Mechanism of methanol toxicity pdf

cleaning materials, solvents, paints, varnishes, Sterno fuel, formaldehyde solutions, antifreeze, gascoal, moonlight, wind washer liquid (30-40% methanol) and duplicate liquids depressant of the central nervous system, Methanol is potentially toxic in quantities as small as one mouth When metabolized liver alcohol and aldehyde dehydrogenase, methanol forms formaldehyde and form acid, both of which are toxic eyes, CNS, and gastrointestinal affected formic acid is the main toxin that makes up much of the anionic rupture, metabolic acidosis, and the gastrointestinal tract. Lactic acid also promotes anion rupture Ofmic acid suppresses cytochrome oxidase in the fondue of the eye; Swelling of the axons in the visual disk and swelling lead to visual impairment formaldehyde has a short half-life, lasts only a few minutes Formal acid metabolizes much more slowly, and this bio-accumulates with significant vertigo of methanol intake, blurred vision, fuzzy, foggy, or blizzard-like visual impairment of respiratory depression/death. Auxiliary measures and provision of airway protection. Dialysis may be required to remove methanol and its main toxic metabolite, formate. (Although forced diuresis can be considered, as methanol is excreted renail - dialysis works better and has a lower risk of pulmonary edema, brain swelling, or acute respiratory distress syndrome). Attempting to correct acidosis using sodium bicarbonate is indicated if the pH is less than 7.20; Please note that patients may require large amounts. Alkaline pH makes it more likely that famic acid will exist as its anion (formate), which cannot access the central nervous system and the optic nerve as easily. Administering folic acid (leukovorin) 50 mg IV every 4 hours for a few days to the potentate folic acid depends on the metabolism of form acid to carbon dioxide and water. Consider ethanol infusion in any patient with unexplained osmolar rupture and/or elevated anion-gap metabolic acidosis, which is unaccounted for ethanol until a definitive diagnosis of denial of its introduction is made. delay in the treatment of methanol intoxication can lead to increased morbidity and mortality, and timely treatment is essential for full recovery. International Program on Chemical Safety Poison Information Monograph 335 Chemical methanol Aliphatic alcohol carbinol colonial spirit Colombian alcohol methanol methanol (Italian) methylated alcohol (s) methyl alcohol methyl hydroxide monohydroximetan pyroxylic wood wood wood napl alcohol alcohol alcohol. 1.4.1 CAS Number 67-56-1 1.4.2 Other NIOSH numbers: PC 14OOOOO Local only. It doesn't matter. The main risks are heavy metabolic acidosis with an increase in the rupture of anion caused by the accumulation of mimic acid and in the late stages also lactic acid. Acidosis and metabolite pulp cause depression/toxicity of the central nervous system and visual impairment, which may be Full blindness is possible. Targeted organs: central nervous system and retina. Neurological: Early signs of mild intoxication and drowsiness. Delays appear after 8 - 36 hours: headache, dizziness, drowsiness, coma, and sometimes convulsions. Extended pupils, with a sluggish or absent mild reflex, occur in conscious patients. Visual impairment: Vision becomes blurred or blacked out, and may be enough to impair light perception or cause complete blindness. There is a disturbance of the pupil's response to light, and a shrinking field of vision, a cattle, and flashing lights. Visual impairment can be permanent. Visual disc hyperemia is common in the acute stage. Other: Abdominal pain is common; acute pancreatitis can occur. Severe recurrent metabolic acidosis with an increase in anion rupture is caused by the accumulation of formate and is associated with the severity of poisoning. Osmolal rupture also usually rises in the early stages before methanol metabolizes into formic acid. The amilas serum can be elevated. Hyperkalemia can occur associated with metabolic acidosis, and red blood cells medium body volume can be increased. If the definition of methanol cannot be met, the anion and osmal rupture should always be calculated (Jacobsen and McMartin, 1997). The definition of formate in the blood and urine ensimatic method can also be performed, but rarely available in the acute phase. First aid measure Acute poisoning occurs mainly when ingested. All cases of ingestion must be sent to the hospital. If exposure occurred when inhaled or in contact with the skin, remove the patient from exposure, remove contaminated clothing, and wash the skin and eyes thoroughly. Management Principles: Consider emptying the stomach of gastric tinghing after the recent (1 hour) pumping of large quantities. Correct metabolic acidosis with sodium bicarbonate, regulating the rate of administration in accordance with repeated and frequent measurement of acid-base condition. Administering ethanol or phomepisol as an antidote to inhibiting the formation of toxic metabolites. Hemodialysis removes methanol and its metabolites, and helps in the correction of metabolic acidosis. If specific treatment is started early enough, it can prevent death and irreversible damage to vision. Methanol was originally produced as a result of destructive wood distillation, but is now commonly produced from hydrogen and carbon monoxide or carbon dioxide, as well as by hydrocarbon oxidation (Windholz, 1983). Formula: CH3OH Molecular Weight: 32.04 3.3.1 Color Color, Smell: Pulp, Colorless Liquid, with a slight alcoholic smell. 3.3.2 Condition/Form Normal state at room temperature: liquid. 3.3.3 Boiling Point Description: 65 degrees Celsius Melting Temperature: 97.8 degrees Celsius Flash point: 12 degrees Celsius (54 degrees Fahrenheit) Auto-preparation temperature: 470 degrees Celsius (air and l): d20/4: 0.7915 Relative vapour density (air and l): 1.11 pairs of pressure pressure 25 degrees Celsius: 125 mm Hg. (16.2 KP) at 20 degrees Celsius: 94 mm Hg. (vol.