

PRODUCT MONOGRAPH

ATGAM* STERILE SOLUTION

(lymphocyte immune globulin, anti-thymocyte globulin [equine])

50 mg/mL

(For Intravenous Use Only)

Immunosuppressant

Pfizer Canada Inc
17,300 Trans-Canada Highway
Kirkland, Quebec H9J 2M5

Date of Approval:
September 1, 2004

Control No. 086555

* TM Pharmacia & Upjohn Company
Pfizer Canada Inc, Licensee
© Pfizer Canada Inc 2004

PRODUCT MONOGRAPH

ATGAM* STERILE SOLUTION

(lymphocyte immune globulin, anti-thymocyte globulin [equine])
50 mg/mL

Immunosuppressant

ACTION AND CLINICAL PHARMACOLOGY

ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]) is the purified concentrated, and sterile gamma globulin, primarily monomeric IgG, from hyperimmune plasma of horses immunized with human thymus lymphocytes.

ATGAM is a lymphocyte-selective immunosuppressant as is demonstrated by its ability to reduce the number of circulating, thymus-dependent lymphocytes that form rosettes with sheep erythrocytes. This antilymphocyte effect is believed to reflect an alteration of the function of the T-lymphocytes which are responsible in part for cell mediated immunity and are involved in humoral immunity. In addition to its antilymphocyte activity, ATGAM contains low concentrations of antibodies against other formed elements of the blood. In rhesus and cynomolgus monkeys, ATGAM reduces lymphocytes in the thymus-dependent areas of the spleen and lymph nodes. It also decreases the circulating sheep-erythrocyte-rosetting lymphocytes that can be detected, but ATGAM does not cause severe lymphopenia.

In general, when ATGAM is given with other immunosuppressive therapy, such as antimetabolites and corticosteroids, the patient's own antibody response to horse gamma globulin is minimal. In a small clinical study, ATGAM administered with other immunosuppressive therapy and measured as horse IgG had a serum half-life of 5.7 ± 3 days.

INDICATIONS AND CLINICAL USE

ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]) is indicated for any patient in whom reduction of peripheral T-lymphocyte function as measured by rosette-forming cell assay could be desirable.

- A. During controlled clinical trials, this immunosuppression has been demonstrated in renal allograft recipients treated with ATGAM. When administered with conventional therapy at the time of rejection, it increases the frequency of resolution of the acute rejection episode. The drug has also been administered as an adjunct to other immunosuppressive therapy to delay the onset of the first rejection episode.

- B. In non-controlled clinical studies, ATGAM has been administered to other patients in whom reduction of T-cell function could be desirable. They had aplastic anemia, T-cell malignancies, or graft-versus-host disease, or had received skin, cardiac, liver, or bone-marrow transplants. Anecdotal reports of benefit have been published, but to date controlled studies to establish safety and efficacy in circumstances other than renal transplantation have not been completed.

CONTRAINDICATIONS

ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]) should not be administered to a patient who has had a severe systemic reaction during prior administration of ATGAM or any other equine gamma globulin preparation.

WARNINGS

Only physicians experienced in immunosuppressive therapy and management of renal transplant patients should use ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]).

Patients receiving ATGAM should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources.

Treatment with ATGAM should be discontinued if any of the following occurs:

1. Anaphylaxis (see **ADVERSE REACTIONS**)
2. Severe and unremitting thrombocytopenia
3. Severe and unremitting leukopenia

This product is manufactured using components of human blood which may contain the causative agent of hepatitis and other viral diseases. Prescribed manufacturing procedures utilized in blood collection centres and the plasma testing laboratories are designed to reduce the risk of transmitting viral infection. However, the risk of viral infectivity from this product cannot be totally excluded.

PRECAUTIONS

Because ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]) is an immunosuppressive agent ordinarily given with corticosteroids and antimetabolites, patients should be monitored carefully for signs of leukopenia, thrombocytopenia or concurrent infection. If infection occurs, appropriate adjunctive therapy should be instituted promptly. The physician should decide whether or not to continue therapy with ATGAM depending on clinical circumstances.

