INTRODUCTION — Beta adrenergic antagonists (beta blockers) have been in clinical use for more than 30 years, and are employed in the management of a range of disorders, including hypertension, ischemic heart disease, heart failure, arrhythmias, migraine headache, tremor, portal hypertension, and aortic dissection. Although safe for most patients when taken as prescribed, beta blocker toxicity is associated with significant morbidity and mortality. In 2006, there were 9041 single beta blocker exposures reported to poison centers in the United States. Of these, there were 613 moderate or major adverse outcomes and four deaths [1]. Complications following beta blocker overdose are related to excessive beta adrenergic blockade, and occasionally the proarrhythmic (membrane-stabilizing) activity of these agents on cardiac conduction [2]. Ingestion of other cardioactive agents in association with beta blockers increases mortality following overdose [2,3]. Common and potentially dangerous coingestions include calcium channel blockers, cyclic antidepressants, and neuroleptics [2]. An overview of beta blocker intoxication will be presented here. A summary table to facilitate emergent management is provided (table 1). A general approach to an adult patient with possible drug intoxication, and an overview of adverse effects of beta blockade, are discussed separately. (See "General approach to drug poisoning in adults" and "Major side effects of beta blockers".)

PHARMACOLOGY

Receptor types and general mechanism — There are at least three distinct types of beta receptors:

- Beta 1, which are found primarily in heart muscle. Activation of these receptors results in an increase in heart rate, contractility, atrioventricular (AV) conduction, and a decrease in AV node refractoriness.
- Beta 2, which are present in heart muscle but are more prominent in bronchial and peripheral vascular smooth muscle. Activation of these receptors results in vasodilation and bronchodilation.
- Beta 3, which are found in adipose tissue and the heart. Activation of these receptors may mediate catecholamine-induced thermogenesis and may reduce cardiac contractility.

Competitive antagonism of the beta receptor decreases cellular levels of cyclic adenosine monophosphate (cAMP). Beta-1 selective blockade results in depressed myocardial contractility, decreased automaticity in pacemaker cells, and decreased conduction velocity through the atrioventricular node [3]. The lungs, peripheral blood vessels, glucose metabolism, and central nervous system are all affected by beta blockade. Nonselective beta blockade results in systemic effects including bronchoconstriction, impaired gluconeogenesis, and decreased insulin release. (See "Major side effects of beta blockers".)

CELLULAR TOXICOLOGY — There are many beta blockers available for clinical use, and although they all inhibit the beta-adrenoreceptor, there are several characteristics that differ among these agents. Following overdose, manifestations of toxicity are observed in varying degrees, depending on the specific agent and dose involved [3,4]. In addition to beta-adrenoreceptor blockade, three properties that affect toxicity include the membrane stabilizing activity (MSA), lipophilicity, and intrinsic sympathomimetic activity (ISA) of the ingested agent (table 2).

- Membrane stabilizing activity (MSA) – Membrane stabilizing agents (eg, propranolol, acebutolol) inhibit myocardial fast sodium channels, which can result in a widened QRS interval and may potentiate other dysrhythmias.
Beta blocker poisoning

- Intrinsic sympathomimetic activity (ISA) – Many agents demonstrate a partial agonist effect at the beta receptor site, resulting in less bradycardia and hypotension in therapeutic and supratherapeutic doses. Bronchoconstriction is also less likely to occur with compounds that possess intrinsic sympathomimetic activity (ISA), or beta-1 selectivity. However, the protective effects of ISA do not completely prevent cardiovascular toxicity following intentional or accidental overdose.

TOXICITY OF SPECIFIC AGENTS — Of all the variables contributing to toxicity, membrane stabilizing activity (MSA) appears to have the greatest influence on adverse cardiovascular effects (table 2). Agents with significant MSA, such as propranolol, acebutolol, betaxolol, and oxprenolol. The effect of MSA is thought to be negligible at therapeutic doses, but in overdose can cause significant cardiovascular morbidity. In one retrospective study, 94 percent (15 out of 16) of patients with cardiovascular toxicity had a history of ingesting beta blockers with MSA [2].

