth and is rarely clinically important. Healing of wounds may be impaired and infections and thinning of the skin may occur; spread of infections may result from modification of tissue reactions.

Adrenal suppression occurs during prolonged therapy with corticosteroids, with development of adrenal atrophy which may persist for years after stopping. Abrupt withdrawal after a prolonged period may lead to acute adrenal insufficiency, hypotension or death (see Withdrawal of Systemic Corticosteroids, below). Withdrawal may also be associated with fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and weight loss.

### **CORTICOSTEROID COVER DURING STRESS**

To compensate for a diminished adrenocortical response caused by prolonged corticosteroid treatment, any significant intercurrent illness, trauma, or surgery requires a temporary increase in corticosteroid dose, or if already stopped, a temporary re-introduction of corticosteroid treatment. Anaesthetists **must** therefore know whether a patient is taking or has been taking a corticosteroid, to avoid a precipitous fall in blood pressure during anaesthesia or in the immediate postoperative period. A suitable regimen for corticosteroid replacement, in patients who have taken more than 10 mg prednisolone daily (or equivalent) within 3 months of surgery, is:

*Minor surgery under general anaesthesia:* usual oral corticosteroid dose on the morning of surgery or hydrocortisone 25-50 mg intravenously at induction; the usual oral corticosteroid dose is recommenced after surgery

*Moderate or major surgery:* usual oral corticosteroid dose on the morning of surgery and hydrocortisone 25-50 mg intravenously at induction, followed by hydrocortisone 25-50 mg 3 times a day by intravenous injection for 24 hours after moderate surgery or for 48-72 hours after major surgery; the usual preoperative oral corticosteroid dose is recommenced on stopping hydrocortisone injections.

INFECTIONS. Prolonged courses of corticosteroids increase susceptibility to infections and increase their severity; clinical presentation of infections may also be atypical. Serious infections, for example septicaemia and tuberculosis, may reach an advanced stage before being recognised, and amoebiasis or strongyloidiasis may be activated or exacerbated (exclude before initiating a corticosteroid in those at risk or with suggestive symptoms). Fungal or viral ocular infections may also be exacerbated.

[Mercy Ships notes: See WHO Model Formulary 2008 for further notes on chickenpox and measles infection risk management.]

WITHDRAWAL OF SYSTEMIC CORTICOSTEROIDS. The rate of withdrawal of systemic glucocorticoids is dependent upon several factors including size of dose, duration of treatment, individual response and the likelihood of relapse of the underlying disease. If there is uncertainty about suppression of the HPA axis, withdrawal should be gradual to enable the adrenal gland to recover. Patients should be advised not to stop taking glucocorticoids abruptly unless permitted by their doctor.

*Gradual withdrawal* should be considered in those whose disease is unlikely to relapse and who have:

- recently received repeated courses (particularly if taken for > 3 weeks)
- taken a short course within 1 year of stopping long-term therapy
- other possible causes of adrenal suppression
- received more than 40 mg daily prednisolone (or equivalent)
- been given repeat doses in the evening
- received more than 3 weeks' treatment

*Abrupt withdrawal* may be considered in those whose disease is unlikely to relapse *and* who have received treatment for 3 weeks or less *and* who are not included in the patient groups described above.

During corticosteroid withdrawal the dose may be reduced rapidly down to the physiological dosage (equivalent to 7.5 mg prednisolone daily) and then reduced more slowly. Assessment of the disease may be needed during withdrawal to ensure that relapse does not occur.

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GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
<b>Triamcinolone Acetonide Inj 10mg/ml, 2ml (Adcortyl, Kenalog-10)</b>  <b>[Not for IM use]</b>		<i>Intra-articular inj</i> , Adult 2.5-15mg (depending on joint size & severity). <i>Intradermal inj</i> , Adult 2-3mg (depending on lesion size) max 30mg (not > 5mg at any one site). See product leaflet for detail.

**COMMENT/CAUTIONS:**

- **Equivalent anti-inflammatory corticosteroid doses**  
[NOTE. This table takes no account of mineralocorticoid effects nor does it take account of variations in duration of action]:
- **Prednisolone 5mg**
  - ≡ Betamethasone 750 micrograms
  - ≡ Dexamethasone 750 micrograms
  - ≡ Methylprednisolone 4 mg
  - ≡ Cortisone 25 mg
  - ≡ Hydrocortisone 20 mg
  - ≡ Triamcinolone 4 mg
- **Patient counselling:** Advise patients on prolonged courses of systemic corticosteroids to consult their doctor promptly if they come into close contact with anyone who has chickenpox or shingles, or if they become ill.
- **Dexamethasone** 1 mg = dexamethasone phosphate 1.2 mg = dexamethasone sodium phosphate 1.3 mg.

