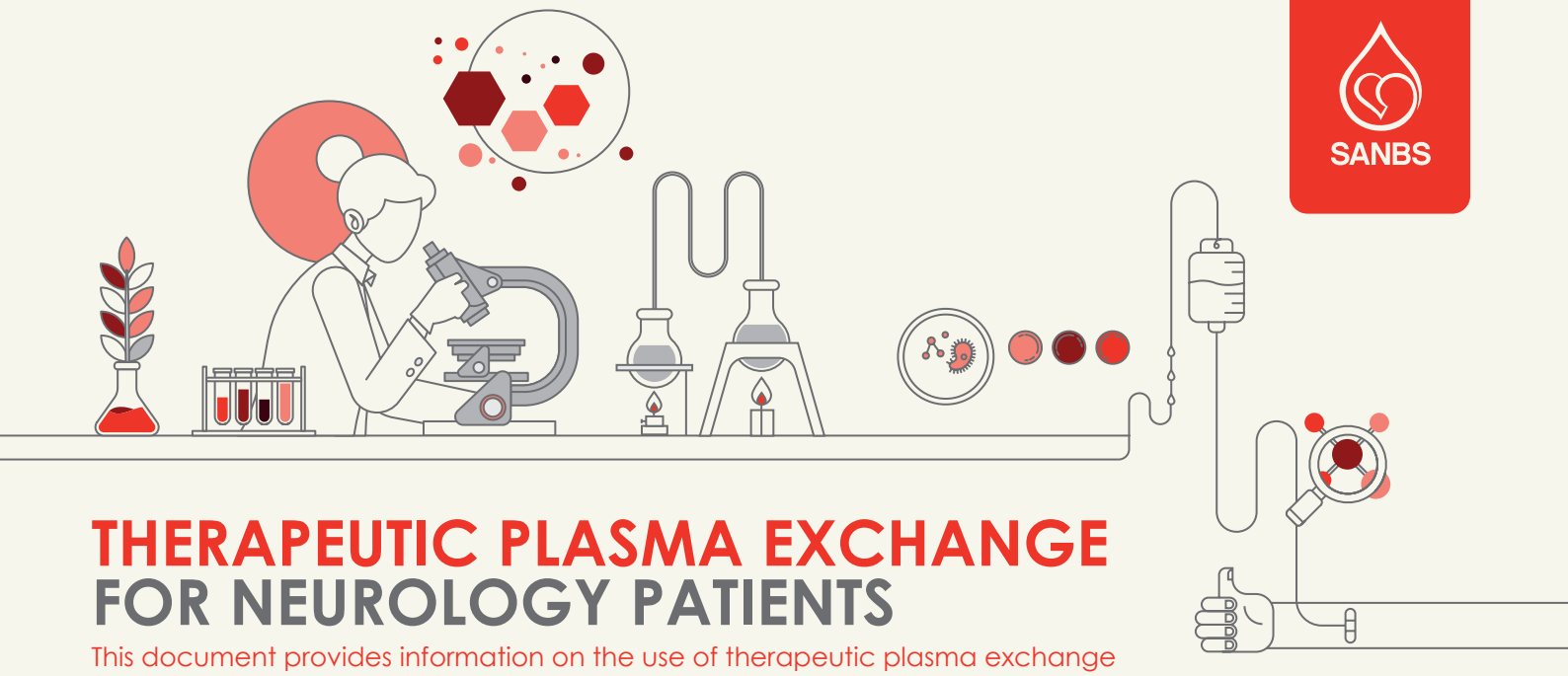

THERAPEUTIC PLASMA EXCHANGE FOR NEUROLOGY PATIENTS

This document provides information on the use of therapeutic plasma exchange (TPE) for patients suffering from a variety of neurological conditions. In addition, it gives information on specialised clinical apheresis services provided by the South African National Blood Service (SANBS) and how to refer your patient for treatment.

