



## Emergency Management of Cyanide Toxicity: An Evidence-Based Reference for Healthcare Assistants, Paramedics, and Health Informatics Professionals- An Updated Review

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### Abstract

**Background:** Cyanide toxicity is a rare but rapidly fatal medical emergency that results from inhibition of mitochondrial oxidative phosphorylation, leading to cellular hypoxia despite adequate oxygen delivery. Exposure occurs through inhalation of hydrogen cyanide gas, ingestion of cyanide salts or cyanogenic foods, occupational accidents, structural fires, and certain pharmaceutical agents. Owing to its nonspecific clinical presentation and rapid progression, early recognition and prompt treatment are essential for reducing morbidity and mortality.

**Aim:** This review aims to provide a comprehensive overview of cyanide toxicity, including its epidemiology, etiology, pathophysiology, clinical manifestations, diagnostic evaluation, emergency management, prognosis, and complications, with emphasis on evidence-based practices relevant to emergency medicine, healthcare assistants, paramedics, and health informatics professionals.

**Methods:** A narrative literature review was conducted using current peer-reviewed studies, toxicology references, and clinical guidelines addressing cyanide poisoning, its underlying mechanisms, diagnostic approaches, antidotal therapy, and supportive management.

**Results:** Cyanide poisoning primarily disrupts aerobic cellular respiration through inhibition of cytochrome c oxidase, resulting in histotoxic hypoxia, profound lactic acidosis, and multiorgan dysfunction. Diagnosis remains predominantly clinical, supported by elevated serum lactate, metabolic acidosis, and characteristic exposure history. Immediate stabilization, decontamination when indicated, and early administration of hydroxocobalamin constitute the cornerstone of treatment. Delayed intervention significantly increases mortality and the risk of persistent neurological sequelae, including Parkinsonian syndromes.

**Conclusion:** Cyanide toxicity remains a time-critical emergency requiring rapid clinical recognition and immediate intervention. Early diagnosis, multidisciplinary management, and prompt antidotal therapy substantially improve survival and neurological outcomes. Ongoing education of frontline healthcare professionals and adherence to evidence-based emergency protocols are essential to optimize patient care and minimize the devastating consequences of cyanide poisoning.

**Keywords:** Cyanide toxicity; Cyanide poisoning; Hydrogen cyanide; Histotoxic hypoxia; Cytochrome c oxidase; Hydroxocobalamin; Sodium thiosulfate; Emergency medicine; Toxicology; Smoke inhalation; Metabolic acidosis; Antidote.

### Introduction

Cyanide toxicity is an uncommon but rapidly life-threatening medical emergency that requires immediate recognition and prompt intervention to prevent irreversible cellular injury and death. Although relatively rare compared with other forms of poisoning, cyanide intoxication is associated with exceptionally high morbidity and mortality because of its ability to rapidly inhibit cellular respiration and oxidative phosphorylation. Cyanide exerts its toxic effects by binding to the ferric ion of mitochondrial cytochrome c oxidase (complex IV) within the electron transport chain, thereby preventing oxygen utilization at the cellular level despite adequate oxygen delivery. This results in histotoxic hypoxia, anaerobic metabolism, excessive lactate production, profound metabolic acidosis, and rapid failure of vital organs,

particularly the brain and heart, which have the highest oxygen demands. Without immediate diagnosis and administration of appropriate antidotal therapy, cyanide poisoning may rapidly progress to cardiovascular collapse, respiratory failure, coma, and death. Historically, cyanide has been implicated in numerous high-profile incidents involving intentional, accidental, and occupational exposures. It has been used in mass suicide events, including the Jonestown tragedy in 1978, as a homicidal agent, and as a chemical warfare agent in both military conflicts and the Holocaust through the use of hydrogen cyanide-containing Zyklon B [1,2]. Despite these historical associations, contemporary cyanide poisoning is more commonly encountered in civilian emergency practice, where exposure results from industrial accidents, smoke inhalation during structural fires, accidental ingestion, occupational hazards, and intentional self-poisoning.