Acebutolol, a cardioselective agent with partial agonist activity and significant MSA, is one of the most toxic beta blockers in overdose [6]. Acebutolol toxicity may predispose the patient to ventricular repolarization resulting in arrhythmias [6].

Sotalol combines class III antidysrhythmic properties with beta adrenergic antagonism. Sotalol prolongs the action potential duration and increases the refractory period by blocking delayed potassium channels. This leads to prolongation of the QTc interval, and can contribute to the development of Torsades de Pointes [7]. (See "Therapeutic use and major side effects of sotalol" and "Acquired long QT syndrome", section on 'Drug-induced TdP'.)

Carvedilol has been associated with toxic epidermal necrolysis at therapeutic levels [8].

PHARMACOKINETICS — In therapeutic use, most beta blockers have half-lives ranging from two to eight hours, but kinetics can change in overdose (table 2). Ingestion of sustained release preparations can delay the onset of symptoms and substantially prolong the duration of toxicity.

Many beta blockers are metabolized via the liver. Esmolol is metabolized by erythrocyte esterases. Atenolol, bisoprolol, labetalol, and sotalol are eliminated by the kidney.

CLINICAL FEATURES OF OVERDOSE — Diagnosis of beta blocker intoxication is made on the basis of history and clinical presentation.

History — Data obtained should include the specific agent, amount ingested, time of ingestion, and any coingestions. Historical features that suggest increased risk for severe toxicity include:

- Coingestion of other cardioactive agents
- Underlying cardiac disease (eg, heart failure)
- Ingestion of sotalol or another agent with membrane-stabilizing activity (eg, propranolol or acebutolol) (see "Toxicity of specific agents" above)

Any possible witnesses and emergency medical services (EMS) personnel who may have recovered pill bottles at the scene should be contacted. The patient’s pharmacy may provide valuable information regarding prescribed medications, the date of the most recent refill, and the total number of pills dispensed.

Physical findings — Most patients who overdose on beta blockers become symptomatic within two hours following ingestion, and nearly all develop symptoms within six hours [2,9]. Exceptions to this general rule include ingestions of sustained release medications and sotalol [10]. In these cases, delayed toxicity up to 24 hours after ingestion can occur.

Bradycardia and hypotension are the most common effects, and in severe overdoses can result in profound myocardial depression and cardiogenic shock. Ventricular dysrhythmias are seen more frequently following propranolol and acebutolol exposures, probably because of the increased membrane-stabilizing activity (MSA) of these agents (table 2). Other potential effects of severe toxicity include mental status change, seizure, hypoglycemia, and bronchospasm.

Mental status changes, including delirium, coma, and seizures, occur most frequently in patients with severe poisoning.

Sci-Hub
http://www.uptodate.com/contents/beta-blocker-poisoning?source=search_result&search=poisoning+betablock&selectedTitle=1%7E18
the minimum pulse and systolic and diastolic ranges were not significantly different between groups, 29 percent of the propranolol group experienced seizures versus none in the non-propranolol group. This difference is probably due to the increased lipophilicity of propranolol, allowing rapid diffusion into the central nervous system.

In addition to the cardiovascular and neurologic manifestations, bronchospasm and hypoglycemia can complicate acute beta blocker intoxication. Early recognition and prompt treatment of hypoglycemia is critical. (See 'Management' below.)

LABORATORY EVALUATION

Laboratory studies — Although serum concentrations of most beta blockers can be measured, they cannot be obtained in time to be clinically useful and are generally performed only for academic or forensic purposes.

In patients with beta blocker overdose, we generally obtain the following studies: an electrocardiogram (ECG), fingerstick glucose, serum electrolytes including calcium, and blood urea nitrogen and creatinine levels. If calcium channel blockers are administered repeatedly, levels should be measured every four to six hours. If an insulin/glucose treatment regimen is used, glucose and potassium levels must be measured every 30 to 60 minutes. (See 'Insulin and glucose' below and 'Calcium' below.)

