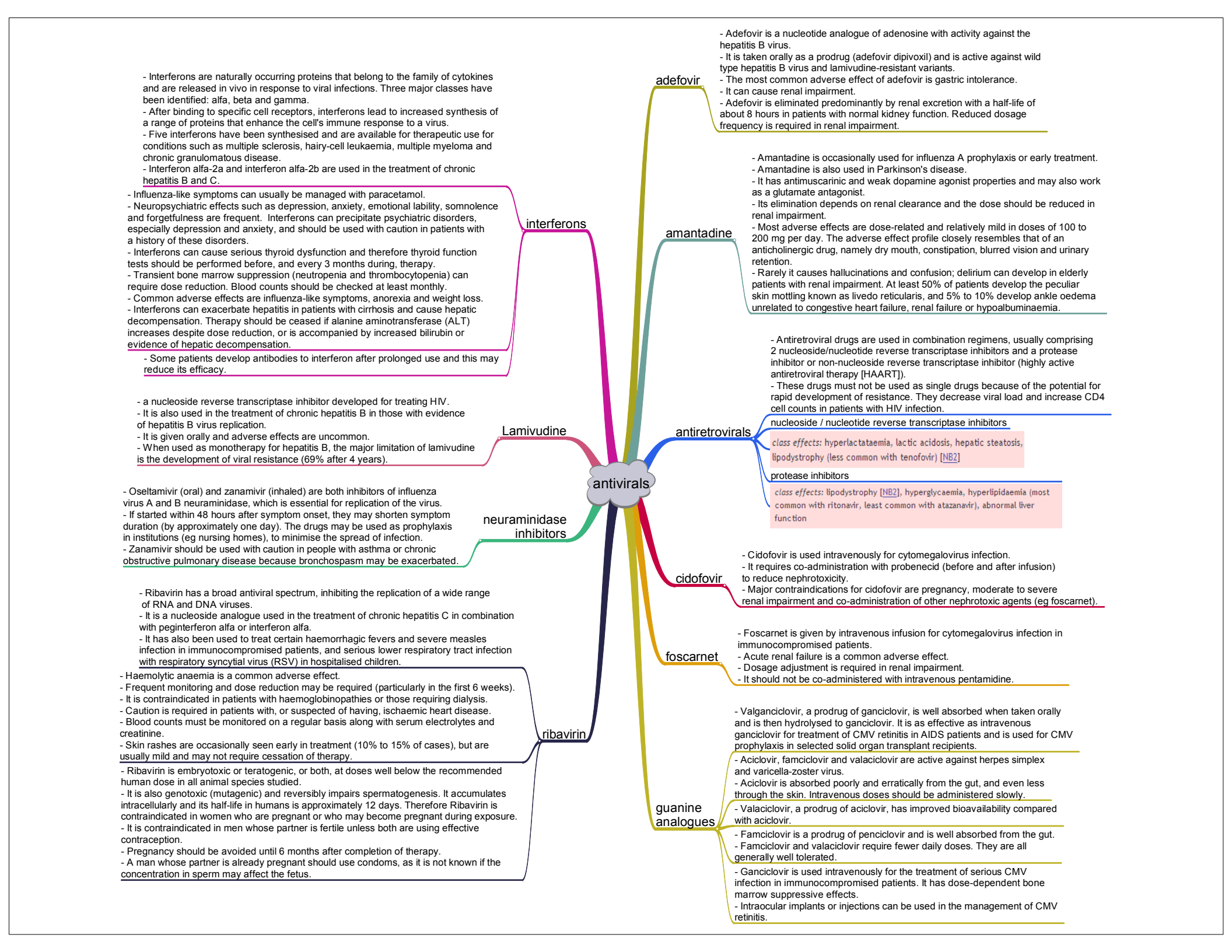
antivirals
interferons
- Interferons are naturally occurring proteins that belong to the family of cytokines and are released in vivo in response to viral infections. Three major classes have been identified: alfa, beta and gamma.
- After binding to specific cell receptors, interferons lead to increased synthesis of a range of proteins that enhance the cell's immune response to a virus.
- Five interferons have been synthesised and are available for therapeutic use for conditions such as multiple sclerosis, hairy-cell leukaemia, multiple myeloma and chronic granulomatous disease.
- Interferon alfa-2a and interferon alfa-2b are used in the treatment of chronic hepatitis B and C.
- Influenza-like symptoms can usually be managed with paracetamol.
- Neuropsychiatric effects such as depression, anxiety, emotional lability, somnolence and forgetfulness are frequent. Interferons can precipitate psychiatric disorders, especially depression and anxiety, and should be used with caution in patients with a history of these disorders.
- Interferons can cause serious thyroid dysfunction and therefore thyroid function tests should be performed before, and every 3 months during, therapy.
- Transient bone marrow suppression (neutropenia and thrombocytopenia) can require dose reduction. Blood counts should be checked at least monthly.
- Common adverse effects are influenza-like symptoms, anorexia and weight loss.
- Interferons can exacerbate hepatitis in patients with cirrhosis and cause hepatic decompensation. Therapy should be ceased if alanine aminotransferase (ALT) increases despite dose reduction, or is accompanied by increased bilirubin or evidence of hepatic decompensation.
- Some patients develop antibodies to interferon after prolonged use and this may reduce its efficacy.
Lamivudine
- a nucleoside reverse transcriptase inhibitor developed for treating HIV.
- It is also used in the treatment of chronic hepatitis B in those with evidence of hepatitis B virus replication.
- It is given orally and adverse effects are uncommon.