% in the air): 6.0 to 36.5 Dangers associated with steam, its dissipation and possible ignition: the liquid is flammable and at normal room temperatures develops vapors that form explosive mixtures in a wide range of concentrations. The risk of inhaling fumes depends on the concentration and duration of exposure (Parmeggiani, 1983). Possible chemical reactions: violent reaction with oxidizing substances such as CrO3, Pb (ClO4)2, HClO4, P2O3, (Lewis, l996). Fire hazards: dangerous when exposed to heat, flames or oxidative agents (Aquilonius et al., 1978). Spontaneous heating: no (Sax et al., 1989). Danger of explosion: modest when exposed to flames (Sax et al., 1989). See also the possible chemical reactions, above. In some countries, dye is added to methanol to distinguish it from ethanol (e.g. in the United Kingdom, purple dye). 4.1.1 Use of industrial/commercial products designed to remove non-home; Industrial - Another removal product; Industrial fuel/ignition source; Industrial - Fuel; Liquid Industrial solvent; Maintenance of industrial vehicles; Industrial - antifreeze (vehicle); Industrial - Fuel supplement; Industrial - Screenwash; Industrial industrial operation - Denaturant; Industrial chemicals used in synthesis; Otherwise, the household/leisure material for drawing the product is not specified; Domestic - stripper paint; Internal fuel/ignition source Domestic - fuel liquid; Maintenance of domestic vehicles; Domestic - antifreeze; Vehicle; Domestic - Screenwash; Domestic Food/Food Pollutant Drinks - Chemical Food Pollutant 4.1.2 Description of Industrial Solvent. Raw materials for the manufacture of formaldehyde and methyl esters of organic and inorganic acids. Antifreeze for radiators and air brakes. Ingredient of gasoline and diesel oil antifreeze. Liquids for washing the windshield. Liquid fuel for small engines used in hobby Fuel for picnic furnaces / solder torches (Windholz; Merck Index, 1983) Solvent for ink, dyes, resins and adhesive ingredients for the removal of paint and varnish (Parmeggiani, l983). A denature for ethanol, which is not intended for human consumption, in concentrations of up to 5% or more (accidental use). Most poisonings occur when ingested. Industrial exposure to methanol vapors is also possible. Sporadic cases of methanol poisoning are usually caused by accidental or suicidal use of a product that may be available in chemical laboratories, and sometimes at home. Poisoning epidemics create very serious problems and are usually the result of the reception of falsified perfumes. Exposure can occur in works related to different uses of the product. Workers should not be exposed to harmful concentrations of steam. However, there is ample evidence from the photographic film industry that repeated exposure to air level exceeding the 200 ppm threshold does not cause significant discomfort or illness (Finkel et al., 1983). In any case, persons with any CNS disorder and/or reduced visual acuity should not be exposed to methanol (Parmeggiani, 1983). Note: Since methanol poisoning often occurs as accidents involving many people, the doctor often deals with medicine catastrophes, and has to change the approach to treatment respectively (Jacobsen and McMartin, 1986). Poisoning can occur as a result of ingestion, inhalation or percutaneous absorption (Dutkiewicz et al., l980; Kahn and Blum, l979). Finished absorbed. Finished absorbed. Finished absorbed. It's possible. It's possible. There are no data. Methanol is easily absorbed from the gastrointestinal tract and respiratory tract, as well as by percutaneous pathway (Dutkiewicz et al., 1980; Kahn and Blum, 1979). After absorption, methanol is widely distributed in the total water of the body with a distribution volume of 0.6 to 0.7 liters/kg (Jacobsen and McMartin, 1997). There is no protein binding (Jacobsen and McMartin, 1986). Undissociated pulp easily crosses the hem-brain barrier. Therefore, aggressive alkaline treatment is important in order to ensure that most formic acids are separated (Jacobsen and McMartin, 1997). It spreads poorly in fatty tissues. The elimination of methanol has zero order at a rate of 8.5 g/l/hour, i.e. about half of ethanol (Jacobsen et al., 1988). If the metabolism of methanol is blocked by ethanol or fomepisol, the removal of methanol occurs very slowly (about 50 hours) and occurs in pulmonary and renal excretion (Brent et al., 2001, Jacobsen et al., 1983). Most methanol is converted into formaldehyde, mainly in the liver, by dehydrogenase alcohol. Formaldehyde is converted into aldehyde dehydrogenase and other enzymes (Jacobsen and McMartin, 1997). In monkeys and rats, methanol is additionally metabolized into carbon dioxide using a folic-dependent single-carbon pathway pool (Vale and Meredith, 1981; Gosselin et al., 1984; Jacobsen and McMartin, 1986). Studies have shown that the rate of oxidation oxidation is regulated by hepatic concentrations of tetrahydrofolate (Eells et al., l982). Concentrations of tetrahydrofolate in the livers of monkeys and humans are significantly lower than in the liver of rats (Johlin et al., 1986), which probably explains the slower metabolism of milling in primates (Jacobsen and McMartin, 1986). Metabolism and methanol toxicity are characterized by important differences between species; in non-primate laboratory animals, methanol itself, rather than its metabolites, is a major toxic agent (Roe, 1982, Gosselin et al., 1984). (See also sections 6.4 and 7.2.2.) Methanol oxidation also occurs in the kidneys (Winchester, l983). The metabolic rate does not depend on plasma concentration, slowly, and is about one-seventh that of ethanol. Full oxidation and methanol may take several days. Since ethanol has an affinity for alcohol