OVERVIEW

SANBS Specialised Therapeutic Services (STS) provides life-saving clinical apheresis services for a range of clinical specialities including haematology, neurology, oncology and nephrology, to adult and paediatric patients in private and public hospitals across eight provinces in South Africa. Our team comprises more than 25 staff which includes therapeutic nursing specialists, a quality team, administrative staff and specialist doctors. Patients are treated by our internationally certified therapeutic specialists, at the hospital bedside or at our base of operation in Parktown, Gauteng. SANBS services in excess of 2000 therapeutic plasma exchange patients annually.

We offer:

- A flexible and responsive service 365 days per year to both public and private patients
- Experienced medical, technical and logistic teams
- A robust quality management system
- A comprehensive range of therapies including therapeutic plasma exchange, leucopheresis, stem cell collection, thrombocytapheresis and red cell exchange

THERAPEUTIC PLASMA EXCHANGE –THE DETAILS

During a TPE procedure whole blood is removed from the patient. The plasma is separated out from the rest of the blood using a cell separator machine and the red cells, white cells and platelets are returned to the patient. In this way any disease causing substances in the plasma are removed. A plasma replacement fluid is given to the patient too, to compensate for the plasma that has been removed. Citrate, an anticoagulant, is added to the extra corporeal circulation to prevent clotting.

Replacement fluid:

The fluid used to replace the removed plasma is usually human albumin for neurological conditions and fresh frozen plasma (FFPs) for haematological conditions. TPE removes coagulation factors with the plasma, therefore when albumin is used as a replacement fluid, monitoring of coagulation factors is required. American Society for Apheresis (ASFA) guidelines recommend INR, PTT and fibrinogen testing prior to the first TPE procedure and on alternate days thereafter. When coagulation abnormalities are present, FFP, cryo-poor plasma and/or cryoprecipitate may be added to the albumin replacement.

Vascular access:

Good venous access is essential for all TPE procedures to ensure continuous blood flow to and from cell separator machine. Peripheral vein access may be used where appropriate, however when peripheral veins cannot support the required blood flow rates (especially when multiple procedures are necessary), central venous access will be required. Our staff are available to perform a vein assessment and guide you on the appropriate venous access for your patient.

AMERICAN SOCIETY FOR APHERESIS (ASFA) GUIDELINES

The American Society for Apheresis (ASFA) publishes evidence-based guidelines for the use TPE which are updated every three years (the 8th edition is available at: https://www.ammtac.org/docs/articulos/ASFA%202019%20guidelines.pdf). These guidelines provide recommendations on the level of evidence, frequency and number of treatments and replacement fluids to be used for each condition. All conditions are categorised as level I-IV namely:

- I - apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment;
- II - apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment;
- III - Optimum role of apheresis therapy is not established and decision making should be individualized;
- IV - published evidence demonstrates or suggests apheresis to be ineffective or harmful.

SANBS uses these guidelines to prioritise patient referrals and to guide treatment plans.