Some studies have suggested an increase in the incidence of cytomegalovirus infection in patients receiving ATGAM. Some physicians have found that it may be possible to reduce this by decreasing the dosage of other immunosuppressive agents which might be administered concomitantly with ATGAM.

Dilution of ATGAM in dextrose infusion solution is not recommended, as low salt concentration may result in precipitation. The use of highly acidic infusion solutions is also not recommended because of possible physical instability over time.

Drug Interactions

When the dose of corticosteroids and other immunosuppressants is being reduced, some previously masked reactions to ATGAM may appear. Under these circumstances, observe patients especially carefully during therapy with ATGAM.

Use in obstetrics or in nursing mothers:

ATGAM has not been evaluated in either pregnant or lactating women.

Use in children:

Experience with children has been limited. ATGAM has been administered safely to a small number of pediatric renal, liver and bone marrow allograft recipients and aplastic anemia patients at dosage levels comparable to those in adults.

ADVERSE REACTIONS

The primary clinical experience with ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]) has been in renal allograft patients, who were also receiving concurrent standard immunosuppressive therapy (azathioprine, corticosteroids).

In controlled clinical trials, investigators have reported with an incidence greater than 5% the following adverse reactions; chills (14%), fever (33%), leukopenia (14%), thrombocytopenia (11%) and dermatological reactions such as pruritus, rash, urticaria, wheal and flare (12.5%).

In controlled clinical trials, investigators have reported with an incidence of 1 to 5% the following adverse reactions; arthralgia, chest and/or back pain, clotted A/V fistula, diarrhea, dyspnea, headache, hypotension, nausea and/or vomiting, night sweats, pain at the infusion site, peripheral thrombophlebitis and stomatitis.

The incidence of adverse reactions has been higher in patients being treated for aplastic anemia. Frequently reported adverse reactions among patients enrolled in aplastic anemia studies were arthralgia, chills, fever, skin rashes and thrombocytopenia. The high incidence of skin rashes and arthralgia was believed by investigators to represent serum sickness. In patients with aplastic anemia and other haematologic abnormalities who have received ATGAM, abnormal tests of liver function (SGOT, SGPT, alkaline phosphatase) and renal function (serum creatinine) have been observed. In some trials, clinical and laboratory findings of serum sickness have been seen in a majority of patients.

Other reactions reported in renal allograft or aplastic anemia patients receiving therapy have included: back pain, chest pain, clotted A/V fistula, diarrhea, dyspnea, headache, hypotension, nausea, night sweats, pain at the infusion site, peripheral thrombophlebitis, stomatitis and vomiting.

Reactions reported **rarely** have been: agitation, anaphylaxis, dizziness, edema, epigastric pain or hiccoughs, herpes simplex reactivation, hyperglycemia, hypertension, iliac vein obstruction, infection, laryngospasm, lymphadenopathy, malaise, paresthesia, periorbital edema, pleural effusions, possible encephalitis, proteinuria, pulmonary edema, renal artery thrombosis, seizure, tachycardia, toxic epidermal necrosis, weakness or faintness, and wound dehiscence.

Post Marketing Experience

During approximately five years of post-approval marketing experience, the frequency of adverse reactions in voluntarily reported cases is as follows; chills (16%), fever (51%), leukopenia (14%), rashes (27%), systemic infection (13%), thrombocytopenia (30%).

Events reported with a frequency of 5 to 10% include; abnormal renal function tests, arthralgia, chest, back or flank pain, diarrhea, dyspnea/apnea, nausea and/or vomiting and serum sickness-like symptoms.

Events reported with a frequency of < 5% include; abnormal involuntary movement or tremor, abnormal liver function tests, abdominal pain, acute renal failure, anaphylaxis, anemia, aplasia or pancytopenia, confusion or disorientation, cough, deep vein thrombosis, dizziness, edema, enlarged or ruptured kidney, eosinophilia, epigastric or stomach pain, faintness, GI bleeding or perforation, haemolysis or haemolytic anemia, headache, Herpes Simplex infection, hyperglycemia, hypertension, hypotension, localized infection, lymphadenopathy, malaise, myalgias or leg pains, neutropenia or granulocytopenia, nosebleed, pain, swelling or redness at infusion site, paresthesias, pulmonary edema or congestive heart failure, renal artery thrombosis, rigidity, seizures, sore mouth-throat, sweating, laryngospasm/edema, tachycardia, thrombophlebitis, vasculitis, and viral hepatitis.

