# ANTI-LYMPHOCYTE GLOBULIN (King's College Hospital Protocol)

**INDICATION:** Aplastic anaemia

**Preparations of ATG:** Horse ATG (ATGAM – anti-thymocyte globulin, 250mg ATG per vial)

**Prior to treatment**

- This needs to be obtained from Pfizer on a named patient basis. A request form and letter from the prescribing consultant stating the reason for treatment needs to be completed. Pharmacy will provide the request form.
- It may take some time to obtain the drug, and therefore the patient must not be admitted until it is confirmed the ATG has arrived in Pharmacy. As the drug is given over 4 days, it is preferable for this to start on a Monday morning, so the drug can be given during the working week.
- Do not give ATG if there is evidence of active infection or previous anaphylaxis with ATG
- Patients should have a class I HLA type sent to Sheffield in case HLA matched platelets are required
- Patients may not respond to ATG and an allogeneic transplant may be required. It therefore is prudent to send a tissue type to both Manchester & Sheffield, and type any siblings.
- Ensure patient has a Hickman line in situ - severe thrombophlebitis occurs if given via peripheral vein.
- Inform blood transfusion lab on admission that all blood and platelet transfusions must be irradiated
- Exclude active infection
- All patients should have an ECG & CXR pre-treatment. Patients with a cardiac history and all those >60 years old should have a baseline echocardiogram.
- ATG may cause anaphylactic reactions. Historically a skin test was used as the test dose for horse ATG (ATGAM), but because of a high incidence of false positives and false negatives, current practice in Europe is to use an intravenous infusion test dose. Therefore, the skin test is no longer required.
- <u>Procedure for intravenous infusion test dose:</u>
- Precede the test dose with methylprednisolone 1mg/kg IV as a 30 minute infusion, 30 minutes before the dose. Also give chlorpheniramine (Piriton) 10mg IV
- The test dose must be supervised by a doctor with epinephrine (see anaphylaxis protocol), chlorphenamine (10mg IV) and hydrocortisone (100mg IV) drawn up beforehand
- Run the infusion slowly at 5ml/hr for the first hour of the first day's dose
- A severe systemic reaction or anaphylaxis to the test dose is an absolute contraindication to proceeding with ATG treatment.

**Prior to each dose**

- Premedicate with methylprednisolone 1mg/kg IV, chlorpheniramine (Piriton) 10mg IV and Paracetamol 1g PO STAT and then QDS PRN.
- The drug is made up on the ward by the nursing staff.
- Dilute in 1000ml Normal saline and give through a 0.22 micron filter (can be obtained from pharmacy). Maximum concentration is 4mg/ml. **Do NOT use glucose 5%.**
- Nursing staff need to ensure that no air hits the product. Therefore when the drawn up solution is added to the bag of normal saline it must be ejected straight into the diluent i.e. do not hold the bag upside down. **The bag should not be shaken**.
- Note that ATG will also cause immediate worsening of neutropenia and thrombocytopenia. If platelets are <30 on day of ATG transfuse 1 dose of platelets before the ATG. Patients may need more than bag of platelets per day.
- Note that blood or platelet transfusions are never to be given while ATG infusion in progress.
- Note that ATG may cause glycosuria and proteinuria – do regular urinalysis and fluid balance

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| **Day 1** | ATG 40mg/kg IV in 1 litre normal saline<br>Slow IV infusion as a test dose as above<br>*If there is anaphylaxis or a severe systemic reaction do not proceed with further treatment*<br>Infuse the remainder of the infusion over 12 – 18 hours. If tolerated, subsequent infusions can be given over 12 hours. |
| **Day 2** | ATG 40mg/kg IV in 1 litre normal saline over 12 hours |
| **Day 3** | ATG 40mg/kg IV in 1 litre normal saline over 12 hours |
| **Day 4** | ATG 40mg/kg IV in 1 litre normal saline over 12 hours |
| **Day 5** | Commence prednisolone 1mg/kg/day |
| **Day 5** | Start ciclosporin 2.5mg/kg bd orally if <60 years old. Start at 1.25mg/kg bd if >60 years old<br>• Regular monitoring of trough cyclosporin levels is required, aiming for a level of 150-200 mcg/litre.<br>• Posaconazole can increase ciclosporin levels |
| **Day 10** | If no serum sickness has occurred begin reducing prednisolone by halving dose every 5 days |

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| **Other medications:** | Omeprazole 20mg daily and continue until prednisolone stopped |
| | Posaconazole tablets 300mg bd for 1 day, then 300mg od. Stop when neutrophils >1.0 for 2 consecutive days |
| | Norethisterone 5mg tds for menstruating females |
| | Acyclovir 400mg bd |
| | Cotrimoxazole is not required – King's College in London have not had a case of PCP following ATG treatment |
| | Ciprofloxacin 500mg bd unless on IV antibiotics. Start when neutophils <1.0. |
| | GCSF is not required to be given following ATG |

Discontinue antifungal and antibiotic prophylaxis when prednisolone has finished but continue if neuts < 0.5

### Immediate reactions to ATG

- Anaphylaxis should be managed according to the hospital protocol.
- Fevers, rigors and rashes are common but usually worse on the first day. They usually respond to extra doses of hydrocortisone and Piriton.
- Fluid retention and hypertension may also occur. It should be managed with IV frusemide.
- If fever occurs blood cultures must be taken and intravenous antibiotics given as per departmental protocol for neutropenic fever - *do not assume fever is due to the ATG*.

### Serum sickness

- This usually develops 7-14 days after starting treatment and is usually prevented by prednisolone.

- Clinical features are fever, rash, arthralgia, myalgia, nausea and vomiting, proteinuria, splenomegaly, lymphadenopathy and increased platelet dependence. The rash is classically serpiginous and palmar-plantar but may be maculopapular, urticarial or purpuric.
- Management is with hydrocortisone 100mg 6-hourly IV for 24-48 hours with continuation of oral prednisolone

**Dose modifications**

- For renal impairment - limited information – clinical decision
- For liver impairment - limited information - clinical decision

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| **Written by** | Dr PA Cahalin, Consultant Haematologist |
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