Routine laboratory evaluation of any poisoned patient should include acetaminophen and salicylate levels, to rule out these common coingestions, and a pregnancy test in women of childbearing age.

A serum lactate concentration above 3 mmol/L is used to predict life-threatening overdose of some medications. However, this may be an insensitive finding with beta blocker overdose. In one retrospective study, four of nine deaths associated with beta blocker poisoning were associated with serum lactate concentrations below 3 mmol/L.

Additional tests are obtained based upon clinical findings. As an example, a plain chest radiograph is obtained in patients with signs of pulmonary edema.

Electrocardiogram — Beta blockers decrease conduction velocity across the atrioventricular (AV) node, resulting in PR prolongation; they also slow automaticity within the sinoatrial (SA) node, causing bradycardia.

QRS prolongation occurs more commonly when beta blockers with membrane stabilizing activity (MSA) are ingested. Significant QTc prolongation can develop following sotalol overdose as a result of its independent Class III antiarrhythmic activity. In severe poisoning, the electrocardiogram (ECG) can show any bradydysrhythmia, and can progress to asystole. (See "Advanced cardiac life support (ACLS) in adults", section on 'Asystole and pulseless electrical activity'.)

A Brugada-like ECG pattern has been reported in the setting of propranolol poisoning, suggesting that other beta blockers that are lipophilic or possess membrane stabilizing activity might have similar effects.

DIAGNOSIS — The diagnosis of beta blocker poisoning is made clinically on the basis of the history and clinical presentation. Typically there is a history of overdose combined with findings of bradycardia and hypotension, which can be profound in severe overdose, resulting in cardiogenic shock. Other findings can include ventricular dysrhythmia, altered mental status, seizure, hypoglycemia, and bronchospasm. Although serum concentrations of most beta blockers can be measured, such measurements cannot be obtained in time to be clinically useful.

DIFFERENTIAL DIAGNOSIS — Many drugs can cause profound hypotension or bradydysrhythmia in overdose. Calcium channel blockers, digoxin, clonidine, and cholinergic agents must be considered when evaluating bradydysrhythmia potentially caused by a toxic ingestion.

Calcium channel blockers are less likely than beta blockers to produce alterations in mental status, and frequently do not do so unless the patient is in profound shock. Hyperglycemia occurs more often with calcium channel blocker toxicity, while beta blockers are associated with hypoglycemia. (See "Calcium channel blocker poisoning".)

Nausea and vomiting occur more often with digoxin toxicity than beta blocker toxicity. Digoxin may cause characteristic changes in an electrocardiogram, such as scooped ST segment depressions. Digoxin is more likely to produce rhythms of increased automaticity, such as atrial tachycardia with atrioventricular block, premature ventricular contractions, or ventricular arrhythmias. (See "Digitalis (cardiac glycoside) poisoning".)
**MANAGEMENT**

**Acute stabilization and overview of therapy** — First, secure the airway and provide advanced cardiac life support as necessary (table 1). **Atropine** should be given early in bradycardic patients and as a pretreatment agent when rapid sequence intubation is required [16]. Establish intravenous access and provide continuous cardiac monitoring. A summary table to facilitate emergent management is provided (table 1). (See "Rapid sequence intubation for adults outside the operating room" and "Advanced cardiac life support (ACLS) in adults".)

Treat hypotension with intravenous (IV) boluses of isotonic fluid; treat symptomatic bradycardia with **atropine**. Atropine is given in a dose of 0.5 to 1 mg every three to five minutes up to a total of 0.03 to 0.04 mg/kg. **Sodium bicarbonate** and magnesium may be needed to treat some arrhythmias. (See 'Other therapies' below.)