The recommended management for some of the adverse reactions that could occur during treatment with ATGAM follows:

1. **ANAPHYLAXIS** is uncommon but serious and may occur during therapy with ATGAM. If this condition does occur, infusion of ATGAM should be discontinued immediately; 0.3 mL aqueous epinephrine (1:1,000 dilution) should be administered intramuscularly along with steroids.

Respiration should be assisted and other resuscitative measures provided. DO NOT resume therapy with ATGAM.

2. **HAEMOLYSIS** can usually be detected only in the laboratory. Fulminant haemolysis has been reported rarely. Appropriate treatment of haemolysis often includes transfusion of erythrocytes; if necessary, administer intravenous mannitol, furosemide, sodium bicarbonate, and fluids. Severe and unremitting haemolysis may necessitate discontinuation of therapy with ATGAM.
3. **THROMBOCYTOPENIA AND LEUKOPENIA** are usually transient. Platelet and white cell counts generally return to adequate levels without interrupting therapy and without transfusions. If thrombocytopenia and leukopenia become severe, it may be helpful to decrease the dose of concomitant immunosuppressant (particularly azathioprine). If after one or two days the situation does not improve, the dose of ATGAM may also be reduced. (see **WARNINGS**)
4. **RESPIRATORY DISTRESS** may indicate an anaphylactoid reaction. Infusion of ATGAM should be discontinued. If distress persists, antihistamine, epinephrine, corticosteroid, or some combination of the three should be administered.
5. **PAIN IN CHEST, FLANK OR BACK** may indicate anaphylaxis or haemolysis. Treatment is the same as for respiratory distress or, if haemolysis has occurred, the same as listed in (2) above.
6. **HYPOTENSION** may indicate anaphylaxis. Infusion of ATGAM should be discontinued and blood pressure stabilized with pressors if necessary.
7. **CHILLS AND FEVER** occur frequently in patients receiving ATGAM. ATGAM may release endogenous leukocyte pyrogens. Prophylactic and/or therapeutic administration of antihistamines, or corticosteroids generally controls this reaction.
8. **CHEMICAL PHLEBITIS** can be caused by infusion of ATGAM through peripheral veins. This often can be avoided by administering the infusion solution into a high-flow vein. A subcutaneous arterialized vein produced by a Brescia fistula is also a useful administration site.

9. **ITCHING AND ERYTHEMA** probably result from the effect of ATGAM on blood elements. Antihistamines generally control the symptoms.
10. **SERUM SICKNESS-LIKE SYMPTOMS** in aplastic anemia patients that have been treated with oral and IV corticosteroids. Resolution of symptoms has generally been prompt and long-term sequelae have not been observed. Prophylactic administration of corticosteroids may decrease the frequency of this reaction.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Because of its mode of action and because it is a biologic substance, the maximum tolerated dose of ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]) would be expected to vary from patient to patient. To date, the largest single daily dose administered to a patient (renal transplant recipient) was 7,000 mg administered at a concentration of approximately 10 mg/mL of saline, seven times the recommended total dose and infusion concentration. In this patient, the administration of ATGAM was not associated with any signs of acute intoxication or late sequelae.

The greatest number of doses (10 to 20 mg/kg/dose) that can be administered to a single patient has not yet been determined. Some renal transplant patients have received up to 50 doses in 4 months, and others have received 28-day courses of 21 doses followed by as many as 3 more courses for the treatment of acute rejection. The incidence of toxicologic manifestations did not increase with any of these regimens.