**7.02 THYROID & ANTITHYROID MEDICINES**

**WHO MODEL FORMULARY 2008 NOTES:**

THYROID AGENTS are natural or synthetic agents containing **levothyroxine** (thyroxine) or **liothyronine** (tri-iodothyronine). The principal effect is to increase the metabolic rate. They also exert a cardiostimulatory effect which may be the result of a direct action on the heart. Thyroid hormones are used in hypothyroidism (myxoedema) and also in diffuse non-toxic goitre, Hashimoto thyroiditis (lymphadenoid goitre) and thyroid carcinoma. Neonatal hypothyroidism requires prompt treatment for normal development. **Levothyroxine sodium** (thyroxine sodium) is the treatment of choice for maintenance therapy. It is almost completely absorbed from the gastrointestinal tract but the full effects are not seen for up to 1 to 3 weeks after beginning therapy; there is a slow response to dose change and effects may persist for several weeks after withdrawal. Dosage of levothyroxine in infants and children for congenital hypothyroidism and juvenile myxoedema should be titrated according to clinical response, growth assessment and measurement of plasma thyroxine and thyroid-stimulating hormone.

ANTITHYROID DRUGS such as **propylthiouracil** and carbimazole are used in the management of thyrotoxicosis. They are also used to prepare the patient for thyroidectomy. They are usually well-tolerated, with mild leukopenia or rashes developing in a few percent of cases, usually during the first 6-8 weeks of therapy. During this time the blood count should be checked every 2 weeks or if a sore throat or other signs of infection develop. The drugs are generally given in a high dose in the first instance until the patient becomes euthyroid, the dose may then be gradually reduced to a maintenance dose which is continued for 12-18 months, followed by monitoring to identify relapse. There is a lag time of some 2 weeks between the achievement of biochemical euthyroidism and clinical euthyroidism. Beta-blockers (usually propranolol) may be used as a short-term adjunct to antithyroid drugs to control symptoms but their use in heart failure associated with thyrotoxicosis is controversial.

Treatment can be given, if necessary, in pregnancy but antithyroid drugs cross the placenta and in high doses may cause fetal goitre and hypothyroidism. The lowest dose that will control the hyperthyroid state should be used (requirements in Graves disease tend to fall during pregnancy). Propylthiouracil appears in breast milk but does not preclude breastfeeding as long as neonatal development is closely monitored and the lowest effective dose is used.

If surgery (partial thyroidectomy) is contemplated, it may be necessary to give **iodine** for 10 to 14 days in addition to antithyroid drugs to assist control and reduce vascularity of the thyroid. Iodine should not be used for long-term treatment since its antithyroid action tends to diminish. In patients in whom drug therapy fails to achieve long-term remissions definitive treatment with surgery or (increasingly) radioactive iodine is preferable.

GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
<b>Carbimazole Tab 5mg (Neomercazole)</b>  <b>Antithyroid</b>	IDA	<i>By mouth</i> , Adult initially 15-40mg daily in 2-3 divided doses; maintenance 5-15mg daily; Child initially 250 micrograms/kg/DOSE given 3 times daily adjusted according to response.
<b>Propylthiouracil Tab 50mg</b>  <b>Antithyroid</b>	D  EML	Hyperthyroidism: <i>by mouth</i> , Adult 300-600 mg daily in divided doses or once daily, until patient becomes euthyroid; then reduce dose gradually, usual maintenance dose 50-150 mg daily.

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### 7.03 INSULINS

#### WHO MODEL FORMULARY 2008 NOTES:

**Diabetes mellitus** is characterized by hyperglycaemia and disturbances of carbohydrate, fat and protein metabolism. There are 2 principal types of diabetes. *Type 1 diabetes or insulin-dependent diabetes mellitus* is due to a deficiency of insulin caused by autoimmune destruction of pancreatic beta cells. Patients require administration of insulin. *Type 2 diabetes or non-insulin dependent diabetes mellitus* is due to reduced secretion of insulin or to peripheral resistance to the action of insulin. Patients may be controlled by diet alone, but often require administration of oral antidiabetic drugs or insulin. The energy and carbohydrate intake must be adequate but obesity should be avoided. In type 2 diabetes, obesity is one of the factors associated with insulin resistance. Diets high in complex carbohydrate and fibre and low in fat are beneficial. Emphasis should be placed on exercise and increased activity. The aim of treatment is to achieve the best possible control of blood-glucose concentration and prevent or minimize complications including microvascular complications (retinopathy, albuminuria, neuropathy). Diabetes mellitus is a strong risk factor for cardiovascular disease; other risk factors such as smoking, hypertension, obesity and hyperlipidaemia should also be addressed.