Human exposure to cyanide occurs through multiple routes, including inhalation, ingestion, dermal absorption, and, less commonly, parenteral administration. Among these, ingestion and inhalation represent the predominant routes associated with severe toxicity. Intentional ingestion of cyanide salts, particularly potassium cyanide and sodium cyanide, is frequently encountered in suicide attempts, whereas inhalational exposure commonly occurs during enclosed-space fires where combustion of nitrogen-containing synthetic materials releases hydrogen cyanide gas [3,4]. Modern construction materials, plastics, synthetic textiles, polyurethane foam, and other polymer-based products produce significant quantities of hydrogen cyanide when burned, making smoke inhalation one of the leading causes of cyanide poisoning in emergency medicine [6]. Consequently, victims rescued from enclosed structural fires frequently experience combined carbon monoxide and cyanide poisoning, significantly increasing mortality and complicating clinical management. Additional sources of cyanide exposure include naturally occurring cyanogenic glycosides found in certain plants and foods. Cassava root, bitter almonds, apricot kernels, peach pits, and several other plant species contain compounds capable of releasing cyanide following enzymatic hydrolysis during digestion. Improper preparation or excessive consumption of these foods has resulted in both acute poisoning and chronic neurological disorders in populations relying heavily on cassava as a dietary staple [5]. Certain pharmaceutical agents, industrial chemicals, electroplating compounds, mining operations, and laboratory reagents also represent potential sources of occupational or accidental cyanide exposure. Although dermal absorption and injection are uncommon routes of poisoning, they remain clinically important in industrial settings involving highly concentrated cyanide solutions. The nonspecific clinical manifestations of cyanide poisoning, including headache, dizziness, confusion, dyspnea, hypotension, seizures, and altered mental status, often resemble other toxicological and medical emergencies, making early diagnosis particularly challenging. Therefore, healthcare assistants, paramedics, emergency clinicians, and health informatics professionals play essential roles in recognizing potential exposure scenarios, facilitating rapid diagnosis, initiating supportive care, and implementing evidence-based treatment protocols. Increased awareness of cyanide toxicity, coupled with timely administration of antidotal therapy and advanced supportive measures, remains critical for improving patient survival and reducing the devastating consequences associated with this rapidly progressive toxicological emergency.

### **Etiology and Individuals at Risk of Cyanide Exposure**

Cyanide toxicity arises from exposure to cyanide-containing compounds through inhalation, ingestion, dermal absorption, or, less frequently, parenteral administration. The likelihood of poisoning depends on the route of exposure, the concentration of cyanide, the duration of contact, and the individual's physiological condition. Although cyanide poisoning remains relatively uncommon, certain occupational, environmental, and clinical settings significantly increase the risk of exposure. Understanding the various etiological factors and identifying high-risk populations are essential for timely diagnosis, appropriate preventive measures, and rapid therapeutic intervention. Inhalation of hydrogen cyanide (HCN) gas represents the most common cause of acute cyanide poisoning. Hydrogen cyanide is rapidly absorbed through the respiratory tract because of its high volatility and ability to diffuse readily across the alveolar-capillary membrane. The majority of inhalational exposures occur during structural and residential fires involving the combustion of nitrogen-containing synthetic materials such as plastics, polyurethane foam, nylon, wool, rubber, and other polymer-based products [7–12]. Victims trapped in enclosed fires are particularly vulnerable because hydrogen cyanide frequently coexists with carbon monoxide, resulting in combined toxic exposure that markedly increases morbidity and mortality. Firefighters, emergency medical personnel, and rescue workers may also be exposed during firefighting operations, particularly when appropriate respiratory protective equipment is unavailable or inadequately used.

Intentional ingestion of cyanide salts remains the leading cause of cyanide poisoning associated with suicide attempts. Sodium cyanide and potassium cyanide are the compounds most frequently involved because of their rapid dissolution in gastric acid, producing hydrogen cyanide gas that is readily absorbed through the gastrointestinal tract. Acute ingestion results in rapid onset of neurological and cardiovascular symptoms, often progressing to respiratory arrest and death if antidotal therapy is delayed. Accidental ingestion may also occur through laboratory accidents, improper storage of industrial chemicals, or contamination of food and beverages. Natural dietary sources constitute another important, although less common, cause of cyanide exposure. Several plants contain cyanogenic glycosides that release hydrogen cyanide following enzymatic hydrolysis during chewing or digestion. Cassava root represents the most clinically significant dietary source, particularly in regions where it serves as a staple food. Inadequate processing of cassava can result in substantial cyanide exposure, as demonstrated during the 2017 outbreak in Uganda, where highly cyanogenic cassava flour was identified as the cause of poisoning in 33 individuals [14]. Other cyanogenic

foods include bitter almonds, apricot kernels, apple seeds, peach pits, and flax seeds, all of which contain naturally occurring cyanogenic compounds capable of causing toxicity when consumed in excessive quantities or prepared improperly [15]. Occupational exposure remains a significant concern among workers employed in industries that utilize cyanide-containing compounds. Individuals working in electroplating facilities, metal extraction and mining operations, jewelry manufacturing, chemical synthesis, photography, and laboratory research may experience chronic low-level exposure or acute poisoning following industrial accidents [17]. Chemical spills, equipment malfunction, inadequate ventilation, and failure to follow occupational safety protocols increase the likelihood of cyanide intoxication in these environments. Dermal absorption, although relatively uncommon compared with inhalation or ingestion, may occur following direct contact with concentrated cyanide solutions or contaminated clothing. Secondary contamination may also develop in emergency responders or healthcare personnel when patients exposed to cyanide are not adequately decontaminated before medical assessment and treatment [13].