DOSAGE AND ADMINISTRATION

1. **Renal-Allograft Recipients**

Adult renal allograft patients have received ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]) at the dose of 10 to 30 mg/kg of body weight daily. The few children studied received 5 to 25 mg/kg daily. ATGAM has been used to delay the onset of the first rejection episode^{5,9,19,27} and at the time of the first rejection episode^{7,14,18,21,25}. Most patients who received ATGAM for the treatment of acute rejection had not received it starting at the time of transplantation.

Usually, ATGAM is used concomitantly with azathioprine and corticosteroids, which are commonly used to suppress the immune response. Exercise caution during repeat courses of ATGAM; carefully observe patients for signs of allergic reactions.

Delaying the Onset of Allograft Rejection: The recommended dose is 15 mg/kg daily for 14 days, then every other day for 14 days for a total of 21 doses in 28 days. The first dose should be administered within 24 hours before or after the transplant.

Treatment of Rejection: The first ATGAM dose can be delayed until the diagnosis of the first rejection episode. The recommended dose is 10 to 15 mg/kg daily for 14 days. Additional alternate-day therapy up to a total of 21 doses can be given.

2. **Other Allograft Recipients**

ATGAM has been used in liver transplant recipients²⁶ at daily doses of 8 to 15 mg/kg. The duration of therapy averaged 13 days. In heart transplant patients,^{13,16,23} intermittent daily doses average 8 mg/kg (range: 5 to 11 mg/kg, duration of therapy averaged four months, and the number of doses averaged 29 (range: 7 to 49). In burn patients who have received temporary skin allografts,^{3,4,8} ATGAM dosage ranged from 10 to 15 mg/kg for up to 24 doses. All patients received the first ATGAM dose in the 24-hour period immediately before or after the surgical procedure.

3. **Bone Marrow Transplantation**

Several different ATGAM dosage regimens have been used in patients receiving bone marrow transplants.^{17,20,28,29} Generally patients received ATGAM 7 to 20 mg/kg for 3 to 14 doses. The first dose was given 9 days before transplant for pre-conditioning, 7 to 30 days after transplant for prophylaxis of graft-versus-host disease or when graft-versus-host disease was diagnosed.

4. **Aplastic Anemia**

Patients with aplastic anemia,^{1,2,6,7,10,11,24} have received ATGAM in several regimens, generally 10 to 20 mg/kg for 8 to 21 doses.

5. **Other Indications**

ATGAM has also been used in patients with Sezary syndrome, T-cell leukemia,^{12,15} and nephrotic syndrome. Although some patients have received multiple high doses intermittently over long periods, a standard dosage regimen has not been established.

PREPARATION AND ADMINISTRATION

1. **Skin Testing**

Before the first intravenous infusion of ATGAM, it is **strongly** recommended that skin testing potential recipients take place before commencing treatment. First the patient should receive an epicutaneous (prick) testing with undiluted ATGAM. If a wheal does not develop 10 minutes after pricking, then proceed to intradermal testing with 0.02 mL of a 1:1000 v/v saline dilution of ATGAM with a separate saline control injection of similar volume. After 10 minutes read the results. A wheal at the ATGAM site of 3 mm or larger in diameter compared to the saline control site suggests clinical sensitivity and an increased possibility of a systemic allergic reaction.

Where an ATGAM skin test causes a locally positive reaction, serious consideration should be given to alternative forms of therapy. The risk to benefit ratio must be carefully weighed. If therapy with ATGAM is deemed appropriate following a locally positive skin test, treatment should be administered in a setting where intensive life support facilities are immediately available and a physician familiar with the treatment of potentially life threatening allergic reactions is in attendance.

A systemic reaction such as generalized rash, tachycardia, dyspnea, hypotension, or anaphylaxis precludes an additional administration of ATGAM.

NOTE: The predictive value of this test has not been clinically proven. Allergic reactions to ATGAM can occur in the presence of a negative skin test. Also, as described above, skin testing will not predict for later development of serum sickness. See **WARNINGS, PRECAUTIONS** and **ADVERSE REACTIONS**.

2. **Infusion Instructions**

- (i) Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Because ATGAM is a gamma globulin product, it can be transparent to slightly opalescent, colourless to faintly pink or brown, and may develop a slight granular or flaky deposit

during storage. ATGAM (diluted or undiluted) should not be shaken because excessive foaming and/or denaturation of the protein may occur.