Treat symptomatic hypoglycemia with IV dextrose. For adults, administer boluses of 50 percent dextrose in water (D50W); for children administer an appropriate IV bolus of dextrose (0.25 g/kg body weight). In infants and young children this is usually given as 2.5 mL/kg of 10 percent dextrose solution. Multiple doses of dextrose may be necessary. Treatment of hypoglycemia in children is discussed in detail separately. (See "Approach to hypoglycemia in infants and children".)

Treat seizures with benzodiazepines (eg, **lorazepam**). (See "Convulsive status epilepticus in adults: Classification, clinical features, and diagnosis".)

IV fluid and **atropine** often do not completely reverse the cardiotoxic effects of beta blocker overdose. In such cases, we give additional treatments based upon the severity of the presentation. These treatments may include:

- **IV glucagon**
- **IV calcium salts**
- **Vasopressor**
- **High dose insulin and glucose infusions**
- **Lipid emulsion therapy**

These therapeutic options are discussed below. (See 'Approach to the selection of specific therapies' below.)

Hemodialysis may be needed in specific circumstances, although this is uncommon. In such cases a nephrologist should be contacted early in the patient’s course. (See 'Other therapies' below.)

Many patients with isolated beta blocker overdose remain asymptomatic and can be discharged after a period of observation. (See 'Disposition' below.)

**Approach to the selection of specific therapies** — Although it is ideal to institute treatments individually to assess their success or failure, this is often not possible in patients who are severely ill from a beta blocker poisoning. Our suggested approaches to therapy based upon the severity of the clinical presentation are described here; a summary table to facilitate emergent management is provided (table 1).

**Severely symptomatic patients** — Our suggested approach to patients manifesting signs of severe beta blocker poisoning (profound hypotension and/or severe bradycardia, depressed mental status) consists of multiple **simultaneous** interventions, including all of the following treatments [17,18]:

- Stabilization of the airway as necessary (avoid induction agents that exacerbate hypotension)
- Additional IV boluses of isotonic crystalloid
- **IV glucagon**
- **IV calcium salts**
- **Vasopressor** (eg, **epinephrine**)
- **IV high-dose insulin and glucose**
- **IV lipid emulsion therapy**

Dosing for each of these therapies is provided below. (See 'Specific therapies' below.)
succession based upon patient response. As an example, we begin treatment with glucagon if IV crystalloid does not adequately improve the patient’s blood pressure, but if hypotension resolves following treatment with glucagon, we do not proceed to IV calcium salts or any other treatment.

- IV glucagon
- IV calcium salts
- IV high-dose insulin and glucose
- IV vasopressor (eg, epinephrine)
- IV lipid emulsion therapy

A period of 15 minutes is reasonable to determine the effectiveness of a specific therapy before proceeding to the next treatment. Dosing for each of these therapies is provided below. (See ‘Specific therapies’ below.)

**Asymptomatic patients** — Many patients with an isolated beta blocker overdose remain asymptomatic and may be discharged after a period of observation, unless the overdose was intentional. (See ‘Disposition’ below.)

**Specific therapies**

**Glucagon** — Despite limited data, glucagon is considered first-line, antitodal treatment for beta blocker overdose [19,20]. Glucagon may be effective initially for a brief period, but prolonged treatment may become ineffective due to tachyphylaxis. Intravenous (IV) glucagon is given as a slow bolus dose followed by continuous infusion. An initial bolus of 5 mg intravenously is administered over one minute; if there is no increase in pulse or blood pressure after 10 to 15 minutes, a second bolus should be administered. The initial pediatric dose is 50 mcg/kg. An effect should be observed within one to three minutes, with a peak response at five to seven minutes. If there is no observed effect after 10 minutes following a second dose, it is unlikely an infusion will provide benefit.

If there is an increase in pulse or blood pressure, an infusion is started at a rate of 2 to 5 mg/hour (pediatric dose 70 mcg/kg/hour). The goal is to maintain a mean arterial pressure of 60 mmHg. If this cannot be achieved, additional therapies are implemented in a sequential manner, beginning with calcium salts. When used as a sole agent in humans, glucagon has been associated with treatment failures.