Iatrogenic cyanide toxicity represents another important etiology encountered in clinical practice. Sodium nitroprusside, a potent intravenous vasodilator widely used for the management of hypertensive emergencies and acute heart failure, contains multiple cyanide moieties that are released during metabolism. Under normal therapeutic conditions, cyanide is rapidly detoxified to thiocyanate by the mitochondrial enzyme rhodanese. However, prolonged infusion, high-dose administration, renal impairment, or hepatic dysfunction may overwhelm endogenous detoxification pathways, resulting in cyanide accumulation and systemic toxicity [16]. Although cyanide toxicity associated with sodium nitroprusside is relatively rare, accumulation of its metabolite, thiocyanate, occurs more frequently and may produce neurological manifestations, particularly in critically ill patients receiving prolonged therapy [16]. Several factors increase an individual's susceptibility to cyanide poisoning, including prolonged exposure in confined environments, inadequate use of personal protective equipment, impaired hepatic detoxification, malnutrition, vitamin B12 deficiency, and preexisting cardiopulmonary disease. Healthcare professionals, paramedics, firefighters, industrial workers, laboratory personnel, and emergency responders should maintain a high index of suspicion for cyanide toxicity when evaluating patients with unexplained metabolic acidosis, altered mental status, cardiovascular instability, or smoke inhalation injuries. Early recognition of exposure risk remains fundamental for prompt diagnosis, rapid initiation of antidotal therapy, and improved clinical outcomes.

### Epidemiology

Cyanide poisoning is an uncommon but highly lethal toxicological emergency that accounts for a relatively small proportion of poisoning cases worldwide while contributing disproportionately to poisoning-related mortality. Its epidemiology varies considerably according to geographical location, occupational activities, industrial development, and the prevalence of residential fires involving synthetic materials. Although cyanide exposure is relatively infrequent compared with other toxic agents, rapid onset of toxicity and high fatality rates make it a major concern for emergency physicians, toxicologists, paramedics, and public health authorities. Epidemiological surveillance systems continue to provide valuable information regarding exposure patterns, affected populations, and clinical outcomes, thereby facilitating the development of preventive strategies and evidence-based emergency response protocols. According to annual reports from the National Poison Data System (NPDS), a total of 853 cyanide exposure cases were documented between 2019 and 2023, resulting in 14 deaths and an overall fatality rate of approximately 1.6% [7,9–12]. Adults represented the overwhelming majority of reported cases, accounting for approximately 86.5% of all exposures, whereas only 4.2% occurred in children younger than five years of age. Most exposures were accidental, with approximately 68.2% classified as unintentional, while intentional self-harm accounted for 7.6% of reported cases [7,9–12]. These findings indicate that occupational accidents, environmental exposure, and residential incidents remain more common than intentional poisoning, although suicidal ingestion continues to represent the most severe clinical presentation. Demographic analyses have consistently demonstrated a predominance of cyanide poisoning among males. Approximately 68% of cyanide ingestions occur in male patients, with a mean age of 34 years, reflecting increased occupational exposure among working-age adults as well as greater involvement in industrial environments where cyanide-containing compounds are frequently encountered [4]. Occupational sectors such as mining, electroplating, metal extraction, jewelry manufacturing, chemical production, and laboratory research continue to represent important sources of chronic and accidental cyanide exposure. In these settings, inadequate safety measures, accidental spills, equipment failure, or improper handling of cyanide compounds may result in acute poisoning incidents.

Route of exposure also demonstrates distinct epidemiological patterns. A retrospective study reviewing 49 years of cyanide poisoning cases involving 65 patients found that ingestion accounted for 84.3% of all exposures, followed by inhalation (7.8%), dermal exposure (1%), and intravenous administration (1%) [8]. While ingestion remains the predominant route in intentional poisoning, inhalational exposure has become increasingly important in emergency medicine because hydrogen cyanide generated during structural fires is now recognized as one of the leading causes of cyanide toxicity worldwide. Victims of enclosed-space fires frequently experience simultaneous exposure to both cyanide and carbon monoxide, producing synergistic toxicity associated with increased mortality and neurological complications. Dietary exposure through improperly processed cassava and other cyanogenic foods remains endemic in several low-resource countries where cassava constitutes a staple food, contributing to outbreaks of acute poisoning and chronic neurological disorders. Collectively, these epidemiological observations highlight the importance of

public health education, occupational safety regulations, poison surveillance systems, and rapid emergency response in reducing cyanide-related morbidity and mortality.