- When used as monotherapy for hepatitis B, the major limitation of lamivudine is the development of viral resistance (69% after 4 years).
neuraminidase inhibitors
- Oseltamivir (oral) and zanamivir (inhaled) are both inhibitors of influenza virus A and B neuraminidase, which is essential for replication of the virus.
- If started within 48 hours after symptom onset, they may shorten symptom duration (by approximately one day). The drugs may be used as prophylaxis in institutions (eg nursing homes), to minimise the spread of infection.
- Zanamivir should be used with caution in people with asthma or chronic obstructive pulmonary disease because bronchospasm may be exacerbated.
ribavirin
- Ribavirin has a broad antiviral spectrum, inhibiting the replication of a wide range of RNA and DNA viruses.
- It is a nucleoside analogue used in the treatment of chronic hepatitis C in combination with peginterferon alfa or interferon alfa.
- It has also been used to treat certain haemorrhagic fevers and severe measles infection in immunocompromised patients, and serious lower respiratory tract infection with respiratory syncytial virus (RSV) in hospitalised children.
- Haemolytic anaemia is a common adverse effect.
- Frequent monitoring and dose reduction may be required (particularly in the first 6 weeks).
- It is contraindicated in patients with haemoglobinopathies or those requiring dialysis.
- Caution is required in patients with, or suspected of having, ischaemic heart disease.
- Blood counts must be monitored on a regular basis along with serum electrolytes and creatinine.
- Skin rashes are occasionally seen early in treatment (10% to 15% of cases), but are usually mild and may not require cessation of therapy.
- Ribavirin is embryotoxic or teratogenic, or both, at doses well below the recommended human dose in all animal species studied.
- It is also genotoxic (mutagenic) and reversibly impairs spermatogenesis. It accumulates intracellularly and its half-life in humans is approximately 12 days. Therefore Ribavirin is contraindicated in women who are pregnant or who may become pregnant during exposure.
- It is contraindicated in men whose partner is fertile unless both are using effective contraception.
- Pregnancy should be avoided until 6 months after completion of therapy.
- A man whose partner is already pregnant should use condoms, as it is not known if the concentration in sperm may affect the fetus.
adefovir
- Adefovir is a nucleotide analogue of adenosine with activity against the hepatitis B virus.
- It is taken orally as a prodrug (adefovir dipivoxil) and is active against wild type hepatitis B virus and lamivudine-resistant variants.
- The most common adverse effect of adefovir is gastric intolerance.
- It can cause renal impairment.
- Adefovir is eliminated predominantly by renal excretion with a half-life of about 8 hours in patients with normal kidney function. Reduced dosage frequency is required in renal impairment.
amantadine
- Amantadine is occasionally used for influenza A prophylaxis or early treatment.
- Amantadine is also used in Parkinson's disease.
- It has antimuscarinic and weak dopamine agonist properties and may also work as a glutamate antagonist.
- Its elimination depends on renal clearance and the dose should be reduced in renal impairment.
- Most adverse effects are dose-related and relatively mild in doses of 100 to 200 mg per day. The adverse effect profile closely resembles that of an anticholinergic drug, namely dry mouth, constipation, blurred vision and urinary retention.
- Rarely it causes hallucinations and confusion; delirium can develop in elderly patients with renal impairment. At least 50% of patients develop the peculiar skin mottling known as livedo reticularis, and 5% to 10% develop ankle oedema unrelated to congestive heart failure, renal failure or hypoalbuminaemia.
antiretrovirals
- Antiretroviral drugs are used in combination regimens, usually comprising 2 nucleoside/nucleotide reverse transcriptase inhibitors and a protease inhibitor or non-nucleoside reverse transcriptase inhibitor (highly active antiretroviral therapy [HAART]).
- These drugs must not be used as single drugs because of the potential for rapid development of resistance. They decrease viral load and increase CD4 cell counts in patients with HIV infection.
nucleoside / nucleotide reverse transcriptase inhibitors
class effects: hyperlactataemia, lactic acidosis, hepatic steatosis, lipodystrophy (less common with tenofovir) [NB2]
protease inhibitors
class effects: lipodystrophy [NB2], hyperglycaemia, hyperlipidaemia (most common with ritonavir, least common with atazanavir), abnormal liver function
cidofovir
- Cidofovir is used intravenously for cytomegalovirus infection.
- It requires co-administration with probenecid (before and after infusion) to reduce nephrotoxicity.
- Major contraindications for cidofovir are pregnancy, moderate to severe renal impairment and co-administration of other nephrotoxic agents (eg foscarnet).
foscarnet
- Foscarnet is given by intravenous infusion for cytomegalovirus infection in immunocompromised patients.
- Acute renal failure is a common adverse effect.
- Dosage adjustment is required in renal impairment.
- It should not be co-administered with intravenous pentamidine.
guanine analogues
- Valganciclovir, a prodrug of ganciclovir, is well absorbed when taken orally and is then hydrolysed to ganciclovir. It is as effective as intravenous ganciclovir for treatment of CMV retinitis in AIDS patients and is used for CMV prophylaxis in selected solid organ transplant recipients.
- Aciclovir, famciclovir and valaciclovir are active against herpes simplex and varicella-zoster virus.
- Aciclovir is absorbed poorly and erratically from the gut, and even less through the skin. Intravenous doses should be administered slowly.
- Valaciclovir, a prodrug of aciclovir, has improved bioavailability compared with aciclovir.
- Famciclovir is a prodrug of penciclovir and is well absorbed from the gut.
- Famciclovir and valaciclovir require fewer daily doses. They are all generally well tolerated.
- Ganciclovir is used intravenously for the treatment of serious CMV infection in immunocompromised patients. It has dose-dependent bone marrow suppressive effects.
- Intraocular implants or injections can be used in the management of CMV retinitis.