- (ii) ATGAM should be diluted for intravenous infusion in an inverted bottle of sterile vehicle, so that the undiluted ATGAM does not contact the air inside. Add the total daily dose of ATGAM to the sterile vehicle, with a concentration not exceeding 4 mg of ATGAM Sterile Solution per mL. The diluted solution should be gently rotated or swirled to effect complete mixing. Once diluted, ATGAM has been shown to be physically and chemically stable for up to 24 hours at concentration of up to 4 mg per mL in the following diluents:

- 0.9% Sodium Chloride Injection

- 5% Dextrose and 0.225% Sodium Chloride Injection

- 5% Dextrose and 0.45% Sodium Chloride Injection

Adding ATGAM to dextrose injection is not recommended, as low salt concentrations can cause precipitation. Highly acidic infusion solutions can also contribute to physical instability over time.

- (iii) ATGAM should not be kept in a diluted form for more than 24 hours (including actual infusion time). It is recommended that diluted ATGAM be stored in a refrigerator if it is prepared prior to time of infusion. The diluted ATGAM solution should be allowed to reach room temperature before infusion.
- (iv) During the clinical trials, most investigators chose to infuse ATGAM into a vascular shunt, arterial venous fistula, or a high-flow central vein through an in-line filter with a pore size of 0.2 to 1.0 micron. The in-line filter should be used with all intravenous infusions to prevent the inadvertent administration of any insoluble material that may develop in the product during storage.
- (v) Using high-flow veins will minimize the occurrence of phlebitis and thrombosis.
- (vi) Do not infuse a dose of ATGAM in less than 4 hours.
- (vii) Always keep a tray containing epinephrine, antihistamines, corticosteroids, syringes, and an airway at the patient's bedside while ATGAM is being administered.
- (viii) Observe the patient continuously for possible allergic reactions throughout the infusion (see **ADVERSE REACTIONS**).

PHARMACEUTICAL INFORMATION

International non-proprietary name (INN): Lymphocyte Immune Globulin, Anti-thymocyte Globulin [Equine]

Molecular weight: The molecular weight as determined by electrophoresis is approximately 150,000.

Description: Lymphocyte immune globulin, anti-thymocyte globulin [equine] is a purified, concentrated and sterile gamma globulin, primarily monomeric IgG, from hyperimmune serum of horses immunized with human thymus lymphocytes.

Composition: Each mL of ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]) contains 50 mg of horse gamma globulin stabilized in 0.3 molar glycine to a pH of approximately 6.8.

Stability and Storage Recommendations: Store ATGAM ampoules in the refrigerator at 2° to 8°C.

DO NOT FREEZE. Protect the ampoules from light by storing in the carton.

Parenteral Products: ATGAM can be diluted to a concentration of up to 4 mg/mL using the following diluents;

0.9% Sodium Chloride Injection, 5% Dextrose and 0.225% Sodium Chloride Injection,
5% Dextrose and 0.45% Sodium Chloride Injection.

The diluted solution is stable for up to 24 hours if stored in a refrigerator. Allow the diluted ATGAM solution to reach room temperature before infusion. ATGAM is appropriately administered into a vascular shunt, arterial venous fistula, or a high-flow central vein through an in-line filter with a pore size of 0.2 to 1.0 micron. The in-line filter should be used with all infusions of ATGAM to prevent the administration of any insoluble material that may develop in the product during storage. The use of high-flow veins will minimize the occurrence of phlebitis and thrombosis. Do not infuse a dose of ATGAM in less than 4 hours. Adding ATGAM to dextrose injection is not recommended, as low salt concentrations can cause precipitation. Highly acidic infusion solutions can also contribute to physical instability over time.

AVAILABILITY OF DOSAGE FORMS

ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]) is supplied in cartons of 5 X 5 mL ampoules containing 250 mg protein per ampoule. Each mL of ATGAM contains 50 mg of horse gamma globulin.