dehydrogenase, which is at least 20 times more than methanol, it predominantly serves as a substrate for this enzyme (Gossel and Bricker, 1984). The administration of ethanol (or phomepisol) reduces the rate of methanol oxidation and delays its clinical and biochemical effects. Thirty percent of the ingested dose is excreted without changes in the airways. The kidney emits less than 5% of immutable methanol. Formate is found in urine 4 to 10 days after one exposure (Baselt, 1982a). The release of urine for 70 mg/24 hours confirms the diagnosis of methanol intoxication (Bozza-Marrubini et al., l987). This is comparable to the average concentration of 2-30 mg/L in non-exposure subjects (Baselt, 1982a; Schaller and Tribeg, 1985). The average ratio of urine concentration in the blood to methanol in humans is 1.30 (Baselt, 1982a). Methanol poisoning is characterized by metabolic acidosis and eye damage. The toxicity of methanol is caused by its metabolites, not methanol itself. The severity of toxicity correlates with the degree of metabolic acidosis, not with the concentration of methanol (Jacobsen and McMartin, 1986; 1997; Schwartz et al., 1981). The mechanism of eye damage is not fully understood (Jacobsen and McMartin, 1997). Experimental results show that eye damage is due to the toxicity of formate, regardless of acidosis. However, acidosis probably causes faster development of eye damage (Jacobsen and McMartin, 1986; Martin-Amat et al., 1977; Martin-Amat et al., 1978). Severe metabolic acidosis is typical for methanol poisoning. Initially, acidosis is caused by the cream acid itself. At a more advanced stage, it is also supported by milk acidosis, which may be caused by the inhibition of cytochrome oxidase (see section 7.2.3.3) due to tissue hypoxia (Jacobsen and McMartin, 1986). Concentrations of pulp acid in the blood are proportional to the widening gap in the anion (Sejersted et al., 1983). For this reason, serum bicarbonate levels and baseline excess values are reliable early indicators of the severity of methanol poisoning (Bozza-Marrubini et al., 1987). Pathological results in the autopsy of the liver, kidneys and heart show parenchimatous degeneration. The lungs show desquamation of epithelial, emphysema, swelling, congestion and pneumonia. The brain can show swelling, hyperemia, petehia and heart attack of confuseds, which in severe cases can be hemorrhagic (McLean et al., 1980; Aquilonius, etc., 1980). The eye shows degenerative changes in the retina and swelling of the visual disk, and there may be optic nerve atrophy. The epithelium of the cornea can show degenerative changes. There was also pancreatic necrosis (Bennet et al., 1952). 7.2.1 Human data 7.2.1.1 Adults (volunteers Clinical Case Data) Volunteers After taking 4 ml methanol, urinary minoan acid levels reach a maximum of about 56 mg/l for 2 hours and then decline rapidly (Kendal and Ramanathan, 1953). The peak concentration of methanol in the blood of 117 mg/L (3.6 mmol/L) was reached 1 hour after an adult male volunteer weighing 78.5 kg swallowed 7 ml methanol (Leaf and zatan, 1952). Data on occupational effects in workers exposed to methanol at vapour concentrations of 85 to 134 ppm increased from an average of 13 mg/l in the morning to 20 mg/l by evening (Baselt, 1982a). Clinical data on cases of acute intake of 4 to 10 ml of methanol can cause permanent blindness (Vale s Meredith, 1981; Bozza-Marrubini et al., 1987; Gossel and Bricker, 1984; Litovic, 1986). However, individual susceptibility varies widely, possibly due to frequent simultaneous intake of ethanol and recovery after taking 500 to 600 ml was recorded (Gossel and Bricker, 1984; Litowitz, 1986). A retrospective analysis of data on large-scale methanol poisoning by falsified wine in Italy l986 showed that no one with urine less than 200 mg/L developed any true symptoms or objective clinical signs. Other Human Data (Sax et al., 1989): Human inhaling TCLo: 86,000 mg/m3: IRR Human Eye: 5 ppm. 7.2.1.2 A very limited experience of children with infants suggests that the clinical picture is similar in adults in all important ways (Gosselin et al., 1984), but that children may be more sensitive to toxic effects (Bozza-Marri et al., 1987). Poisoning occurred in a child at the age of 10 weeks, when methanol was mistaken for distilled water and mixed in the child's food (Wenzl et al., 1968). Child poisoning can occur as a result of skin absorption or inhalation (Litovitz, l986). An 8-month-old baby died of methanol toxicity after a cold, rubbing his chest with olive oil and then applying warm methanol compresses (Kahn and Blum, 1979). 7.2.2 Appropriate oral rat animal data: LD50: 5628-l3000 mg/kg oral dog: LDLo: 7500 mg/kg oral monkey: LDLo: 7000 mg/kg rabbit skin: LD50: 20 g/kg inhalation monkey: LCLo: l000 ppm inhalation rat: LC50: 64,000 ppm/4H (Sax et al. l989) Metabolism and methanol toxicity vary markedly between species (Jacobsen and Martin, 1986). In primates and humans, methanol causes metabolic acidosis and eye damage. However, in non-primate laboratory animals it acts as a depressant of the CENTRAL National SN (Gosselin et al., 1984; Rowe, 1982). 7.2.3 Relevant in vitro Data Several enzyme systems involved in the metabolism of methanol have been reported, including specific formaldehyde dehydrogenases found in numerous species and tissues (Tephly and l984). The rate of oxidation of washing out is regulated by the hepatic concentration of tetrahydrofolate (Eells et al., 1982) 1982) Section 6.4). This observation may explain some differences in methanol toxicity between species and justifies therapeutic trials of folic acid (Jacobsen and McMartin, 1986). Formate can inhibit the activity of cytochrome C oxidase in pristine mitochondria, in subsenochondrial particles and in isolated cytochrome aa3. Inhibition increases with the reduction of pH (Nicholls, 1976). This finding may explain the formation of lactate, which occurs at the late stage of severe methanol poisoning (Jacobsen and McMartin, 1986). 