Vomiting is common following administration of glucagon. We suggest prophylactic or concurrent administration of a serotonin antagonist antiemetic (eg, ondansetron). (See “Characteristics of antiemetic drugs”.)

**Glucagon** activates adenylate cyclase at a site independent from beta-adrenergic agents, causing an increase in adenosine 3’-5’-cyclic monophosphate (cAMP). Elevations in cAMP increase the intracellular pool of calcium available for release during depolarization, augmenting contractility. The successful use of glucagon to manage beta blocker toxicity has been documented in many case reports, but no controlled trials involving humans have been conducted [21]. One review of the available controlled trials in animal models found that glucagon increased heart rate (HR), at least transiently, but had minimal effect on mean arterial pressure (MAP) [19].

In 2006, a trial comparing vasopressin with glucagon in a swine model of propranolol overdose found no difference in survival at four hours [22]. No difference was detected in HR, MAP, systolic BP, or cardiac output, except in the first hour, when vasopressin caused a marked increase in MAP and systolic BP. Notably, cardiac output did not improve following glucagon administration.

**Calcium** — A number of case reports demonstrate the efficacy of IV calcium salts in treating beta blocker toxicity [23,24]. Either calcium chloride or calcium gluconate may be given.

**Calcium chloride**, 1 g of a 10 percent solution (10 mL), is given as a slow push, and should be administered via a central venous catheter. The dose may be repeated up to a total of 3 g. The pediatric dose is 20 mg/kg (maximum dose is 1 g); up to 60 mg/kg may be given.

**Calcium gluconate** should be given if only peripheral IV access is available. The percentage of elemental calcium in calcium gluconate is one-third that of the calcium chloride salt, so 30 mL of a 10 percent solution should be administered as an initial dose. In children, give 60 mg/kg per dose (maximum dose is 3 g).
Vasopressor (catecholamine) — In animal models and human case reports, treatment of beta blocker overdose with catecholamine infusion alone has resulted in poor outcomes [27-29]. Catecholamines may be added if the combination of atropine, IV fluids, glucagon, and IV calcium salts are unsuccessful in improving cardiovascular performance, or as a temporizing measure until high dose insulin therapy starts to take effect. The vasopressor can then be titrated downward as tolerated. (See "Use of vasopressors and inotropes").

An infusion of epinephrine at 1 mcg/minute can be started and titrated upwards to maintain a MAP of 60 mmHg. Pediatric dosing starts at 0.1 mcg/kg/minute and is titrated upwards based upon the patient’s MAP. High infusion rates may be necessary to overcome competitive inhibition. An arterial line may be needed to monitor blood pressure.

Catecholamines exert positive inotropic and chronotropic activity on the myocardium by stimulating adrenergic receptors and increasing the concentration of cAMP. One possible explanation for the lack of effectiveness of catecholamines in beta blocker overdose is that high doses are often required to achieve a therapeutic effect. Higher doses may increase the risk of arrhythmia. In addition, some speculate that unopposed alpha constriction increases the cardiac workload, diminishing stroke volume and cardiac output.

Insulin and glucose — High-dose insulin is being used with greater frequency to treat beta-blocker overdose. In patients who manifest hemodynamic instability refractory to the other therapies described above, we suggest that a trial of high-dose insulin and glucose be administered, possibly in combination with other agents depending on the clinical scenario, and titrated upward until blood pressure stabilizes. (See 'Approach to the selection of specific therapies' above.)

The dosing regimen for high-dose insulin is described in detail separately. Of note, hypoglycemia is a possible complication of this treatment since the dose of insulin is much higher (approximately 10-fold) than that typically given for diabetic ketoacidosis. When necessary, euglycemia can be maintained by means of a continuous IV infusion of 5 to 10 percent dextrose. A hemodynamic response to high-dose insulin therapy is delayed for 30 to 60 minutes, therefore simultaneous implementation of other therapies to support the patient’s pulse and blood pressure are generally required. Repletion of potassium and magnesium may be needed. (See "Calcium channel blocker poisoning", section on 'Insulin and glucose'.)

