The pH of stored blood ranges from 6.80 to 6.22 and may exceed a maximum of 6.4. Tromethamine effectively corrects this acidity. Tham Solution may be added directly to the blood used to prime the pump-oxygenator. When ACD blood is brought to a normal pH range the blood appears in the urine after eight hours.Urinary excretion of bicarbonate continues over a period of three days.

INDICATIONS AND USAGE
Tham Solution (tromethamine injection) is indicated for the prevention and correction of severe metabolic acidosis. In the following conditions it may help to sustain vital functions and thus provide time for treatment of the primary disease:

1. Metabolic Acidosis Associated with Cardiac Bypass Surgery.

Tham Solution has been found to be primarily beneficial in correcting metabolic acidosis which may occur during or immediately following cardiac bypass surgical procedures.


It is well known that ACD blood is acidic and becomes more acidic on storage. Tromethamine effectively corrects this acidity. Tham Solution may be added directly to the blood used to prime the pump-oxygenator. Tromethamine may be indicated during cardiac bypass surgery should metabolic acidosis appear.

3. Metabolic Acidosis Associated with Cardiac Arrest.

Acidosis is nearly always one of the consequences of cardiac arrest and, in some instances, may even be a causative factor in arrest. It is important therefore, that the correction of acidosis should be started promptly.
1. Large doses of Tham Solution may depress ventilation, as a result of increased blood pH and reduced CO₂ concentration. Thus, dosage should be adjusted so that blood pH is not allowed to increase above normal. In situations in which respiratory acidosis may be present concomitantly with metabolic acidosis, the drug may be used with mechanical assistance to ventilation.

2. Care must be exercised to prevent perivascular infiltration since this can cause inflammation, necrosis and sloughing of tissue. Venospasm and intravenous thrombosis, which may occur during infusion, can be avoided by minimizing by insuring that the injection needle is well within the largest available vein and that solutions are slowly infused. Intravenous catheters are recommended. If perivascular infiltration occurs, institute appropriate countermeasures. See ADVERSE REACTIONS.

3. Tham Solution (tromethamine injection) should be administered slowly and in amounts sufficient only to correct the existing acidosis, and to avoid overdosage and alkalosis. Overdosage in terms of total drug and/or too rapid administration, may cause hypoglycemia of a prolonged duration (several hours). Therefore, frequent blood glucose determinations should be made during and after therapy.

4. Extreme care should be exercised in patients with renal disease or reduced urinary output because of potential hypernatremia and the possibility of a decreased excretion of tromethamine. In such patients, the drug should be used cautiously with electrocardiographic monitoring and frequent serum potassium determinations.

5. Because clinical experience has been limited generally to short-term use, the drug should not be administered for a period of one day except in a life-threatening situation.

The intravenous administration of Tham Solution can cause fluid and/or solute overriding resulting in dilution of serum electrolyte concentrations, overhydration, congested states or pulmonary edema.

Admixtures may be incompatible. Consult with pharmacists, if available. When introducing additives, use aseptic technique, mix thoroughly and do not store.

PRECAUTIONS

1. Blood pH, P CO₂, bicarbonate, glucose and electrolyte determinations should be performed before, during and after administration of Tham Solution.

2. While it has not been shown that the drug increases exsanguination time in humans, this possibility should be kept in mind since this has been noted experimentally in dogs. Do not administer unless solution is clear and seal is intact. Discard unused portion.

3. Pregnancy Category C: Animal reproduction studies have not been conducted with tromethamine. It is also not known whether tromethamine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Tromethamine should be given to a pregnant woman only if clearly needed.

4. Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when THAM Solution is administered to a nursing mother.

5. Carcinogenesis, Mutagenesis, Impairment of Fertility: Studies with THAM Solution have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility.