INSULIN. Appropriate insulin regimens should be worked out for each patient. Insulin requirements may be affected by variations in lifestyle (diet and exercise)—drugs such as corticosteroids, infections, stress, accidental or surgical trauma, puberty and pregnancy (second and third trimesters) may increase insulin requirements; renal or hepatic impairment and some endocrine disorders (for example Addison disease, hypopituitarism) or coeliac disease may reduce requirements. In pregnancy insulin requirements should be monitored frequently.

**Insulin** must be given by injection because it is inactivated by gastrointestinal enzymes. Generally, insulin is given by subcutaneous injection into the upper arms, thighs, buttocks, or abdomen. There may be increased absorption from a limb site, if the limb is used in strenuous exercise following the injection. It is essential to use only syringes calibrated for the particular concentration of insulin administered. Insulin preparations can be classified according to duration of action after subcutaneous injection as follows:

- those of short duration which have a relatively rapid onset of action, for example soluble or neutral insulin;
- those with an intermediate action, for example isophane insulin;
- those with a relatively slow onset and long duration of action, for example protamine zinc insulin.

**Soluble insulin**, when injected subcutaneously, has a rapid onset of action (after 30-60 minutes), a peak action between 2 and 4 hours, and a duration of action up to 8 hours. Soluble insulin by the IV route is reserved for urgent treatment and fine control in serious illness and perioperatively. When injected intravenously, soluble insulin has a very short half-life of only about 5 minutes and its effects disappear within 30 minutes. When injected subcutaneously, **intermediate-acting insulins** have an onset of action of approximately 1-2 hours, a maximal effect at 4-12 hours and a duration of action of 16-24 hours. They can be given twice daily together with short-acting insulin or once daily, particularly in elderly patients. Most can be mixed with soluble insulin in the syringe, essentially retaining properties of each component. **Long-acting insulins** have an onset of action approximately 4 hours after subcutaneous injection; peak activity is between 10 and 20 hours, and duration of action up to 36 hours. Mixed insulin zinc suspension can be classified as either intermediate or long-acting.

*The duration of action of different insulin preparations varies considerably from one patient to another and this needs to be assessed for every individual.* The type of insulin used and its dose and frequency of administration depend on the needs of each patient. For patients with acute onset diabetes mellitus, treatment should be started with soluble insulin given 3 times daily with medium-acting insulin at bedtime. For those less seriously ill, treatment is usually started with a mixture of pre-mixed short- and medium-acting insulins (for example 30% soluble insulin with 70% isophane insulin) given twice daily. The proportions of soluble insulin can be increased in patients with excessive post-prandial hyperglycaemia.

Regimens should be developed by each country.

**MONITORING.** If possible patients should monitor their own blood-glucose concentration using blood glucose strips. Since blood-glucose concentration varies throughout the day, patients should aim to maintain blood-glucose concentration between 4-9 mmol/litre (72-180 mg/dl) for most of the time (4-7mmol/litre before meals and less than 9 mmol/litre after meals) while accepting that on occasions it will be higher; strenuous efforts should be made to prevent blood-glucose concentrations falling below 4 mmol/litre (72 mg/dl) because of the risk of hypoglycaemia. Patients should be advised to look for troughs and peaks of blood glucose and to adjust their insulin dosage only once or twice a week. Insulin doses are determined on an individual basis, by gradually increasing the dose to optimise blood-glucose concentration while avoiding hypoglycaemia. In the absence of blood-glucose monitoring strips, urine-glucose monitoring strips can be used (method of personal choice for many patients with Type 2 diabetes mellitus). It is less reliable than blood glucose but is easier and costs much less. All patients should monitor either blood- or urine-glucose concentration daily.

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[Mercy Ships note: For full notes on hypoglycaemia please refer to the WHO Model Formulary 2008, notes on glucagon edited as it is not on our formulary.]