PHARMACOLOGY

ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]) is a transparent to slightly opalescent aqueous protein solution, colourless to light brown, and nearly odourless. It may develop a slight granular or flaky deposit during storage. (For information about in-line filters, see Infusion Instructions.)

Before release for clinical use, each lot of ATGAM is tested to assure its ability to inhibit rosette formation between human peripheral lymphocytes and sheep red blood cells in vitro. In each lot, antibody activity against human red blood cells and platelets is also measured and determined to be within acceptable limits. Only lots that test negative for anti-human serum protein antibody, antiglomerular basement membrane antibody and pyrogens are released.

ANIMAL TOXICOLOGY

In the development of ATGAM (lymphocyte immune globulin, anti-thymocyte globulin [equine]) aliquots of the various clinical lots have been infused intravenously to either Macaca rhesus or Macaca irus monkeys. Two dosage regimens have been used: 100 mg/kg on day 0, 200 mg/kg on day 2, and 400 mg/kg on day 4 or, currently, 50 mg/kg on days 0, 2, 4 and 7. A three-week observation period has followed that last infusion in either dosage regimen.

The observed changes could have been anticipated on the basis of the antilymphocyte activity of ATGAM. Within 24 hours after infusion, decreased peripheral blood lymphocytes and increased total leukocyte and neutrophil counts occurred. Decreased thymus size with involution or atrophy or both and decreased lymphocyte populations in the thymus-dependent areas of the spleen and lymph nodes were noted. The atrophy was most prevalent in animals that received the higher doses.

In animals receiving either dosage regimen, packed cell volume, total erythrocyte counts, and haemoglobin concentrations have decreased and reticulocytes and nucleated erythrocytes have increased enough to be classified an anemia.

An occasional death believed to have resulted from anemia has occurred. Transient decreases in blood platelet counts have also occurred. Thrombus formation occurred frequently along the route of infusion, i.e., the saphenous and femoral veins. However, the incidence of thrombi has decreased since in-line filters have been used during infusion. In these animals no evidence of DIC (disseminated intravascular coagulation) has appeared.

REFERENCES

1. Amare M, Abdou NL, Robinson MG, Abdou NI. Aplastic anemia (AA) associated with bone marrow suppressor T-cell hyperactivity: Successful treatment with antithymocyte globulin (ATG). *Am J Hematol* 1978;5:25-32.
2. Bukowski RM, Hewlett JS, Hoffman GC, Rothman Hamburger SA. Antithymocyte globulin (ATG) therapy of severe aplastic anemia (AA). *Meet Abstr Blood* 1978;52(suppl 1):77.
3. Burke JF, Quinby WC, Bondoc CC. Early excision and prompt wound closure supplemented with immunosuppression. *Surg Clin North Am* 1978;58:1141-50.
4. Burke JF, Quinby WC, Bondoc CC, Cosimi AB, Russell PS, Szyfelbein SK. Immunosuppression and temporary skin transplantation in the treatment of massive third degree burns. *Ann Surg* 1975;182:183-97.
5. Butt KMH, Zielinski CM, Parsa I, Elberg AJ, Wechter WJ, Kountz SK. Trends in immunosuppression for kidney transplantation. *Kidney Int* 1978;13(suppl 8):S95-8.
6. Champlin R, Gale RP. Antithymocyte globulin (ATG) treatment of aplastic anemia (AA) -- a randomized controlled study. *Meet Abstr Blood* 1981;58(5)(suppl 1):40.
7. Cosimi AB. The clinical value of antilymphocyte antibodies. *Transplant Proc* 1981;13(1):462-8.
8. Cosimi AB, Burke JF, Russell PS. Transplantation of skin. *Surg Clin North Am* 1978;58:435-51.
9. Cosimi AB, Wortis HH, Delmonico FL, Russell PS. Randomized clinical trial of antithymocyte globulin in cadaver renal allograft recipients: Importance of T cell monitoring. *Surgery* 1976;80:155-63.
10. Doney KC, Torok-Storb B, Buckner CD, Weiden P, Storb R. Treatment of aplastic anemia (AA) with antithymocyte globulin (ATG) and androgens with or without mismatched bone marrow infusion. *Meet Abstr Blood* 1981;58(5)(suppl 1):40.
11. Doney KC, Weiden PL, Buckner CD, Storb R, Thomas ED. Treatment of severe aplastic anemia using antithymocyte globulin with or without an infusion of HCA haploidentical marrow. *Exp Hematol* 1981;9(8):829-34.
12. Edelson RL, Raafat J, Berger CL, Grossman M, Troyer C, Hardy M. Antithymocyte globulin in the management of cutaneous T-cell lymphoma. *Cancer Treat Rep* 1979;63:675-80.
13. English TAH, Cooper DKC, Cory-Pearce R. Recent experience with heart transplantation. *Br Med J* 1980;281:699-702.
14. Filo RS, Smith EJ, Leapman SB. Reversal of acute renal allograft rejection with adjunctive ATG therapy. *Transplant Proc* 1981;13(1):482-90.