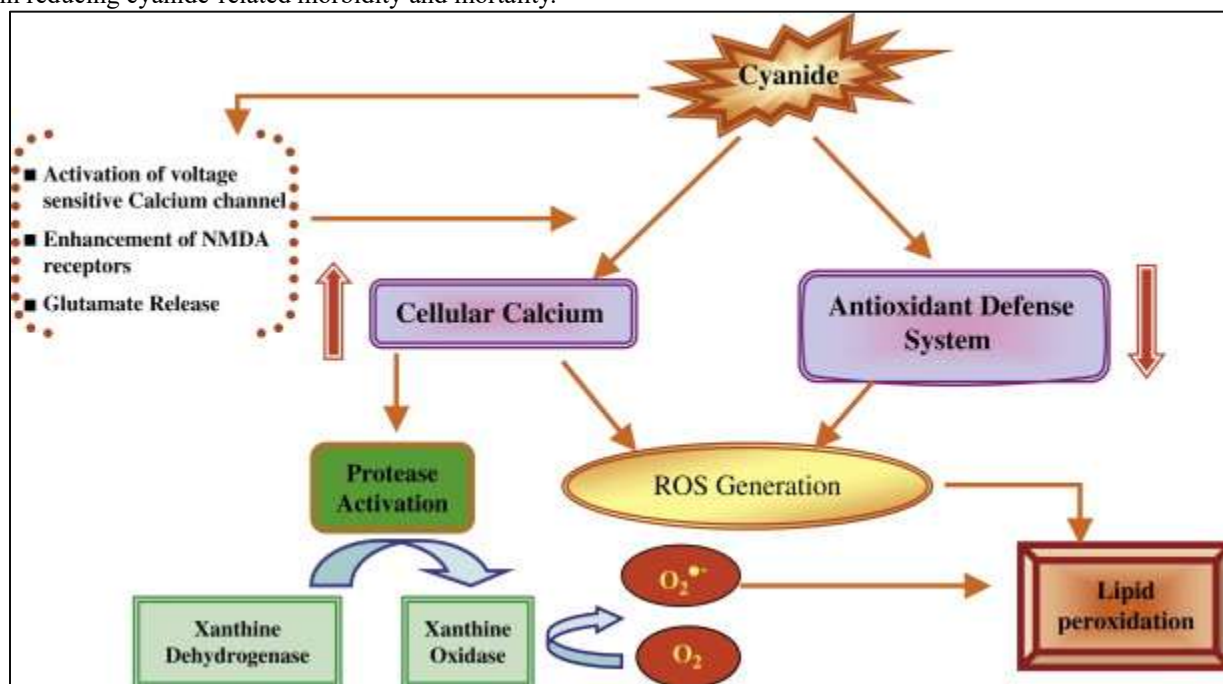


Fig. 1: Cyanide Toxicity.

### Pathophysiology

The pathophysiology of cyanide toxicity is characterized by rapid interruption of aerobic cellular metabolism, resulting in profound cellular hypoxia despite adequate oxygen delivery and normal arterial oxygen saturation. Cyanide exerts its toxic effects primarily at the mitochondrial level, where it inhibits oxidative phosphorylation, the principal biochemical process responsible for adenosine triphosphate (ATP) production. Because ATP serves as the universal energy source for cellular functions, inhibition of mitochondrial respiration produces widespread cellular dysfunction and rapid failure of metabolically active organs, particularly the brain and myocardium. The primary molecular target of cyanide is cytochrome c oxidase (Complex IV), a critical enzyme within the mitochondrial electron transport chain. Cyanide exhibits a high affinity for the ferric ( $\text{Fe}^{3+}$ ) and copper centers of cytochrome c oxidase, preventing the transfer of electrons to molecular oxygen during oxidative phosphorylation [18]. This mechanism closely resembles the toxic actions of hydrogen sulfide and, to a lesser extent, carbon monoxide, both of which interfere with mitochondrial respiration through inhibition of cellular oxygen utilization. As electron transport ceases, oxidative phosphorylation stops completely, ATP production rapidly declines, and cells lose their ability to maintain normal physiological processes. Despite adequate oxygen delivery to tissues, cyanide poisoning produces a state known as histotoxic hypoxia, in which oxygen cannot be utilized because mitochondrial respiration is blocked. Consequently, cells are forced to rely exclusively on anaerobic glycolysis to generate energy. Although anaerobic metabolism temporarily produces limited ATP, it simultaneously generates excessive amounts of lactate. The accumulation of lactate results in profound metabolic acidosis, one of the characteristic biochemical hallmarks of cyanide poisoning [18]. Severe lactic acidosis often develops rapidly and serves as an important diagnostic indicator, particularly in patients presenting after smoke inhalation or suspected cyanide ingestion. Cellular energy failure has widespread physiological consequences affecting virtually every organ system. The central nervous system is particularly vulnerable because neurons possess minimal energy reserves and depend almost entirely on continuous aerobic metabolism. As ATP production declines, neurological manifestations progress rapidly from headache, dizziness, and confusion to seizures, coma, and respiratory depression. Similarly, myocardial cells experience impaired contractility, arrhythmias, hypotension, and ultimately cardiovascular collapse. Failure of sodium-potassium ATPase pumps results in intracellular sodium and calcium accumulation, cellular edema, membrane dysfunction, oxidative stress, and activation of inflammatory pathways that further exacerbate tissue injury. Without rapid administration of antidotal therapy and restoration of mitochondrial function, irreversible cellular damage progresses quickly, leading to multiorgan failure and death.