**HYPOGLYCAEMIA** is a potential complication in all patients treated with insulin or less frequently with sulfonylureas. The consequences of hypoglycaemia include confusion, seizures, coma and cerebral infarction. Initial treatment of hypoglycaemia involves glucose 10–20 g given by mouth either in liquid form or as granulated sugar (2 teaspoons) or sugar lumps (3 lumps). If necessary this may be repeated in 10–15 minutes. Alternatively, 25 ml of glucose intravenous infusion 50% (section 8.03) may be given, but this higher concentration is more irritant and viscous, which makes administration difficult. Glucose intravenous infusion 10% may also be used but a larger volume is needed. Close monitoring is necessary in the case of an overdose with a long acting insulin because further administration may be required. Patients whose hypoglycaemia is caused by a sulphonylurea should be transferred to hospital because the hypoglycaemic effects of these drugs may persist for many hours.

**DIABETIC KETOACIDOSIS** is a potentially lethal condition caused by an absolute or relative lack of insulin; it commonly occurs when adjustments to insulin dosage fail to compensate for increases in insulin requirements, for example during severe infection or major intercurrent illness. Diabetes ketoacidosis occurs mostly in patients with Type 1 diabetes mellitus. It also occurs in Type 2 diabetics who have a temporary need for insulin. Diabetic ketoacidosis is characterized by hyperglycaemia, hyperketonaemia and acidaemia with dehydration and electrolyte disturbances. It is essential that soluble insulin (and intravenous fluids) is readily available for its treatment.

**INFECTIONS** are more likely to develop in patients with poorly controlled diabetes mellitus. These should be treated promptly and effectively to avoid diabetic ketoacidosis.

**SURGERY.** Particular attention should be paid to insulin requirements when a patient with diabetes undergoes surgery that is likely to need IV infusion of insulin for longer than 12 hours. Soluble insulin should be given in IV infusion of glucose and potassium chloride (provided the patient is not hyperkalaemic), and adjusted to provide a blood-glucose concentration 7-12 mmol/litre (126-216 mg/dl). The duration of action of IV insulin is only a few minutes therefore the infusion must not be stopped unless the patient becomes frankly hypoglycaemic. For non-insulin dependent diabetics, insulin treatment is almost always required during surgery (oral hypoglycaemic drugs having been omitted). [Mercy Ships note: please continue oral hypoglycaemics during surgery unless directed otherwise.]

GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
<b>Insulin, Soluble 100 units/ml (Neutral insulin, R) (e.g. Actrapid HM, check current brand in stock)</b>	EML	SC, IM, IV or IV infusion, Diabetes mellitus, Adult & Child dose according to individual requirements. See WHO notes above.
Note: Only short-acting insulin can be given IV. Insulins are °Fridge Items unless currently in use.		

**COMMENT/CAUTIONS:**

- **Acute illness:** Insulin requirement may vary - consider transfer to soluble insulin *by SC route* every 6 hours; never reduce or stop insulin in patients with vomiting as extra insulin may be needed.
- **Beta-blockers** especially non-selective ones may mask the onset of hypoglycaemic symptoms.
- **Administration:** when mixing insulins draw up the shorter-acting one first and administer directly after mixing. Patients should only be transferred from one brand of insulin to another under medical supervision and in most instances they can be initiated at the same dose and schedule.
- **Diabetic ketoacidosis:** Give soluble insulin *by IV infusion*, well-diluted to 1unit/ml in NS at a rate of 6 units/hour (Adult) or 0.1unit/kg/hour (Child). When plasma glucose level is acceptable reduce rate to 3units/hour (Adult) or 0.02unit/kg/hour (Child), until SC insulin regime is restarted.

**7.04 ORAL HYPOGLYCAEMIC AGENTS**

**WHO MODEL FORMULARY 2008 NOTES:**

Oral antidiabetic (hypoglycaemic) drugs are used for non-insulin-dependent diabetes mellitus in patients who do not respond to dietary adjustment and an increase in physical exercise. They are used to supplement the effect of diet and exercise. There are various types of oral antidiabetic agents. The most commonly used are the **sulfonylureas** and the **biguanide** metformin.