7.2.4 TLV Workplace Standards (limit threshold): 200 ppm (Sax et al., 1989) TWA (weighted average) OSHA:200 ppm 260 mg/m3 NIOSH: 800 ppm/15 minutes short-term exposure limit of 7.2.5 Acceptable daily intake of food additives and contaminants The Committee recommended that methanol should be used as a solvent in food only for extraction purposes, and recommended a maximum concentration of 8 ppm in food. There are no data. Methanol is associated with birth defects in rats after both oral (Infurna et al., 1986) and inhalation exposure (Nelson, et al., 1985; Rogers et al., 1993; Bologna et al., 1994). There are no data. The main metabolic interaction occurs with ethanol, and is detailed in sections 6.4 and 10.6. 8.1.1 Sampling and sampling 8.1.1.1.1 Collection of blood and urine samples must be collected to identify methanol and folic acid. 8.1.2 Storage of laboratory samples and samples 8.1.2.1 Toxicological analyses of methanol and formate are stable in biological samples. Methanol, however, is a volatile substance and samples must be stored in tightly restricted containers. During all procedures, precautions should be taken to minimize the loss of alcohol by evaporation. If long-term storage is required prior to analysis, it is recommended to keep samples frozen at -20 degrees Celsius 8.2.2 Test for biological samples 8.2.2.1 Simple quality tests Fast procedures for detecting methanol in the blood (point test): no protein serum filter (1 ml) is added to the 0.1 ml KMnO4 solution (5 g in 100 ml H2O). The test tube should be gently twisted and, after 5 minutes, enough powdered sodium bisulfite should be added to decolonize the permanganate. Freshly prepared solution of chromotropic acid (0.2 ml, 0.5 g at 100 ml H2O) and 6 ml concentrated H2SO4 should be added and mixed and heated in a boiling water bath for 5 minutes. The red-purple color is positive and specific to methanol. 8.2.2.3 Simple quantitative quantification methods can be done with a coloratheria of 570 nm. This method involves measuring the intensity of color after methol oxidation by formaldehyde, and then developing color by reacting formaldehyde with chromotropic acid (CTA). Availability of ethanol oxidized methanol procedure followed by the development of the CTA color if the calibration curve was established using pure methanol methanol Thus, this method can be used for initial detection of methanol, but is unsuitable for monitoring blood methanol levels during anti-dose ethanol treatment (false results) (Tietz, 1986). 8.2.2.4 Advanced quantitative methods of measuring methanol in the blood, gaschmatography is the method of choice. Plasma is diluted: equal volume of internal standard (2 ml methylethylketon in 1:1 water, procedure A (Baselt, 1982b) or: 1:10 with internal standard (3 ml 1 propanol in 1:1 water), procedure B (Blanke, 1975). It is highly recommended to use a pre-column. Column 125 KK; detector 200 degrees Celsius. nitrogen flow rate, 17 ml/minute. Procedure: introduction of 0.5 ml sample; storage time: methanol 0.6 minutes; (ethanol 0.9 minutes); 2.3 minutes. Procedure B: gas chromatographer with interchangeable glass injector, sleeve and flame ionization detector; 5' x 1/4 glass column containing l0% polyethylene glycol (PEG) 400 per 100 to 120 Anaknom 80. Injector 110 degrees Celsius, column 85 degrees Celsius, l25 C detector. nitrogen flow rate, 70 ml/minute Procedure: injecting 1 ml sample; Storage time: methanol 0.585 minutes, ethanol 0.654 minutes, internal standard 6 minutes. A quality control sample containing 1 g/l of each chemical is analyzed daily. 8.2.2.5 Other specialized methods of measuring formate in blood and urine are available by several methods. The Enzyme Method Shaller and Triebig (1985), modified by zuppi and Motalbetti (1986), is accurate (cv by 1 mmol / l 1.5%), simple, This should be the method of choice for large-scale screening in the event of a methanol poisoning epidemic (Soppi and Montalbetti, 1986) if the gas chromatographic definition of methanol cannot be met. In addition, it is easy to give out the enzyme definition of a comrade (zuppi and Montalbetti, 1986). : Fremic acid oxidizes NED in the presence of dehydrogenase (FDH). The amount produced by NADH, measured at 340 nm, is equivalent to the amount acids are present in the sample. HCOOH and NAD' FDH CO2 - NADH - H' Optimal PH for FDH is between between and 7.5; the reaction occurs at ambient temperature. Formate can be measured in any biological fluid (urine, plasma, serum, or whole blood) deproteinized with perchloric acid 0.33 mmol/L Apparatus: Hitachi 705 (Boheringer Mannhein; Rotochem CFA 2000 (Kontron s.p.a.). Detailed procedure and its advantages over other enzyme methods are discussed by zuppi and Montalbetti (1986). HPLC principle: Phamic acid is separated on the column (250 mm x 4 mm) nucleosyl - 10 C18, having as a mobile phase a dual distilled H2O with pH, set at 3.53 sulfuric acid (flow 1 ml/minute pressure on the column 75 bar). Eluate is controlled at 210 Nm. The retention time at pH 3.53 for famic acid is 3.03 minutes. Gas chromatography of gas chromatography of pulpic acid can be performed by two procedures: degradation of fodder acid with benzoic acid or: oxidation of fodder acid to CO and catalytic reduction on the pole to methane; methane is measured by ionizing the flame. 