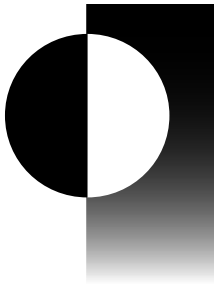
Botulism Antitoxin Bivalent (Equine) Types A and B

R2-0705 USA

Sanofi Pasteur Limited
Toronto Ontario Canada

Botulism Antitoxin Bivalent (Equine)
Types A and B

℞ only



For Prevention or Treatment of Botulism, Types A and B[1]

DESCRIPTION

Botulism Antitoxin Bivalent (Equine), as supplied by Sanofi Pasteur Limited, is a refined and concentrated preparation of horse globulins modified by enzymatic digestion and contains phenol 0.4% as a preservative.

INDICATIONS

Experimental evidence concerning the amount of circulating antitoxin needed to counteract botulism toxin poisoning by antitoxin therapy is not fully documented. The outcome of treatment depends, as it does in other comparable conditions, largely on the time interval elapsing after onset of symptoms before the peak of absorbed antitoxin is reached. This principle is illustrated in reported animal experiments.[1]

One or more vials of this mixture may be necessary to provide adequate circulating antibody of each type, depending upon the severity of the toxemia.

Precautionary Measures in the Administration of any Serum or Antitoxin

Before administering any serum or antitoxin to a patient, physicians are well advised to ascertain whether the patient has a history of asthma or hay fever, and particularly whether the patient suffers distress when in proximity to horses. Patients with such a history may develop serious reactions of an anaphylactic character upon the administration of serum of equine origin either subcutaneously, intramuscularly or intravenously. It should be borne in mind, also, that a patient who has been given a previous injection of serum of equine origin may develop a marked reaction when given a second injection, especially if the previous injection was intravenous in character.

Epinephrine Hydrochloride Solution (1:1,000) and other appropriate agents must be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs.[2]

TESTS FOR SENSITIVITY TO SERUM OR ANTITOXIN

A test for sensitivity to serum or antitoxin should be carried out each time a serum or antitoxin is administered, unless it is being given daily.

Sensitivity to any particular serum or antitoxin may be gauged by one of the following methods.

1. **Scratch, prick, or puncture test.** Apply one drop of a 1:100 dilution of the serum in normal saline to the site of a superficial scratch, prick, or puncture on the volar aspect of the forearm. Positive (histamine) and negative (physiologic saline) control tests should also be applied. A positive test is a wheal with surrounding erythema at least 3 mm larger than the negative control test, read at 15 to 20 minutes. The histamine control must be positive for valid interpretation. If the scratch test is negative, an intradermal test is performed.[3]

2. **Intradermal test.** A dose of 0.02 mL of 1:1,000 saline-diluted serum (enough to raise a small intradermal wheal) is administered. If the test is negative, it should be repeated using a 1:100 dilution.

   In persons with negative history for animal allergy and for prior exposure to equine serum, only the 1:100 dilution may be used.
   Interpretation of the intradermal test is done as with the scratch test.
   Positive and negative control tests should be applied as described above.[3]

Whereas intradermal skin tests have resulted in fatalities, the scratch test is usually safe. Therefore, scratch tests should always precede the intradermal tests.

A serum should never be injected, nor a skin test performed unless a syringe containing Epinephrine Hydrochloride Solution (1:1,000) is within immediate reach.

Skin tests should always be performed by trained personnel familiar with the treatment of acute anaphylaxis.[3]

A negative skin test does not entirely preclude the possibility of the occurrence of serum reactions.

ADVERSE REACTIONS

1. Anaphylactic reactions have been reported following administration of equine sera.

2. Thermal Reaction: When this reaction occurs, it usually develops in from twenty minutes to one hour after the injection of serum or antitoxin. It is characterized by a chilly sensation, slight dyspnoea and a rapid rise in temperature.

3. Serum Sickness: The symptoms of serum sickness include fever, urticaria, or maculopapular rash, arthritis or arthralgia, and lymphadenopathy. These symptoms may appear individually, or in combination, within fourteen days after the administration of a serum or antitoxin.