Sulfonylureas act mainly by augmenting insulin secretion and are therefore only effective if there is some residual pancreatic beta-cell activity. They may occasionally lead to hypoglycaemia 4 hours or more after food. This usually indicates excessive dose and it occurs more frequently in the elderly and with long-acting sulfonylureas e.g. **glibenclamide**. Disadvantage: may encourage weight gain. They should not be used during breastfeeding and caution is required in the elderly and those with renal or hepatic insufficiency because of the risk of hypoglycaemia. Insulin therapy is generally required during intercurrent illness such as myocardial infarction, coma, infection, and trauma, during surgery and also during pregnancy.

**Metformin** exerts its effect by decreasing gluconeogenesis and by increasing peripheral utilization of glucose. Metformin can only act in the presence of endogenous insulin therefore is effective only in diabetics with some residual functioning pancreatic islet cells. It is used as a first-line treatment in overweight non-insulin-dependent diabetic patients and in others when strict dieting and sulfonylureas have failed to control the disease. Gastrointestinal adverse effects are common on initial treatment and may persist, particularly when very high doses (such as 3 g daily) are given. In order to reduce gastrointestinal effects, initiate with a low dose which may be gradually increased. Metformin may provoke lactic acidosis which is most likely to occur in patients with renal impairment; it should not be used in patients with even mild renal impairment. One major advantage of metformin is that it does not usually cause hypoglycaemia. It may be used together with insulin (but weight gain and hypoglycaemia can be problems) or sulfonylureas (but possibility of increased adverse effects with such combinations). During medical and surgical emergencies insulin treatment is almost always required; insulin should be substituted for metformin before elective surgery and in pregnancy.

GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
<b>Glibenclamide (Glyburide) Tab 5mg (Daonil)</b> [Sulphonylurea]	IDA  EML	<i>By mouth</i> , Adult initially 5 mg once daily with breakfast (Elderly 2.5 mg, but avoid—see WHO notes above), adjusted according to response (maximum 15 mg daily).
<b>Metformin Tab 500mg (Glucophage)</b> [Biguanide]	IDA  EML	<i>By mouth</i> , Adult initially 500 mg with breakfast for at least 1 week then 500 mg with breakfast and evening meal for at least 1 week, then 500 mg with breakfast, lunch and evening meal <i>or</i> 850 mg every 12 hours with or after food (max 2g/DAY in divided doses).

**COMMENT/CAUTIONS:**

- **Metformin:** Contraindicated in renal impairment and hepatic disease (see WHO notes above). Adverse effects include GI disturbances, lactic acidosis (increase risk with alcohol). Monitor vitamin B<sub>12</sub> levels yearly.
- **DRUG-INDUCED HYPOGLYCAEMIA:** hypoglycaemia may be potentiated by anticoagulants, chloramphenicol, fluconazole, NSAIDs, and fibrates. Conversely, the hypoglycaemic effects of antidiabetics may be reduced by oral contraceptives, corticosteroids, diuretics.

## 7.05 SEX HORMONES & RELATED MEDICINES

### WHO MODEL FORMULARY 2008 NOTES:

[Mercy Ships note: See WHO Model Formulary 2008 for full HRT & COC notes.]

ESTROGENS are necessary for the development of female secondary sexual characteristics; they also stimulate myometrial hypertrophy with endometrial hyperplasia. They affect bone by increasing calcium deposition. They are secreted at varying rates during the menstrual cycle throughout the period of activity of the ovaries. During pregnancy, the placenta becomes the main source of estrogens. Ovarian secretion declines at the menopause. Estrogen therapy is given cyclically or continuously principally for contraception and for the alleviation of menopausal symptoms. If long-term therapy is required for menopausal hormone therapy a progestogen should be added to prevent cystic hyperplasia of the endometrium (or of endometrial foci in women who have had a hysterectomy) and possible transformation to cancer.

PROGESTOGENS. **Progesterone** is a hormone secreted by the corpus luteum whose actions include induction of secretory changes in the endometrium, relaxation of uterine smooth muscle and production of changes in the vaginal epithelium. Progesterone is relatively inactive following oral administration and produces local reactions at site of injection. This has led to the development of synthetic progestogens including **levonorgestrel**, **norethisterone** and **medroxyprogesterone** [not on Mercy Ships list]. Where endometriosis requires drug treatment, it may respond to synthetic progestogens on a continuous basis. A progestogen may also be used for the treatment of severe dysmenorrhoea but where contraception is also required the best choice is a combined oral contraceptive. In postmenopausal women receiving long-term estrogen therapy for hormone replacement, a progestogen needs to be added for women with an intact uterus to prevent hyperplasia of the endometrium. Progestogens have been used for the treatment of menorrhagia, but they are not as effective as tranexamic acid [not included on WHO Model List]; mefenamic acid [not included on WHO Model List or Mercy Ships list] is particularly useful when dysmenorrhoea is also a problem.