### Toxicokinetics

The toxicokinetic profile of cyanide is characterized by rapid absorption, widespread tissue distribution, limited endogenous detoxification capacity, and efficient renal elimination following metabolic conversion. The onset, severity, and clinical outcome of cyanide poisoning depend on several factors, including the chemical form of cyanide, route of exposure, absorbed dose, duration of exposure, and the individual's metabolic capacity. Because cyanide acts

rapidly after systemic absorption, understanding its toxicokinetic properties is essential for early recognition and prompt treatment. Hydrogen cyanide gas is absorbed almost instantaneously through the pulmonary alveoli following inhalation, allowing symptoms to develop within seconds after exposure [18]. This rapid absorption explains the high mortality associated with enclosed-space fires and industrial accidents involving cyanide gas. Oral ingestion of cyanide salts, including sodium cyanide and potassium cyanide, generally produces symptoms within minutes to several hours, depending on gastric emptying, food intake, and the quantity ingested [18]. Dermal absorption is relatively uncommon because intact skin provides some protection; however, concentrated cyanide solutions or prolonged exposure can produce systemic toxicity within minutes to hours, particularly when skin integrity is compromised [18]. Cyanide toxicity associated with intravenous sodium nitroprusside usually develops after prolonged administration over several days, particularly when detoxification mechanisms become overwhelmed. The principal detoxification pathway involves enzymatic conversion of cyanide to thiocyanate by the mitochondrial enzyme rhodanese, also known as thiosulfate cyanide sulfurtransferase [19,20,30]. Rhodanese utilizes sulfur donated from endogenous thiosulfate to convert highly toxic cyanide into the substantially less toxic thiocyanate, which is subsequently eliminated by renal excretion. During severe poisoning, endogenous sulfur stores become rapidly depleted, limiting cyanide detoxification and allowing toxic concentrations to accumulate. Administration of sodium thiosulfate replenishes sulfur donors, thereby enhancing rhodanese-mediated detoxification. Hydroxocobalamin provides an alternative elimination pathway by directly binding cyanide to form cyanocobalamin (vitamin B12), which is readily excreted in urine [19,20]. The toxic and lethal doses of cyanide vary according to its chemical form and route of exposure. In adults, ingestion of approximately 50–100 mg of sodium or potassium cyanide may produce fatal poisoning, while doses approaching 200 mg are generally considered lethal for most individuals [21]. The estimated average fatal dose is approximately 1.52 mg/kg, although fatalities have occurred at doses as low as 0.52 mg/kg [21]. Clinical outcomes vary considerably depending on the speed of medical intervention and antidote administration. Case reports illustrate this variability, with an 84-year-old man dying after ingestion of 400–800 mg of potassium gold cyanide, whereas an 18-year-old patient survived ingestion of 975–1300 mg but subsequently developed persistent Parkinsonian neurological sequelae [22,23]. These observations emphasize that early diagnosis, rapid supportive care, and prompt antidotal treatment remain the most important determinants of survival following cyanide exposure.

### History and Physical Examination

Accurate diagnosis and timely management of cyanide poisoning rely heavily on obtaining a comprehensive clinical history and performing a focused physical examination. Because cyanide toxicity progresses rapidly and no single bedside diagnostic test is immediately available, clinicians must maintain a high index of suspicion, particularly when evaluating patients with compatible exposure histories and unexplained neurological or cardiovascular deterioration. Early recognition is especially important for emergency physicians, paramedics, healthcare assistants, and prehospital providers, as prompt initiation of antidotal therapy substantially improves survival. The clinical history should begin with identification of the suspected route of exposure, as the onset, severity, and progression of symptoms vary considerably depending on whether cyanide was inhaled, ingested, absorbed through the skin, or administered iatrogenically. Inhalation and ingestion remain the two most common routes of exposure, whereas dermal absorption and injection are relatively uncommon [18]. Determining the duration of exposure, estimated dose, and timing of symptom onset is essential because these factors influence disease severity and therapeutic decision-making. Patients exposed to hydrogen cyanide gas generally develop symptoms within seconds to minutes because of rapid pulmonary absorption. Conversely, individuals who ingest cyanide salts may experience symptom onset ranging from several minutes to a few hours depending on gastric contents, dose ingested, and the chemical formulation [1].

Exposure history should include careful questioning regarding involvement in structural or enclosed-space fires, occupational exposure in industries such as mining, electroplating, chemical manufacturing, jewelry production, and laboratory work, as well as potential intentional ingestion during suicide attempts. Clinicians should also inquire about recent administration of sodium nitroprusside in critically ill patients, particularly when prolonged infusion or renal impairment is present. Dietary history is equally important because ingestion of cyanogenic foods, including improperly processed cassava, bitter almonds, apricot kernels, peach pits, and apple seeds, has been associated with cyanide poisoning outbreaks in several regions of the world [18]. Clinical manifestations are generally nonspecific and involve multiple organ systems because cyanide disrupts aerobic metabolism throughout the body. Neurological symptoms are often among the earliest findings and include headache, dizziness, anxiety, confusion, weakness, agitation, and impaired concentration. As toxicity progresses, patients may develop altered mental status, seizures, coma, and loss of protective airway reflexes. Respiratory manifestations range from tachypnea and dyspnea during the initial compensatory phase to respiratory depression and respiratory arrest in advanced poisoning. Gastrointestinal symptoms such as nausea, vomiting, abdominal pain, and cramping are particularly common following oral ingestion [18]. Physical examination should focus on rapid assessment of airway, breathing, circulation, and neurological status. Cardiovascular abnormalities frequently include tachycardia during early poisoning, followed by ventricular dysrhythmias such as ventricular tachycardia and ventricular fibrillation. Patients may initially exhibit hypertension associated with reflex bradycardia before progressing rapidly to profound hypotension, circulatory shock, and cardiovascular collapse as mitochondrial energy failure worsens [18]. Neurological examination often reveals progressive deterioration in consciousness, while respiratory assessment may demonstrate hyperventilation followed