6. Pediatric Use: The safety and effectiveness of THAM Solution in pediatric patients is based on over 30 years of clinical experience documented in the literature and on safety surveillance. THAM Solution has been used to treat severe cases of metabolic acidosis with concurrent respiratory acidosis because it does not raise P CO₂ in bicarbonate does in neonates and infants with respiratory failure. It has also been used in neonates and infants with hypernatremia and metabolic acidosis to avoid the additional sodium given with the bicarbonate. However, because the osmotic effects of THAM Solution are greater and large continuous doses are required, bicarbonate is preferred to THAM Solution in the treatment of acidic neonates and infants with RDS. Hypoglycemia may occur when this product is used in premature and even full-term neonates. See WARNINGS and ADVERSE REACTIONS.

GERIATRIC USE: Clinical studies of Tham solution did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in response between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

ADVERSE REACTIONS

Generally, side effects have been infrequent.

Respiratory: Although the incidence of ventilatory depression is low, it is important to keep in mind that such depression may occur. Respiratory depression may be more likely to occur in patients who have chronic hypventilation or those who have been treated with drugs which depress respiration. In patients with associated respiratory acidosis, tromethamine should be administered with mechanical assistance to ventilation.

Vascular: Extreme care should be taken to avoid perivascular infiltration. Local tissue damage and subsequent sloughing may occur if extravasation occurs. Chemical phlebitis and venospasm also have been reported.

Hematologic: Transient depression of blood glucose may occur.

Hepatic: Infusion via low-lying umbilical venous catheters has been associated with hepatic necrosis. Reactions which may occur because of the solution or the technique of administration include febrile response, infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection extravasation and hypervolemia. If an adverse reaction does occur, discontinue the infusion, evaluate the patient, institute appropriate therapeutic countermeasures and save the remainder of the fluid for examination if deemed necessary.

OVERTOXIS

Too rapid administration and/or excessive amounts of tromethamine may cause alkalosis, hypoglycemia, overhydration or solute overload. In the event of overdosage, discontinue the infusion, evaluate the patient and institute appropriate countermeasures. See WARNINGS, PRECAUTIONS and ADVERSE REACTIONS.

Dosage and Administration

Tham Solution (tromethamine injection) is administered by slow intravenous infusion, by addition to pump-oxygenator ACB blood or other priming fluid or by injection into the venicular cavity during cardiac arrest. For infusion by peripheral vein, a large needle should be used in the largest antecubital vein or an indwelling catheter placed in a large vein of an elevated limb to minimize chemical irritation of the alkaline solution during infusion. Catheters are recommended.

Dosage and rate of administration shall be carefully supervised to avoid overdosage (alkalosis). Pretreatment and subsequent determinations of the base excess (P CO₂, P CO₂ bicarbonate, glucose and electrolytes) and urinary output should be made as necessary to monitor dosage and progress of treatment. In general, dosage should be limited to an amount sufficient to increase blood pH to normal limits (7.35 to 7.45) and to correct acid-base derangements. The total quantity to be administered during the period of illness will depend upon the severity and progress of the acidosis. The possibility of some retention of tromethamine, especially in patients with impaired renal function, should be kept in mind.

The intravenous dosage of Tham Solution (tromethamine injection) may be estimated from the buffer base deficit of the extracellular fluid as determined by means of the Siggaard-Andersen nomogram. The following formula is intended as a general guide:

Tham Solution (mL of 0.3 M) Required = 9.0 mL/kg (324 mg/kg) has been used in clinical studies with Bypass Surgery.

The LD₅₀ values for the acute intravenous toxicity of THAM are influenced by the rate of infusion of the dose administered.

Intravenous LD₅₀ Mice = 3100 mg/kg
Intravenous LD₅₀ Rats = 2300 mg/kg
Each 100 mL contains tromethamine 3.6 g (30 mEq). pH adjusted with acetic acid (approx. 8.4 mEq/100 mL). A 0.3 molar solution. 389 mOsmol/L (calc.). pH 8.6 (8.4-8.7). Single-dose container. Sterile, nonpyrogenic. Usual dose: For intravenous use. See insert. Use only if clear and vacuum present. Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.] Protect from freezing.