COMBINED ORAL CONTRACEPTIVES (COC). Estrogen plus progestogen combinations are the most widely used hormonal contraceptives. They produce a contraceptive effect mainly by suppressing the hypothalamic-pituitary system resulting in prevention of ovulation; in addition, changes in the endometrium make it unreceptive to implantation.

COC & SURGERY. Estrogen-containing oral contraceptives should preferably be discontinued (and adequate alternative contraceptive arrangements made) 4 weeks before major elective surgery and all surgery to the legs or surgery which involves prolonged immobilization of a lower limb. They should normally be

restarted at the first menses occurring at least 2 weeks after full mobilization. When discontinuation is not possible thromboprophylaxis (with heparin and graduated compression hosiery) is advised.

COCs should be STOPPED IMMEDIATELY if any of the following symptoms occur and resumed only after consultation with a health care provider:

- Sudden severe chest pain (even if not radiating to left arm);
- Sudden breathlessness (or cough with blood-stained sputum);
- Severe pain in calf of one leg;
- Severe stomach pain;
- Serious neurological effects including unusual, severe, prolonged headache especially if first time or getting progressively worse *or* sudden partial or complete loss of vision *or* sudden disturbance of hearing or other perceptual disorders *or* dysphagia *or* bad fainting attack or collapse *or* first unexplained epileptic seizure *or* weakness, motor disturbances, very marked numbness suddenly affecting one side or one part of body;
- Hepatitis, jaundice, liver enlargement;
- Blood pressure above systolic 160 mmHg and diastolic 100 mmHg;
- Detection of 2 or more risk factors for venous thromboembolism or arterial disease, see notes above [Mercy Ships note: refer to WHO formulary.]

PROGESTOGEN-ONLY CONTRACEPTIVES or preparations (POP), such as oral **levonorgestrel** may offer a suitable alternative when estrogens are contraindicated but the oral POPs do not prevent ovulation in all cycles and have a higher failure rate than combined estrogen-containing preparations. POPs carry less risk of thromboembolic and cardiovascular disease than COCs and are preferable for women at increased risk of such complications, for example smokers over 35 years. They can be used as an alternative to estrogen-containing combined preparations prior to major surgery. Oral POPs may be started 3 weeks after birth; breastfeeding women should preferably start at least 6 weeks after birth. Menstrual irregularities (oligomenorrhoea, menorrhagia, amenorrhoea) are common.

**Levonorgestrel** is used for emergency contraception. [see below for dose]. Adverse effects include nausea, vomiting, headache, dizziness, breast discomfort, and menstrual irregularities. If vomiting occurs within 2–3 hours of taking the tablets, replacement tablets can be given with an antiemetic. Advise patient that her next period may be early or late; that she needs to use a barrier contraceptive method until her next period, and she should seek prompt medical attention if lower abdominal pain occurs, or if subsequent menstrual bleed is abnormally light, heavy, brief or absent. There is no evidence of harmful effects to the fetus if pregnancy should occur.