by hypoventilation as respiratory muscle fatigue develops. Several classic physical findings have traditionally been associated with cyanide poisoning, although they are neither sensitive nor consistently present. Cherry-red skin coloration, resulting from impaired peripheral oxygen extraction, occurs in only approximately 11% of patients, while the characteristic bitter almond odor on the breath is detected in approximately 15% of cases and cannot be recognized by many individuals because of inherited genetic differences in olfactory perception [8]. Consequently, the absence of these classical findings should never exclude cyanide poisoning. Instead, diagnosis should be guided by the clinical context, exposure history, rapid symptom progression, and evidence of severe metabolic dysfunction [8, 18].

### Evaluation

The diagnosis of cyanide poisoning remains primarily clinical because no rapid, widely available laboratory test exists to definitively confirm cyanide exposure during the initial emergency evaluation. Consequently, clinicians must integrate exposure history, clinical presentation, physical examination findings, and supportive laboratory abnormalities to establish the diagnosis and initiate treatment without unnecessary delay. Waiting for confirmatory cyanide concentrations may result in irreversible cellular injury or death because laboratory measurement of blood cyanide levels is generally unavailable in most emergency departments and often requires specialized toxicology laboratories with prolonged turnaround times. One of the most valuable laboratory indicators of cyanide poisoning is severe lactic acidosis. Cyanide inhibits mitochondrial oxidative phosphorylation, forcing cells to rely exclusively on anaerobic glycolysis for energy production. The resulting accumulation of lactate produces profound metabolic acidosis that closely correlates with the severity of poisoning. Serum lactate concentrations of 8 mmol/L or greater have demonstrated high sensitivity and specificity for clinically significant cyanide toxicity among patients with suspected exposure, particularly following smoke inhalation or cyanide ingestion [24]. Elevated lactate levels should therefore strongly prompt consideration of cyanide poisoning in patients presenting with unexplained metabolic acidosis. Another important diagnostic finding results from impaired tissue oxygen utilization. Because cyanide prevents cellular oxygen extraction rather than oxygen delivery, venous blood retains unusually high oxygen concentrations, a phenomenon known as arterialization of venous blood. Central venous oxygen saturation values exceeding 90% are highly suggestive of cyanide toxicity, although similar findings may also occur in hydrogen sulfide and carbon monoxide poisoning [25]. Likewise, venous blood may appear unusually bright red because oxygen remains bound to hemoglobin instead of being utilized by peripheral tissues. These findings reflect the underlying mechanism of histotoxic hypoxia characteristic of cyanide poisoning.

Because cyanide poisoning frequently occurs in victims of enclosed-space fires, simultaneous exposure to carbon monoxide is common. Measurement of carboxyhemoglobin concentrations using carbon monoxide co-oximetry is therefore recommended, particularly in critically ill smoke inhalation victims. Identifying concurrent carbon monoxide poisoning is important because dual toxicity is associated with significantly greater neurological injury, cardiovascular compromise, and mortality than either toxin alone. Comprehensive toxicological evaluation should therefore consider both conditions during the initial assessment. Routine laboratory investigations provide valuable information regarding organ function and help exclude alternative diagnoses while monitoring disease progression. Initial investigations should include complete blood count, serum electrolytes, renal function tests, liver function tests, arterial or venous blood gas analysis, serum lactate concentration, coagulation profile, blood glucose, and cardiac biomarkers such as troponin to evaluate myocardial injury. Electrocardiography should be performed to detect arrhythmias, myocardial ischemia, or conduction abnormalities associated with severe poisoning. Chest radiography may be indicated in smoke inhalation victims to evaluate concomitant pulmonary injury, whereas computed tomography of the brain may be considered in patients with persistent neurological deficits after stabilization. Ultimately, cyanide poisoning remains a time-critical clinical diagnosis. Laboratory investigations should support rather than delay treatment, particularly in patients presenting with compatible exposure history, rapidly progressive neurological impairment, cardiovascular instability, severe metabolic acidosis, and markedly elevated serum lactate. Early recognition, immediate supportive care, and prompt administration of specific antidotal therapy remain the most important determinants of patient survival and favorable neurological outcomes [25].