Animal studies and case reports of both isolated beta blocker overdose and combined calcium channel blocker and beta blocker overdose suggest that treatment with high dose insulin and glucose is effective [26,30,31]. However, the role for this therapy in pure beta blocker overdose remains unsettled, despite an increasing number of case reports describing successful treatment of patients with severe beta-blocker and mixed beta-blocker overdoses [32]. Often, such cases involve patients treated with multiple therapies (eg, calcium, atropine, glucagon, vasopressors) before treatment with high dose insulin, making it difficult to determine which therapy was most effective. High dose insulin has been well tolerated in patients, and has been administered for prolonged periods, up to 116 hours in one case [32].

One animal study of insulin therapy in propranolol toxicity was terminated early when every pig in the insulin and glucose treatment group achieved the study goal of four hour survival, while those treated with vasopressin and epinephrine died within 90 minutes [27]. Cardiac output (CO) in animals treated with insulin and glucose increased steadily and consistently, while CO in animals treated with vasopressin and epinephrine decreased until death.

It appears that insulin exhibits a steady dose response curve, and may be titrated upwards until blood pressure improves. One study using a pig model of propranolol overdose, compared treatments with placebo and insulin at doses of 1 unit/kg per hour, 5 units/kg per hour, and 10 units/kg per hour [33]. For each one unit/kg per hour increase of insulin, there was a statistically significant increase in cardiac output, and no ceiling effect was noted.

The pathophysiology of beta blocker intoxication is similar in many respects to that of calcium channel blocker (CCB) intoxication, for which high dose insulin and glucose therapy has been more extensively studied. Although the mechanism is not completely understood, both CCB and beta blocker poisoning appear to interfere with myocyte metabolism. In addition, beta blockers inhibit pancreatic insulin release further reducing available glucose and diminishing CO. Insulin appears to improve inotropy by providing substrate for aerobic metabolism within the myocyte (See "Calcium channel blocker poisoning", section on 'Pathophysiology'.)

Lipid emulsion therapy — Lipid emulsions are the fats used in total parenteral nutrition (TPN). Initially used to

Studies of ILE therapy are preliminary and limited. ILE may have a useful role in the treatment of patients who are hemodynamically unstable from particular poisonings, including beta blockers, after more traditional therapies (eg, in the case of beta blocker poisoning: IV fluids, atropine, glucagon, high dose insulin and glucose, and vasopressors) have failed to restore hemodynamic stability. ILE has been used successfully in documented cases of severe beta blocker overdose [34,35]. Several case reports describe patients treated with both high dose insulin and ILE with good results [36]. ILE may be used early in the treatment of an overdose of a highly lipophilic agent (eg, propranolol), or as an adjunct to other treatments as described above. (See 'Approach to the selection of specific therapies' above.)

Gastrointestinal (GI) decontamination — GI decontamination may involve activated charcoal (AC), whole bowel irrigation, or gastric lavage; therapy is based upon clinical circumstance. (See "Gastrointestinal decontamination poisoned patient").

We suggest treatment with activated charcoal (AC), 1 g/kg by mouth or nasogastric tube, in all patients who have ingested more than one to two hours of a known or suspected beta blocker ingestion, unless there are contraindications to AC administration. Charcoal should be withheld in patients who are sedated and may not be able to protect their airway unless endotracheal intubation is performed first. However, endotracheal intubation should not be performed solely for the purpose of giving charcoal.

Asymptomatic patients who present more than two hours after a reported ingestion are unlikely to benefit from AC, and we do not recommend routine treatment in these patients.

The role of activated charcoal in symptomatic patients who present several hours after ingestion is more controversial. We suggest the administration of AC (1 g/kg by mouth or nasogastric tube) if there are no contraindications to charcoal administration. Although there are no data to suggest improved outcomes with AC in such patients, we believe that AC is a relatively safe intervention whose potential benefits in this situation outweigh its risks.