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GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
<b>Ergometrine Inj 0.5mg/ml</b> [Ergonovine] °Fridge Item	MSL  EML	Uterine bleeding: <i>By IM inj</i> 0.2 mg every 2 to 4 hours; for diagnostic use in angina pectoris, the usual dose is 0.05 to 0.2 mg <i>intravenously</i> .
<b>Estrogen, Conjugated Tab 0.625mg (Premarin)</b> [HRT]		Menopausal/post-menopausal symptoms: <i>by mouth</i> 0.625mg daily, usually on a cyclical basis and in conjunction with an added progesterone for part of the cycle.
<b>Ethinylestradiol 30microgram/ Levonorgestrel 150microgram Tab (e.g. Microgynon 30)</b> [COC]	IDA  EML	<i>By mouth</i> one tablet ('pill') daily taken same time each day for 21 days; subsequent courses repeated after 7-day pill-free interval (during which withdrawal bleeding occurs). Initiate first course on day 1 after the beginning of the menstrual period.
<b>Levonorgestrel Tab 750 micrograms, 2 tablet pack</b>	IDA  EML	Emergency contraception: <i>by mouth</i> , Adult (female) 1.5 mg as a single dose (taken within 120 hours/5 days of unprotected intercourse); <i>or</i> 750 micrograms (taken within 72 hours) followed by a second dose 750 micrograms 12 hours later.
<b>Norethisterone Tab 5mg</b> [HRT]	IDA  EML	<i>By mouth</i> , Endometriosis: Adult 10mg daily starting on day 5 of cycle (increased if spotting occurs to 20-25mg daily, reduced once bleeding has stopped). Menorrhagia: Adult 5mg 3 times daily for 10 days to stop bleeding; to prevent bleeding 5mg twice daily from day 19 to 26 of cycle Dysmenorrhoea: 5mg 2-3 times daily from day 5 to 24 for 3 to 4 cycles. HRT: 5mg daily from day 15 to 26 of each 28-day estrogen HRT cycle.
<b>Oxytocin Inj 10 units/ml</b> °Fridge Item	MSL IDA  EML	Induction & augmentation of labour: <i>IV infusion</i> of 5-10 units in 1000 ml D5/NS/RL solution at a rate of 0.5-5ml/minute titrate to response. Postpartum haemorrhage: <i>IM or IV infusion</i> 5-10 units as above titrate to response (of 10-40 units/ml solution)

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**COMMENT/CAUTIONS:**

- **Ergometrine/Ergonovine:** Contraindicated for labour induction in threatened spontaneous abortion and in hypersensitive patients, not recommended prior to delivery of the placenta. Caution should be exercised in patients with heart, hepatic, or renal dysfunction, hypertension, vascular disease, or sepsis.
- **COC Initiation:** Use another form of contraceptive for day 1-7 of first cycle. Each tablet ('pill') should be taken at approximately the same time each day.
- **COC Missed tablets:** Take the missed tablet as soon as possible and take the next tablet at the usual time, but use an additional method of contraception for 7 days—if the 7 days extend beyond the end of the packet/cycle, a new packet/cycle is started without leaving a gap between packets. If delayed by longer than 24 hours contraceptive protection may be lost. Critical time for loss of protection is when a pill is omitted at beginning or end of a cycle (which lengthens the pill-free interval). Emergency contraception is recommended if either 2 or more pills are missed from the first 7 pills in a packet *or* 4 or more consecutive pills are missed mid-packet.
- Vomiting up to 3 hours after taking an oral contraceptive *or* very severe diarrhoea can interfere with the absorption of the pill. Additional precautions should be used during and for 7 days after recovery. If vomiting and diarrhoea occur during the last 7 pills, the next pill-free period should be omitted.
- **COC Breastfeeding:** Start 12 weeks after delivery to not affect breastfeeding.
- **COC Contraindications:** Thromboembolism or phlebitis (present/history), pregnancy, cerebral vascular or coronary artery disease, estrogen-dependent cancer, unexplained vaginal bleeding or amenorrhoea, diabetes with vascular disease, hypertension, liver/heart/renal/adrenal disease, heavy smoker > 35 yo, headaches with focal neurological symptoms (patient should report any increase in headache frequency or onset of focal symptoms).
- **COC Precautions:** Weight change, lipid/liver/GI/emotional disorders, undiagnosed bleeding irregularities, fluid retention, contact lenses; recommend annual med history/exam.
- **COC Drug Interactions:** reduced contraceptive effect by rifampicin and broad-spectrum antibiotics, griseofulvin and antiepileptics; antagonise anticoagulant effects, may increase side effects of tricyclic antidepressants.
- **HRT Drug Interactions:** Unlikely due to the low dose of oestrogen in HRT.
- **HRT Contraindications:** Estrogen dependent cancer, active thrombo-phlebitis or thromboembolic disorders, liver disease, unexplained vaginal bleeding, pregnancy or breast-feeding.

### 7.06 DRUGS FOR URINARY INCONTINENCE

GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
<b>Oxybutynin HCl Tab 5mg (Cystrin/Ditropan)</b>		VVF patients: Adult and Child > 12yo <i>By mouth</i> initially 5mg 2-3 times daily; increased if needed to max 5mg 4 times daily; Elderly initially 2.5-3mg twice daily; increased to 5mg twice daily according to response and tolerance.

**COMMENT/CAUTIONS:**

- **Oxybutynin:** Please check current VVF standing orders and guidelines. **Not to be confused with hyoscine n-butylbromide (butylscopolamine or Buscopan), see Section 1.04 Antispasmodics.**