### Treatment and Management

The management of cyanide poisoning constitutes a true medical emergency because of the rapid progression from cellular hypoxia to cardiovascular collapse, neurological injury, and death. Successful treatment depends on early recognition, immediate supportive care, rapid decontamination when appropriate, and prompt administration of specific antidotal therapy. Because cyanide inhibits mitochondrial oxidative phosphorylation within minutes of exposure, treatment should never be delayed while awaiting laboratory confirmation. Instead, clinical suspicion based on exposure history and characteristic manifestations should guide immediate therapeutic intervention. Effective management requires close collaboration among emergency physicians, paramedics, critical care specialists, toxicologists, nurses, and other healthcare professionals to ensure rapid stabilization and continuous monitoring. The initial management of patients with suspected cyanide poisoning follows the standard principles of advanced life support, beginning with assessment and stabilization of the airway, breathing, and circulation (ABC). Airway protection is particularly important because neurological deterioration may occur rapidly, resulting in loss of protective airway reflexes, decreased consciousness, seizures, or respiratory arrest. Supplemental oxygen should be administered immediately at the highest available concentration, preferably 100% oxygen delivered through a non-rebreather mask

or mechanical ventilation following endotracheal intubation when indicated. Although oxygen alone does not reverse cyanide-induced histotoxic hypoxia, maximizing oxygen delivery remains essential while definitive therapy is initiated. Patients who develop respiratory insufficiency require prompt ventilatory support with continuous monitoring of oxygen saturation, end-tidal carbon dioxide, and arterial blood gases [26].

Cardiovascular stabilization is equally critical because cyanide poisoning frequently progresses to severe hypotension, dysrhythmias, myocardial depression, and circulatory shock. Continuous electrocardiographic monitoring should be established immediately to detect life-threatening arrhythmias such as ventricular tachycardia or ventricular fibrillation. Intravenous access should be secured promptly to facilitate fluid resuscitation, antidote administration, and vasoactive drug therapy. Isotonic crystalloid solutions are generally administered initially to restore intravascular volume and improve tissue perfusion. If hypotension persists despite adequate fluid replacement, vasopressor agents such as norepinephrine may be required to maintain adequate mean arterial pressure and organ perfusion. Patients with severe poisoning should be managed in an intensive care setting where continuous hemodynamic monitoring and advanced organ support are available. Decontamination is an important component of management when external contamination or recent ingestion is suspected. Patients exposed through dermal contact should undergo immediate removal of contaminated clothing followed by thorough washing of the skin with soap and copious amounts of water to prevent continued absorption and secondary contamination of healthcare personnel. Appropriate personal protective equipment should be worn by medical staff during decontamination procedures, particularly when volatile cyanide compounds are involved. In cases of recent oral ingestion, activated charcoal may be considered if administration can occur within an appropriate time frame and the patient's airway is protected. Activated charcoal has demonstrated the ability to adsorb approximately 35 mg of cyanide for every gram administered, thereby reducing gastrointestinal absorption [26,27]. However, activated charcoal should never be administered to patients with active vomiting, seizures, or impaired consciousness unless endotracheal intubation has been performed because aspiration may result in serious pulmonary complications [26,27].

Specific antidotal therapy remains the cornerstone of definitive treatment for cyanide poisoning. Current guidelines recommend hydroxocobalamin as the preferred first-line antidote because of its rapid mechanism of action, favorable safety profile, and effectiveness across a broad range of exposure scenarios. Hydroxocobalamin is a precursor of vitamin B12 that directly binds cyanide ions to form cyanocobalamin, a stable, nontoxic compound that is subsequently eliminated through renal excretion. The standard adult dose consists of 5 g administered intravenously over approximately 15 minutes, with a second 5 g dose administered if clinical improvement is inadequate or severe poisoning persists, resulting in a maximum recommended dose of 10 g [28]. Although this dose greatly exceeds normal physiological vitamin B12 requirements, hydroxocobalamin is generally well tolerated. Common adverse effects include transient reddish discoloration of the skin, mucous membranes, plasma, and urine, as well as temporary interference with certain laboratory investigations because of specimen discoloration [28]. These effects are benign and should not discourage its administration in suspected cyanide poisoning. Alternative antidotal therapy consists of sodium nitrite combined with sodium thiosulfate, although this regimen has largely been replaced by hydroxocobalamin in many countries because of several important limitations. Sodium nitrite induces the formation of methemoglobin, which competes with cytochrome oxidase for cyanide binding, thereby reducing mitochondrial toxicity. However, excessive methemoglobin formation may impair oxygen transport and produce significant tissue hypoxia, particularly in patients with anemia, smoke inhalation injury, or concurrent carbon monoxide poisoning. Furthermore, sodium nitrite possesses potent vasodilatory properties that may worsen hypotension in critically ill patients already experiencing cardiovascular instability. Sodium thiosulfate acts as a sulfur donor that enhances endogenous detoxification through activation of the mitochondrial enzyme rhodanese, promoting conversion of cyanide into thiocyanate for renal elimination. Although sodium thiosulfate remains an effective adjunctive therapy, its relatively limited penetration into the central nervous system reduces its effectiveness in protecting highly vulnerable brain tissue, including the basal ganglia, where cyanide-induced injury is particularly severe [19]. Following initial stabilization and antidotal treatment, patients require continuous monitoring of neurological status, cardiovascular function, acid-base balance, serum lactate concentrations, renal function, and oxygenation. Management of complications such as seizures, metabolic acidosis, arrhythmias, and multiorgan dysfunction should follow established critical care protocols. Early diagnosis, aggressive supportive care, prompt administration of hydroxocobalamin, and multidisciplinary critical care management remain the most important determinants of survival and favorable neurological recovery in patients with acute cyanide poisoning [19].