Gastric lavage should not be routinely performed, but may be considered for patients who present within one hour following ingestion of a large quantity of medication. Large sustained or controlled release tablets may not pass through the oral gastric tube.

Whole bowel irrigation is reserved for patients who have ingested sustained release or enteric coated preparations, or have suspected drug concretions (pharmacobezoars) in the GI tract.

Other therapies

- **Sodium bicarbonate** – Sodium bicarbonate has been used successfully in the treatment of beta blocker induced arrhythmia [37,38]. Because it is a relatively safe intervention, we suggest giving it as an adjunct for patients with QRS widening.
  
The dose of sodium bicarbonate is 1 to 2 mEq/kg given as an IV push, which may be repeated. If treatment is effective, an infusion can be started. We mix 132 mEq of sodium bicarbonate in 1 L of D5W and infuse at 250 mL/hour in adults, and at twice the maintenance fluid rate in children. The infusion is tapered once the arrhythmia resolves. (See "Tricyclic antidepressant poisoning").

- **Magnesium** – Magnesium may be administered when ventricular arrhythmias are present or hypomagnesemia is suspected. Sotalol has a high propensity to induce ventricular arrhythmias and will often require magnesium, administered as a 2 g IV bolus or as a continuous infusion.

- **Intravenous pacing** – Ventricular pacing may be effective in patients with profound bradycardia, or in patients with combined beta blocker and calcium channel blocker intoxication [39]. However, ventricular pacing frequently fail to capture, or increases the heart rate without a corresponding increase in perfusion [40]. IV pacing can be implemented if there is no response to pharmacologic therapies, and the patient remains bradycardic and hypotensive. Some authors note a decrease in blood pressure with pacing [4]. (See "Temporary cardiac pacing").

- **Intraaortic balloon pump** – The intraaortic balloon pump has been used successfully after failure of pharmacologic management in severe cases of propranolol and atenolol overdose [41,42] and in combined verapamil-SR (sustained release) and atenolol overdose [43]. (See "Intraaortic balloon pump counterpulsation").

- **Hemodialysis** – Hemodialysis has a minimal role in the treatment of beta blocker overdose and is effective only with hydrophilic, minimally protein-bound beta blockers such as atenolol [43], nadolol, atenolol, labetalol, and...
ingested other cardioactive medications that may exacerbate toxicity. In such cases, the emergency clinician should contact a nephrologist early in the patient’s course to avoid delays in preparing for hemodialysis.

Continuous venovenous hemodialysis (VVHD) can be used if the patient is not able to tolerate traditional hemodialysis due to pronounced hypotension. The decision to initiate hemodialysis and the selection of the appropriate type is made in consultation with the nephrologist. (See "Enhanced elimination of poisons".)

**Pediatric considerations** — Hypoglycemia is seen more often in pediatric patients than adults. Management does not significantly differ from that in adults.

We recommend 24 hours of observation in a monitored setting for any initially asymptomatic child who has ingested a sustained release preparation, sotalol, or multiple cardioactive agents. Outside of such cases, the great majority of isolated ingestions by young children are uneventful and they can be discharged after a six hour period of observation [45,46].

Children may be observed safely at home after the witnessed ingestion of a single beta blocker tablet and Poison Control Centers typically manage these exposures via telephone follow-up [47,48]. Should the patient’s family call the Emergency Department (ED) for advice, it is prudent to advise them to bring the child to the ED for evaluation since follow-up can be problematic.

**Disposition** — Patients who have ingested a beta blocker and who manifest hemodynamic instability or an altered mental status should be admitted to a critical care unit for cardiac monitoring and further management.

Sotalol has a long half-life and toxicity may result in ventricular dysrhythmias. Thus, patients require 24 hours of inpatient cardiac monitoring following sotalol overdose, even if they are asymptomatic.