DOSAGE AND ADMINISTRATION

Prevention of Botulism Types A and B

The recommended prophylactic dose for an individual who has eaten food suspected of being infected with *C. botulinum* is 1,500-7,500 IU of Type A and 1,100-5,500 IU of Type B given intramuscularly depending on the amount of food eaten (one-fifth to one vial). This may be followed in 12 to 24 hours by the injection of the contents of a second vial if any signs or symptoms of botulism appear.[4]

Treatment of Botulism Types A and B

The best results in the treatment of botulism are likely to be obtained where very large doses of antitoxin are given early in the disease. The object is to provide an excess of circulating antitoxin as early as possible.

a) **Intravenous injection (IV).** In order to ensure the quickest possible neutralization of all toxin in the tissue and fluids, it is advisable to give immediately 7,500 IU of Type A and 5,500 IU of Type B (one vial) intravenously diluted in 0.9% saline for intravenous infusion at a 1:10 dilution. The preparation should be at ambient temperature before being administered. This may be accomplished with safety simply by holding the vial in one's hand for a minimum of 2 minutes. It should be given by slow intravenous infusion.

b) **Intramuscular injection.** In order to provide a reservoir of antitoxin from which it may be absorbed, an additional 7,500 units of Type A and 5,500 units of Type B (one vial) may be given by intramuscular injection.

Further doses may be indicated in 2 to 4 hours if the signs and symptoms worsen.

Important Points in Injecting the Serum

Intravenous Injection. The serum is injected very slowly intravenously at a dilution of 1:10.

It is advisable that the patient be tested for sensitivity to horse serum and, if necessary, initial intravenous doses should be small and well diluted (see below).

Administration of Antitoxin to Sensitive Persons

Whenever there is a history of allergy, sensitivity to horse serum or manifestations of sensitivity when in proximity to horses, or if the reaction to the skin test is positive, great care must be exercised in the administration of serum (or antitoxin).

No one method can be advised for the administration of serum or antitoxin for sensitive persons as each presents an individual problem. Desensitization of the patient may be carried out by serial injections of diluted antitoxin as indicated below at intervals of 15 minutes, provided no reactions occur.

"Desensitization" to Serum - Intravenous Route[3]

Dose Number*	Dilution of Serum in Normal Saline	Amount of Injection (mL)
1	1:1,000	0.1
2	1:1,000	0.3
3	1:1,000	0.6
4	1:100	0.1
5	1:100	0.3
6	1:100	0.6
7	1:10	0.1
8	1:10	0.3
9	1:10	0.6
10	undiluted	0.1
11	undiluted	0.2
12	undiluted	0.6
13	undiluted	1.0

* Administer consistently at 15-minute intervals.

If signs of anaphylaxis occur, aqueous epinephrine should be administered immediately. Administration of sera under the protection of a desensitization procedure must be continuous. Once administration is interrupted, protection from desensitization is lost.[3]

A separate sterilized syringe and needle should be used for each individual patient to prevent transmission of homologous serum hepatitis and other infectious agents from one person to another.

NOTE: Following the administration of serum (or antitoxin), and particularly in those cases showing a positive skin test, the patient should be kept under close observation for one to two hours and under reasonable close surveillance for a period of twenty-four hours.

STORAGE

Store at 2° to 8°C (35° to 46°F). DO NOT FREEZE.

HOW SUPPLIED

Botulism Antitoxin Bivalent (Equine) Types A and B is supplied in vials, each containing:

Type A – 7,500 International Units, equivalent to 2,381 US Units

Type B – 5,500 International Units, equivalent to 1,839 US Units

CPT® Code: 90287

CPT is a registered trademark of the American Medical Association.

REFERENCES

1. Iida H, Ono T, Karashimada T. Studies on the serum therapy of type E botulism. In: Botulism 1966; Proceedings of the Fifth International Symposium on Food Microbiology, Moscow, July 1966. London, Chapman & Hall. 1967:346-359.

2. National Advisory Committee on Immunization*:* Canadian Immunization Guide, Fourth Edition. Minister of Supply and Services Canada. 1993.

3. American Academy of Pediatrics: Report of the Committee on Infectious Diseases, 23rd ed. Elk Grove Village, IL., The Academy, 1994.

4. Miller ES. Botulism. P. 947. In: Harrison TR, ed. *Principles of internal medicine. 2nd ed.* New York, Blakiston, 1954.

Manufactured by:
Sanofi Pasteur Limited
Toronto Ontario Canada

Printed in Canada
Product Information as of July 2005.

R2-0705 USA