8.2.3 Interpretation of toxicological tests in late stages (severe metabolic acidosis) all ingested methanols can be metabolized and therefore cannot be detected in serum (Jacobsen, 1984). Methanol: To convert conventional units (mg/L) into mmol/L, divide methanol concentrations by 32.04 (Osterloh et al., 1986). Normal blood concentrations: Normal blood methanol concentrations derived from endogenous production and dietary sources, about 15 mg/L (0.05 mmol/L) (range from 2 to 30 mg/L) (Baselt, 1982a). Toxic concentrations in the blood: Recorded concentrations of plasma methanol zgt;5000 mg/L (157 mmol/L) (Gosselin et al., 1984; Gordfoot, 1982). Deadly concentrations: Concentrations of methanol in the blood are not necessarily a reliable predictive index (Baselt, 1982a; Jacobsen and McMartin, 1986). Toxicity clearly correlates with the degree of metabolic acidosis, i.e. the accumulation of pulpic acid. Bennet et al. (1953) reported blood concentrations of 0 to 3900 mg/L (0 to 122 mmol/L) (average 1,300 mg/L or 40 mmol/L) in 11 surviving patients, and concentrations from 0 to 4000 mg/L (0 to 125 mmol/L) (average 1600 mg/L or 50 mmol/L) in 7 who died during treatment (Bennet et al., 1953). Formic acid: Convert conventional units (mg/L) to milliequivalents in L divides formate concentrations 45.02 (Osterloh et al., 1986). Normal blood concentrations: From the literature and experience of collective poisoning of methanol-falsified wine in Italy in 1986, the concentration of pulp acid in normal subjects can vary from 0 to 18 mg/L. According to Baselt (1982a), the concentration of 1982a blood formic acid in normal subjects averages about 5 mg/L, and Osterich et (1986) report that normal formate concentrations are considered to be less than 12 mg/L. In workers exposed to production, the level of mimic acid in the blood increased from 3.2 to 3.2 in pre-received samples up to 7.9 mg/l by evening (Baselt, 1982a). Toxic concentrations in the blood: It has recently been suggested that serum concentrations are more correlated with clinical condition than methanol concentrations, and that the concentrations of the format are a more direct indicator of toxicity (Osterloh et al., 1986; Bozza-Marrubini et al., 1987; Jacobsen et al., 1983a,b; McMartin et al., 1980). It can be expected that blood concentrations exceeding 200 mg/L will lead to eye injuries or

acidosis (Osterloh et al., 1986). Deadly concentrations: Not reported. Concentrations of urine: Normal concentrations of uric acid on average from 2 to 30 mg/L if they are determined by an enmity method (Shaller s Triebig, 1985), and from 2.1 to 289.2 mg/L if they are determined by gas-chromatography (Triebig et al., 1974). According to Baselt (1982a), urine concentrations for the uterine pool range from 2 to 30 mg/L in unexposed subjects as a result of normal metabolism. 8.3.1 Biochemical analysis 8.3.1.1 Blood, plasma or serum of blood arterial gases, serum electrolytes, osmolality, BUN, creatinine and blood glucose. The diagnosis and severity of methanol and ethylene glycol poisoning can also be assessed with reasonable accuracy by indirect methods, i.e. by measuring the degree of metabolic acidosis together with the calculation of anion and osmal clearances (Bozza-Marrubini et al., 1987; Jacobsen and McMartin, 1986; 1997). Acute systemic poisoning can occur when ingested, inhaled, exposed to skin and parenteral irradiation, but ingestion is the main pathway. A summary of the clinical consequences for acute poisoning is provided in section 2.2. 9.1.1 Admission is the main route of impact. Clinical effects after acute poisoning when ingested initially consist of transient intoxication and drowsiness (similar to ethanol poisoning). After a delay period of 6 to 30 hours, the effects of toxic methanol metabolites can cause vomiting, dizziness, abdominal pain, diarrhea, shortness of breath, acidosis (the breath of Kussel), blurred vision, visual disc hyperemia, blindness, dilated pupils (missing light reflex). In very severe cases, anxiety and delusions can occur (Winchester, 1998). Toxic and lethal doses are recorded in section 7.2.3.1. 9.1.2 Inhalation of acute intoxication is rare (Parmeggiani, 1983; Morton Grant, 1986). Indications of intoxication may include irritation of mucous membranes, headache, tinnitus, dizziness, insomnia, nystagmus, dilated pupils, blurred vision, nausea, vomiting, colic and constipation (Parmeggiani, 1983). For toxic effects, see Sections 7.2.1 and 7.2.4. However, the harmful effects described were caused by prolonged exposure to concentrations well above the officially recommended limits 1983). 9.1.3 Skin poisoning by this route was demonstrated in animals (see .9. 7.2.2), and happened in humans (Kahne and Blum, 1979). However, in one case, allegedly related to percutaneous absorption, it is also likely that fumes were inhaled (Kahn s Blum, 1979). 9.1.4 Visual contact of external contact with methanol with the eye causes minor local effects (Morton Grant, 1986) (see section 9.4.9). 9.1.5 Parenteral Exposure No data. Whether there is a chronic form of methanol poisoning remains in question; if it exists, it is very rare (Morton Grant, 1986). Nevertheless, methanol should be regarded as a cumulative poison (Lewis, 1996; Bozza-Marrubini et al., 1987) because of the slowness with which it is eliminated. There is ample evidence that re-exposure to air concentrations well above the 200 ppm threshold does not cause significant discomfort or illness (Finkel et al., 1983). However, people with any central nervous system disorders and/or decreased visual acuity should not be exposed to methanol (Parmeggiani, 1983). 9.2.1 The cumulative effects of eating small but repetitive doses can be very serious (see section 11.2: Observations of the Milan Poison Centre from wine poisoning, falsified methanol in Italy, l986). 9.2.2 Inhalation of daily exposure to methanol vapor can lead to the accumulation of toxic concentrations (Lewis, 1996). Chronic poisoning can occur from inhalation during occupational exposure (Parmeggiani, 1983) to air concentrations of 800 to 3,000 ppm (Leaf and zatman, 1952; Basel, 1982a). In chronic poisoning as a result of inhalation, visual impairment may be the first sign of poisoning. It can start with a slight blurring of vision and progresses to the reduction of visual fields and, theoretically, to complete blindness. 