sanbs.org.za
Toll free: 0800 11 90 31

NEUROLOGICAL INDICATIONS FOR THERAPEUTIC PLASMA EXCHANGE

Disease	Indication	Notes
1. Acute inflammatory demyelinating polyradiculo-neuropathy (Guillain Barré syndrome)	**ASFA category I (first line therapy)**	ASFA 2019 categorises TPE for GBS as a category I criteria (first line therapy) as it removes circulating autoimmune antibodies which are damaging to the peripheral nerve myelin. Several randomised controlled trials comparing plasma exchange to supportive care alone have shown that TPE can accelerate motor recovery, decrease time on the ventilator, and speed attainment of other clinical milestones. TPE has beneficial effect in severely and mildly affected individuals, with a significantly increased proportion of patients able to walk after four weeks. Studies have shown equal efficacy of TPE and IVIG as treatment options in severe disease however TPE was found to be more cost-effective in certain settings. An average of 5-6 TPE procedures over 10-14 days are usually required. SANBS performs almost 100 TPE procedures per year for GBS patients.
2. Myasthenia Gravis (MG)	Acute short-term treatment: **ASFA category I (first line therapy)** Long term treatment in chronic disease: **ASFA category II (second line therapy)**	In MG, ASFA 2019 categorises TPE for acute short-term treatment (moderate-severe disease including myasthenic crisis, unstable or refractory disease, unstable disease activity pre-thymectomy) as a category I criteria (first line therapy) and as a category II criteria (second line therapy) for long-term treatment in chronic disease. There are three major mechanisms of action for TPE in MG: immediate intravascular reduction of autoantibody concentration, pulsed induction of antibody redistribution, and subsequent immunomodulatory changes. TPE works rapidly; clinical effects can be apparent within 24 hours but may take up to a week. In therapy refractory patients TPE may represent an option for long-term management of MG. IVIG and TPE are regarded as equally effective in treating severe MG. The number of TPE procedures depends on the clinical scenario. In acute attack, relapse or unstable disease, 3-6 treatments over 10-14 days are usually required. For chronic treatment, weekly to bi-weekly individually adjusted procedures may be performed. SANBS performs in excess of 50 TPE procedures a year for patients with MG.
3. Chronic Inflammatory Demyelinating Polyradiculo-neuropathy (CIDP)	**ASFA category I (first line therapy)**	ASFA 2019 categorises TPE for CIPD as a category I criteria (first line therapy). There are 3 first-line treatment options: intravenous or oral corticosteroids, which are commonly used, IVIG, or TPE with evidence from randomised controlled trials in favour of IVIG or TPE. TPE is used to remove circulating auto antibodies but therapies need to be initiated early to stop the inflammatory demyelination and prevent secondary axonal degeneration and therefore permanent disability. TPE provides short-term benefit, but rapid deterioration may occur afterwards. This may necessitate maintenance treatment, with repeated TPE and/or other immunomodulation therapies, with frequency tailored to symptoms and tolerability of the individual patient. TPE is usually performed 2-3 times per week until clinical improvement is achieved and then tapered to weekly or monthly. SANBS performs 30-40 TPE procedures per year for patients with CIPD.
4. N-METHYL-D-ASPARTATE RECEPTOR (NMDAR)-Encephalitis	**ASFA category I (first line therapy)**	ASFA 2019 categorises TPE for NMDAR-encephalitis as a category I criteria (first line therapy). First-line therapy includes high dose corticosteroids, IVIG or TPE, and a search for potential underlying tumour (with teratoma excision if present). TPE removes the pathophysiologically relevant antibody and acts an adjunct to immuno-therapy for suppressing active inflammation and antibody production. There is a substantial percentage of patients with NMDAR encephalitis who do not respond to TPE, however TPE remains among the treatment options and is included in the treatment recommendations from the German Network for Research on Autoimmune Encephalitis. An average of 5-12 TPE treatments over 1-3 weeks with individually adjusted number of and intervals between treatments is usually performed.
5. Neuro Myelitis Optica Spectrum Disorders (NMOSD)	Acute attack/ relapse: **ASFA category II (second line therapy)** Maintenance: **ASFA category III (optimum role of apheresis therapy is not established and decision-making should be individualized)**	ASFA 2019 categorises TPE for acute/ relapsing NMOSD as a category II criteria (TPE is a second line therapy). Several case reports have shown TPE benefits in corticosteroid-refractory NMOSD exacerbation, with 50–70% of patients showing improvement (in conjunction with steroids). Prompt initiation of TPE is a strong predictor of beneficial outcome in severe attacks of NMOSD; for every day delay in therapy initiation, the odds of achieving complete remission are reduced by 6.3%. TPE should begin within 5 days of symptom onset and be performed daily or on alternate days for an average of 5 procedures (range 2-20 procedures), depending on clinical response. TPE may be beneficial as a chronic treatment for the prevention of NMOSD relapse in select patients (category III criteria). SANBS performs over 120 TPE procedures per year for patients with NMOSD.
6. Multiple Sclerosis	Acute/ relapsing: **ASFA category II (second line therapy)** Chronic: **ASFA category III (optimum role of apheresis therapy is not established and decision-making should be individualized)**	ASFA 2019 categorises TPE for MS as a category II criteria (second line therapy) for acute / relapsing MS and category III (optimum role of apheresis therapy is not established and decision-making should be individual-ized) for chronic MS. TPE may benefit MS patients through the immediate removal of plasma antibodies and immune complexes, induction of a redistribution of antibodies from the extravascular space, and subsequent immunomodulatory changes. An increasing number of disease-modifying medications have become available in recent years which reduce the likelihood of the development of new white-matter lesions, clinical relapses, and stepwise accumulation of disability. Standard treatment for clinically isolated syndrome (CIS), or acute MS attacks or relapses in adult and paediatric patients without change is intravenous administration of high dose steroids. If patients are unresponsive, which occurs in 20-25%, a second steroid pulse in combination with TPE is recommended after an interval of 10-14 days. TPE is regarded as ineffective for the chronic phase of PPMS/SPMS (Primary progressive multiple sclerosis / Secondary progressive multiple sclerosis) based upon results of several RCTs. TPE has been used for drug removal in MS patients treated with natalizumab who developed progressive multifocal leukoencephalopathy. In acute attack/relapse cases, unresponsive to steroids, 5-7 TPE procedures over 10-14 days is recommended with a response rate of >50%. Early initiation of therapy, within 14-20 days of symptom onset, is a predictor of response. However, response has still been shown in patients treated 60 days after the onset of symptoms.
7. Acute Transverse Myelitis	Unclassified	TPE for the treatment of acute transverse myelitis is not categorised in the ASFA 2019 guidelines but is often used in patients with moderate to aggressive forms who do not improve with intravenous and oral steroids [1]. Although no clinical trial has proven TPE effectiveness, benefit has been shown in retrospective studies of patients with transverse myelitis who received IV steroids followed by TPE. Particular benefit has been shown when started within the acute or subacute stage of the myelitis or in those patients who exhibit active inflammation on MRI. SANBS performs approximately ten TPE procedures per year for patients with transverse myelitis.