Any person who has taken an overdose of a beta blocker with membrane stabilizing activity (table 2) or multiple cardioactive medications is at increased risk of severe toxicity and should be observed in the emergency department for six hours. Patients who remain asymptomatic without need of intervention can be safely discharged. Patients who are asymptomatic at presentation after ingestion of a sustained release beta blocker should be observed for at least six hours to insure that symptoms do not develop [2].

Asymptomatic adults who have inadvertently ingested an amount of beta blocking agent no greater than their total daily dose (excluding sotalol) may be observed safely at home [2].

**ADDITIONAL RESOURCES** — Regional poison control centers in the United States are available at all times for consultation on patients who are critically ill, require admission, or have clinical pictures that are unclear (1-800-222-1222). In addition, some hospitals have clinical and/or medical toxicologists available for bedside consultation and/or inpatient care. Whenever available, these are invaluable resources to help in the diagnosis and management of ingestions or overdoses. The World Health Organization provides a listing of international poison centers at its website: www.who.int/gho/phe/chemical_safety/poisons_centres/en/index.html

**SUMMARY AND RECOMMENDATIONS**

- Although beta blocker overdose generally follows a benign clinical course, patients with significant toxicity require aggressive medical management. A summary table to facilitate emergent management is provided (table 1).

- Toxicity increases greatly when an agent has membrane stabilizing activity (MSA) (table 2) or when other cardioactive agents are ingested concomitantly. Lipophilic agents cross the blood brain barrier and can cause neurologic dysfunction even in the absence of systemic hypotension (table 2). (See ‘Cellular toxicology’ above and ‘Toxicity of specific agents’ above.)

- Sotalol is a unique agent with an extended half-life that can cause QTc interval prolongation and severe ventricular arrhythmias in overdose. Propranolol and acebutolol possess properties that increase their potential toxicity. (See ‘Toxicity of specific agents’ above and ‘History’ above.)

- Most patients who develop toxicity from beta blocker overdose do so within two hours of ingestion, and virtually all do so within six hours. Bradycardia and hypotension are the most common effects. Cardiogenic shock and ventricular dysrhythmias can occur with severe overdose. Other potential effects of severe toxicity include mental status change, seizure, hypoglycemia, and bronchospasm. Hypoglycemia is seen more often in children.
delays can occur, most often a prolonged PR interval. In severe poisoning, ANY bradydysrhythmia can develop, and may progress to asystole. (See 'Laboratory studies' above and 'Electrocardiogram' above.)

- For patients with severely symptomatic beta blocker poisoning (eg, profound persistent hypotension or bradycardia), we suggest simultaneous treatment with all of the following therapies (Grade 2C). Dosing is provided in the text and the rapid overview table (table 1). Severe beta blocker poisoning can be difficult to manage and consultation with a medical toxicologist or regional poison control center is prudent. (See 'Acute stabilization and overview of therapy' above and 'Severely symptomatic patients' above.):
  - Stabilization of the airway as necessary (avoid induction agents that exacerbate hypotension)
  - Additional IV boluses of isotonic crystalloid
  - IV glucagon
  - IV calcium salts
  - Vasopressor (eg, epinephrine)
  - IV high-dose insulin and glucose
  - IV lipid emulsion therapy

- For patients who are mildly symptomatic from beta blocker poisoning, and in whom IV fluids, atropine, and glucagon prove ineffective at reversing signs of cardiotoxicity, we suggest a stepwise treatment approach (Grade 2C). Give the following treatments, in succession, based upon patient response: IV calcium salts, lipid emulsion therapy, vasopressors, and high-dose insulin and glucose. The implementation of each therapeutic option is discussed in the text. (See 'Acute stabilization and overview of therapy' above and 'Specific therapies' above.)

- Sodium bicarbonate and magnesium may be needed to treat some arrhythmias. Hemodialysis may rarely be needed, in which case a nephrologist should be contacted early. (See 'Other therapies' above.)

- The length of observation following inadvertent overdose varies according to the type and number of medications ingested. (See 'Disposition' above.)

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REFERENCES


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