9.2.3 Skin exposure No data. 9.2.4 Eye Contact No data. 9.2.5 Parenteral Exposure No Data. 9.2.6 Other data is not available. The course of methanol, when taken in the body alone, initially causes only mild and transient intoxication and drowsiness. Characteristically, this early stage is followed by a hidden period of 8 to 36 hours (Vale and Meredith, 1981), an average of 12 hours (Proudfoot, 1981). In 2 patients who drank ethanol for 2 days, the hidden period lasted 90 hours (Jacobsen and McMartin, 1986). This hidden period is due to the slow production of formaldehyde and formal acid. Nausea, vomiting, headache, dizziness, or abdominal pain, then a super-emist. Visual impairments such as blurred vision and reduced visual acuity often occur at this stage. Metabolic acidosis with anione rupture and osmolal rupture is typical even in the early stages. Coma, convulsions and death can occur in the later stages of poisoning. The prognosis is theoretically good if treatment is started early. Most patients hospitalized at a late stage and often without to analyze methanol when delays in diagnosis can lead to death (Jacobsen and McMartin, 1986). Severe methanol poisoning is fatal in about 25% of cases (Bozza-Marrubini, 1987). During the epidemic in Atlanta, Georgia, USA, 323 people were poisoned and had a total mortality rate of 6.2% (Bennet et al., l953). After the poisoning of methanol-fake wine in Italy in l986, the Milan Poison Center reported about 34 patients who were hospitalized in several hospitals. Two patients recovered but suffered irreversible visual damage and nine patients died. Bradycardia, hypotension and severe acidosis indicate a poor prognosis (Proudfoot, 1981). In 115 patients with serum bicarbonate levels of less than 20 mek/L, the mortality rate was 19%. An increase of up to 50% in 30 patients with serum bicarbonate levels below 10 mek/L (Bennet et al., 1953). The most common long-term result is visual impairment, usually central scotomatoma or total secondary blindness in relation to optical atrophy. Patients who have gross visual symptoms or signs when received are unlikely to improve (Proudfoot, 1981). Others report that vision is unlikely to show a significant improvement in 6 days (Morton Grant, 1986). Prevention of eye damage depends on surgical treatment to eliminate methanol, and especially its toxic metabolites, from the body. With hemodialysis and cardiopulmonary support, severely poisoned patients who would die will survive (McLean et al., 1980). Unfortunately, they can be forever blind with serious damage to the central nervous system, ranging from moderate polyneuropathy (Aquilonius et al., 1978), to stiffness, spasticity and hypokinesis (Guggenheim et al., 1971), as well as Parkinson's extrapyramidal syndrome with mild dementia (McLean et al., l980). Causes of death are complications of metabolic acidosis, including coma, seizures, cardiovascular collapse, brain swelling and pulmonary edema. Death can be rapid or occur a few hours after being fell into a coma (Winchester, 1996). 9.4.l Cardiovascular patient often looks pale and has cold and sticky limbs (Proudfoot, 1981; Winchester, 1983). Heart rate and blood pressure are usually in order to end during poisoning (Proudfoot, 1981), when cardiovascular failure, bradycardia, hypotension, and myocardial infarction can fade (observations from Milan's poison center). 9.4.2 Respiratory hyperpnoia develops as metabolic acidosis becomes severe and the patient tries to compensate. Respiratory failure can complicate anyone. Pulmonary swelling can be super-news (Bozza-Marrubini et al., 1987). Severe metabolic acidosis is common, but Cuscomaul's breathing (slow, deep breathing) occurs only in 25% of cases (Proudfoot, 9.4.3 Neurological 9.4.3.1 CNS Early: intoxication and drowsiness. These signs are much milder than those caused by (Basel, 1982a; Bozza-Marrubini et al., 1987; Jacobsen and McMartin, 1986). Delay: Headache, dizziness, weakness, motor anxiety. Some patients exhibit a phase of arousal (delirium is possible) to drowsiness and coma superven. Convulsions occur from time to time (Proudfoot, 1981; Bozza Marrubini et al., 1987). Extended pupils with a sluggish or absent light reflex are characteristic, and the disturbance of the pupil's reaction to light is accompanied by a corresponding visual impairment (Morton Grant, 1986). Cerebral swelling and necrosis in Putamen have been documented (McLean et al., 1980). It was reported that the harshness of the nuchals and other signs of menstruation (Litovitz, 1986). 9.4.3.2 Peripheral nervous system The development of visual parallel symptoms or precedes the development of other symptoms (Jacobsen and McMartin, 1986). The visual symptoms described range from spots in front of the eyes and flashing lights, or visual nebula, to markedly reduced visual acuity and complete blindness (Morton Grant, 1986). In the acute phase, visual acuity is usually disturbed by a central or cecocentral scotomata. In the early stages, they are rarely accompanied by a narrowing of peripheral fields. Visual acuity is accompanied by a corresponding disturbance of the pupil's reaction to light; students continue to respond normally to accommodation (Morton Grant, 1986). Visual disc hyperemia is the most common anomaly in acute retinoscopy, and subsides within 2 to 7 days. Peripapilic swelling is also common, but develops more slowly and persists longer (up to 8 weeks) than visual disc hyperemia (Proudfoot, 1981). Venous engorgement and retinal bleeding are not common (Proudfoot, 1981). The subsequent course can range from full recovery, with the disappearance of retinal swelling and the return of normal vision, to persistent retinal swelling within 2 months. Optical atrophy can develop in 1-2 months and vision can be lost (Morton Grant, 1986). Between these extremes there are many cases of partial but permanent visual impairment. Patients whose vision is not restored remain in the central field, and as optical atrophy develops, peripheral fields may shrink (Morton Grant, 1986). Electroretinography in methanol poisoning showed minor changes (b-wave reduction), and in many cases was essentially normal, although patients remained blind. This is consistent with the underlying harmful effects of methanol on retinal ganglion cells and optical nerve fibers (Morton Grant, 1986). 