How to refer patients for Therapeutic Plasma Exchange treatment

If you wish to refer a patient for Plasma Exchange please contact us on 082-555-9294. We aim to perform the first procedure within 20 hours from first call unless requested otherwise by the treating doctor.

Referral Pathway for Plasma Exchange Therapy

The staff member receiving the call will guide you as to what is required in order to complete a safe and successful TPE.

This will include the following to be available prior to the procedure:

1. SANBS TPE Request Form, FRM-STS-049 and the link https://sanbs.org.za/specialised-services/
2. SANBS TPE Consent Form, FRM-STS-048 and the link https://sanbs.org.za/specialised-services/ signed by patient/legal guardian or clinician (where necessary)

*Note: SANBS is not allowed to perform any procedure without these completed, signed documents

3. Patent venous access
4. Blood results, e.g. FBC, CMP and U&E.
5. Availability of emergency equipment and medication (e.g. oxygen, adrenalin, phenergan, solu-cortef, calcium gluconate, etc.) if required during an adverse event.

At SANBS, it is our mission to reliably provide trusted blood products and services to all patients at a world class level of cost and quality. We look forward to assisting you with all your clinical apheresis requirements. Please contact us for any queries, referrals or general information. We can be reached on 082 555 9294 or therapeutics2@sanbs.org.za for any queries or to make a booking.

1. Noland DK, Greenberg BM. Safety and efficacy of plasma exchange in pediatric transverse myelitis. Neurol Clin Pract 2018; 8(4): 327-30.