15. Fisher RI, Kubota TT, Mandell GL, Broder S, Young RC. Regression of a T-cell lymphoma after administration of antithymocyte globulin. *Ann Intern Med* 1978;88:799-800.
16. Greipp RB, Stinson EB, Dong E Jr, Phillips RC, Morrell RM, Shumway NE. Use of antithymocyte globulin in human heart transplantation. *Circulation* 1972;45(suppl 1):147-53.
17. Gengozian N, Edward CL, Vodopick HA, Huebner RF. Bone marrow transplantation in a leukemic patient following immunosuppression with antithymocyte globulin and total body irradiation. *Transplantation* 1973;15:446-54.
18. Hardy MA, Nowygrod R, Elberg A, Appel G. Use of ATG in treatment of steroid-resistant rejection. *Transplantation* 1980;29:162-4.
19. Kountz SL, Butt KHM, Rao TKS, Zielinski CM, Rafi M, Schultz Jr. Antithymocyte globulin (ATG) dosage and graft survival in renal transplantation. *Transplant Proc* 1977;9:1023-5.
20. Meuwissen HJ, Moore EC, Strauss HS, Taft E, Britten A. Successful retransplantation of bone marrow following failure of initial engraftment in a patient with aplastic anemia. *J Pediatr* 1976;89:588-92.
21. Nowygrod R, Appel G, Hardy M. Use of ATG for reversal of acute allograft rejection. *Transplant Proc* 1981;13(1):469-72.
22. Pass RF, Whitley RJ, Drethelm AG, et al. Cytomegalovirus infection in patients with renal transplant: Potentiation by antithymocyte globulin and an incompatible graft. *J Infect Dis* 1980;142:9-17.
23. Reemtsma K, Bregman D, Drusin R, Dobelle W, Edie R, Hardy MA. Cardiac transplantation for patients requiring mechanical circulatory support. *N Engl J Med* 1978;298:670-1.
24. Shadduck RK, Winkelstein A, Zeigler A, et al. Aplastic anemia following infectious mononucleosis: Possible immune etiology. *Exp Hematol* 1979;7:264-71.
25. Shield CH, Cosimi AB, Tolkoff-Rubin N, Rubin R, Herrin J, Russell PS. Use of antithymocyte globulin for reversal of acute allograft rejection. *Transplantation* 1979;28(6):461-4.
26. Starzl TE, Koep LJ, Halgrimson CG, et al. Liver transplantation 1978. *Transplant Proc II* 1979;:240-6.
27. Wechter WJ, Brodie JA, Morrell RM, Rafi M, Schultz Jr. Antithymocyte globulin (ATGAM) in renal allograft recipients. *Transplantation* 1979;28(4):294-302.
28. Weiden PL, Doney K, Storb R, Thomas ED. Antihuman thymocyte globulin (ATG) for prophylaxis and treatment of graft-versus host disease in recipients of allogenic marrow grafts. *Transplant Proc* 1978;10:213-6.
29. Weiden PL, Doney K, Storb R, Thomas ED. Antihuman thymocyte globulin for prophylaxis of graft-versus-host disease. *Transplantation* 1979;27:227-30.