9.4.3.3 No data. 9.4.3.4 Skeletal and Smooth Muscles No Data. Disturbance of the pupil's reaction to light is associated with visual impairment; i.e. this is due to damage to the afferent branch of the light reflex. 9.4.4 Discomfort and abdominal pain of the gastrointestinal tract are very frequent. Violent Colic are common and nausea and vomiting occur in about 50% of cases; only a minority develops diarrhoea. Abdominal pain may precede acute pancreatitis associated with hyperamilasemia and hyperamilasusaria (Gosselin et al., 1984; Winchester, 1983). Back pain may be present (Jacobsen and McMartin, 1986). However, in the only patients who were tested with isoamilas or serum lipase, the striking increase in overall amylase activity in the serum was entirely due to salivary isoamilas, and the activity of lipase in the serum remained perfectly normal. Thus, hyperamilasemia should not be interpreted as a solid evidence of pancreatitis (Eckfeldt et al., 1986). 9.4.5 Liver effects were not reported. The liver of parenchimatous degeneration was described during the autopsy. 9.4.6 Urination 9.4.6.1 Renal cucumber and renal failure can sometimes occur with severe methanol poisoning (Closs et al., 1970). 9.4.6.2 Other data is not available. 9.4.7 Endocrine and reproductive systems (both acute and chronic poisoning) are not reported (Advisory Group, 1985). 9.4.8 Dermatological skin damage can occur as a result of local irritant and dissolved methanol activity (Parmeggiani, 1983). 9.4.9 Eyes, ears, nose, throat (local effects) Visual disturbances arising from methanol system poisoning are detailed in section 9.4.3.2. External contact with the eye is said to cause corneal opacity, but this seems to be the exception, not the rule. Tests in front of the rabbit show that the danger is negligible (Morton Grant, 1986). The staining of the cornea by phforce was observed for 1 month in a patient whose eye was splashed with a mixture of chloroform and methanol (Morton Grant, 1986). In the mucous membranes, the irritating effect of methanol can cause local injuries. 9.4.10 Hematological In one group of patients, the average volume of red cell cells (MCV) was significantly increased in patients with moderate and severe poisoning (Schwarz et al., 1981). 9.4.11 Immunological is not reported (in acute or chronic poisoning). 9.4.12 Metabolic 9.4.12.1 Acid base abnormality The main disorder in methanol poisoning is metabolic acidosis with an increase in anion rupture. Originally acidosis due to the cream acid itself. At a more advanced stage, it is also supported by milk acidosis (see section 7.1). Serum bicarbonate levels and basic excess value are early and reliable indicators of the severity of poisoning (Bozza-Marrubini et al., 1987; Jacobsen and McMartin, 1986). In fact, serum bicarbonate levels are back correlated with the accumulation of formate (McMartin et al., 1980). Metabolic acidosis can be severe and despite the corresponding and repetitive infusions of alkaline solutions (Bozza-Marrubini et al., 1987). 9.4.12.2 Fluid and electrolyte disturbances Increased rupture of anion is a consequence of acid mimic acid (in later stages, lactic acid can also accumulate). Patients poisoned with methanol have an early elevated osmal rupture. The osmal gap is determined by subtracting calculated from measured osmolality (Jacobsen and McMartin, 1986; Saxena et al., 1987). Normal osmolality is 286 mOm/kg H2O, and the normal osmolal gap is 10 mOsm/kg H2O (Litovitz, 1986; Jacobsen and McMartin, 1986; Saxena et al,1987). Calculated osmolality can be obtained using the following equation (Saxena et al., 1987): or by the following formula, using SI units (Jacobsen and McMartin, 1986): (1.86 x Na' urea and glucose) / 0.93 (SI units). The increased osmolal rupture is due to the presence of osmotically active agents such as methanol, ethanol, mannitol, etc. Hyperkalemia can complicate severe metabolic acidosis or rhabdomyolysis. 9.4.12.3 Other data is not available. 9.4.13 Allergic Reactions No Data. 9.4.14 Other Clinical Effects No Data. 9.4.15 Pregnant women are not at any particular increased risk of acute methanol toxicity. Breastfeeding: No data. Enzyme deficiency does not give greater susceptibility to the toxicity of acute or chronic exposure to methanol. There are no reports of toxic effects of methanol on any breeding phase of bird and mammal species or on the human reproductive cycle (Advisory Group, 1985). Based on the available data, it is unlikely that adverse reproductive effects will result in the impact not exceeding the current TLV of 200 ppm (Advisory Group, 1985). There are no data. Treatment consists of: emptying of the stomach (if indicated); correction of acidosis; ethanol or fumepisol administrations inhibit the formation of toxic metabolites; rapidly reducing the load on the body of methanol and emojialse; Intensive support for multiple organ/system failures. Intensive supportive assistance for multiple organ/system failure is often required. Since severe, recurrent metabolic acidosis is the main feature of methanol poisoning, acidosis correction is a must, perhaps, life-saving, and can prevent eye damage (Proudfoot, 1981; Bozza-Marrubini, et al,1987). The degree of acidosis was found to closely