### Differential Diagnosis

The diagnosis of cyanide poisoning can be challenging because its clinical manifestations are nonspecific and overlap with several other toxicological and medical emergencies. Patients commonly present with altered mental status, metabolic acidosis, hypotension, respiratory distress, and cardiovascular instability, findings that are shared by numerous conditions. Carbon monoxide poisoning is the most important differential diagnosis because both toxins are frequently encountered simultaneously in victims of enclosed-space structural fires. Both conditions impair cellular oxygen utilization and may produce neurological dysfunction, myocardial injury, and hypoxia. Hydrogen sulfide poisoning should also be considered because it inhibits mitochondrial cytochrome oxidase through a mechanism similar to cyanide, resulting in severe cellular hypoxia and circulatory collapse. Additional differential diagnoses include septic shock, severe lactic acidosis, opioid overdose, methanol poisoning, ethylene glycol poisoning,

hypoglycemia, and acute ischemic stroke. Classical findings such as cherry-red skin or a bitter almond odor are unreliable and should not be relied upon for diagnosis [8].

### Prognosis

The prognosis of cyanide poisoning depends primarily on the dose of exposure, route of intoxication, rapidity of diagnosis, and timely administration of appropriate antidotal therapy. Patients who receive immediate supportive care and hydroxocobalamin shortly after exposure generally have favorable outcomes, whereas delays in treatment markedly increase mortality and the risk of permanent neurological injury. Severe poisoning frequently results in prolonged tissue hypoxia that predominantly affects highly metabolically active brain regions, particularly the basal ganglia. Survivors may subsequently develop persistent neurological sequelae resembling Parkinson's disease, including bradykinesia, rigidity, hypomimia, slowed speech, cognitive impairment, and gait abnormalities [29]. Overall mortality varies considerably according to the type of exposure. A comprehensive review of cyanide ingestions reported an approximate fatality rate of 26% among ingestion cases [8], whereas National Poison Data System reports between 2019 and 2023 documented an overall fatality rate of 1.6% across all exposure routes and circumstances [7,9–12].

### Complications

Cyanide poisoning can result in numerous acute and long-term complications because of widespread impairment of cellular respiration and tissue oxygen utilization. Neurological complications are among the most common and may include seizures, coma, episodic memory impairment, cognitive dysfunction, dizziness, gait instability, dystonia, and persistent Parkinsonian manifestations caused by injury to the basal ganglia [30,31]. Cardiovascular complications include tachycardia, ventricular arrhythmias, hypotension, myocardial dysfunction, circulatory shock, and cardiac arrest, all of which significantly increase mortality. Respiratory complications range from tachypnea and dyspnea during the early compensatory phase to respiratory failure requiring mechanical ventilation. Gastrointestinal manifestations, including nausea and vomiting, frequently occur following oral ingestion and may contribute to dehydration and aspiration risk. Severe metabolic acidosis resulting from excessive lactate production further worsens organ dysfunction. In survivors, delayed neurological deficits and functional disability may persist for months or become permanent, emphasizing the importance of early diagnosis, prompt antidotal therapy, and comprehensive rehabilitation following acute cyanide intoxication [30,31].

### Conclusion

Cyanide toxicity is a rapidly progressive toxicological emergency characterized by inhibition of mitochondrial oxidative phosphorylation, resulting in cellular hypoxia, severe metabolic acidosis, and multiorgan failure despite adequate oxygen availability. Although uncommon, cyanide poisoning carries substantial mortality if recognition and treatment are delayed. Prompt identification of exposure history, early clinical suspicion, aggressive supportive care, and immediate administration of specific antidotal therapy, particularly hydroxocobalamin, remain the cornerstones of successful management. Laboratory findings such as elevated serum lactate and severe metabolic acidosis support the diagnosis but should not delay treatment. Advances in emergency medicine, critical care, and toxicology have significantly improved patient survival through standardized treatment protocols and rapid antidote availability. Continued education of emergency physicians, paramedics, healthcare assistants, and health informatics professionals is essential to facilitate early recognition, evidence-based decision-making, and multidisciplinary management, ultimately reducing mortality, preventing long-term neurological complications, and improving clinical outcomes for patients with acute cyanide poisoning.

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