correspond to the severity of poisoning (Bozza-Marrubini et al., 1987; Jacobsen et al., 1983; Morton Grant, 1986). A re-evaluation of the acid-base state is necessary. Sodium bicarbonate should be used. Avoid sodium lactate, as lactate metabolism may be disrupted (Bozza-Marrubini et al., 1987; Gosselin et al., 1984). Correction of acidosis may require 400 to 600 mmol of bicarbonate in first few hours (Jacobsen and McMartin, 1986). Fluids should be given orally or intravenously maintaining adequate urine volume (Bozza-Marrubini et al., 1987). Hyperkalemia is usually corrected by the introduction of bicarbonate (see also treatment guide: hyperkalemia). It is possible to consider the special treatment of brain swelling (Bozza-Marrubini et al., 1987; Gosselin et al., 1984). Convulsions should be controlled (see treatment guide: convulsions). Conventional decontamination procedures are necessary in cases of percutaneous exposure or exposure to vapors: removal from exposure, removal of clothing, adequate long-term washing of the skin and eyes. Consider emptying the stomach gastric lavado only after a recent meal (1 hour) of a large amount. Hemodialysis Extracorporeal hemodialysis removes methanol and formate, and, if started early enough, can prevent irreversible damage to vision and death (Proudfoot, 1981; Jacobsen and McMartin, 1986; 1997). Methanol is easily dialisen due to low molecular weight, lack of protein binding and low distribution of 0.7 l/kg (Jacobsen and McMartin, 1986; Gonda et al., 1978). The clearance values are between 150 and 200 ml/minute (Jacobsen and McMartin, 1986), depending on blood flow and surface area in dialysis (Jacobsen and McMartin, 1986). Formate also has a low molecular weight and low distribution (0.5 l/kg) (Jacobsen, 1983b) and clearance values for children range from 140 to 150 ml/minute (Jacobsen, 1983b; Jacobsen and McMartin, 1986). It is difficult to give accurate readings for hemodialysis in methanol poisoning. The only absolute signs are pronounced metabolic acidosis and acidosis in combination with any degree of visual impairment. If fomepisol is given at an early stage of poisoning, before significant acidosis develops, the patient may not need hemodialysis regardless of the concentration of methanol in the blood until acidosis develops. The following may serve as relative indications for hemodialysis: (a) concentrations of methanol in the blood, more than 500-600 mg/L (16-20 mmol/L) (Gonda et al., 1978; Jacobsen and McMartin, 1986; Gosselin et al., 1984; Proudfoot, 1981; Vail and Meredith, 1981; Winchester, 1983; Gossel and Bricker, 1984). Hemodialysis should continue until methanol concentrations fall below 200-300 mg/L (6-10 mmol/L) (Jacobsen and McMartin, 1986; Proudfoot, 1981; Gossel and Bricker, 1984; Winchester, 1983; Gosselin et al, 1984). b) when 20 to 40 ml or more methanol were swallowed by adults (Bozza-Marrubini et al., 1987; Jacobsen and McMartin, 1986; Vail and Meredith, 1981, Gosselin et al., 1984). c) Severe acidosis; base deficit of 15 mmol/L or anony rupture of 30 mmol/L (Gosselin et al., 1984; Vail and Meredith, 1981; Jacobsen and McMartin, 1986). If concentrations of methanol in the blood are not available, hemodialysis should continue for at least 8 hours and repeat quickly if acidosis is repeated (Jacobsen and McMartin, 1986). d) When and do not respond to ethanol and sodium bicarbonate. (e) Oliguria (Closs et al., 1970). (f) Serum blood clot concentration may be a better criterion for hemodialysis than methanol concentrations themselves (Osterloh et al., 1986). It can be expected that concentrations of more than 200 mg/L will be subject to eye injury or acidosis (Osterloh et al., 1986). (g) Some authors suggested that any degree of visual impairment or fondoscopic impairment as signs of hemodialysis (Gonda et al., 1978; Jacobsen and McMartin, 1986). Even during hemodialysis, it is very important to manage bicarbonate and especially ethanol. Since deep acidosis is common, it is prudent to use bicarbonate-based dialysis (Winchester, 1983). In two patients, the average dialysis ratio of ethanol/methanol was recorded as 149/157 and 164/176 ml/minute, respectively (Jacobsen, 1982). In this study, the removal of ethanol hemodialysis was 8.9 and 9.8 g/hour, respectively. This means that in adults the total dose of ethanol from 16 to 20 g/h will need to be replaced by ethanol lost due to metabolism and dialysis. Similar values have been found in other studies (Gonda et al., 1978; Jacobsen and McMartin, 1986). The loss of ethanol in dialysis can be replaced during hemodialysis by increasing the rate of ethanol infusion by 7-10 g/hour (Jacobsen and McMartin, 1986; Vale and Meredith, 1981; Winchester, 1983; Bayer et al., 1984 (103 mg/kg/hour); McCoy et al., 1979). In addition, the addition of ethanol to dialysis (22 mmol/L) (Peterson et al., 1981) was recommended, but this approach has not been tested (Jacobsen and McMartin, l986). The rebound rises in methanol levels to 20 mg/dL after hemodialysis has been reported even up to 36 hours after hemodialysis (Winchester, 1983), which reflects the movement of methanol from tissues into the plasma compartment. Peritoneal dialysis is also sometimes used to eliminate methanol (Wenzl et al., 1968), but much less effective than hemodialysis. Its effectiveness can be significantly increased by adding Alkaline Agent THAM (trometanol or trometamine) to dialysis fluid (Bozza-Marrubini et al., 1987). 10.5.1 Adults there are two alternative antidotes, both of which act by blocking alcohol dehydrogenase-indirectly metabolized methanol: ethanol, fomepisol. (i) ethanol is effective because it has a much greater affinity for alcohol dehydrogenase than methanol. The concentration of ethanol in the blood of 100 mg/DL (22 mmol/L) almost completely blocks the metabolism of methanol (Jacobsen and McMartin, 1986). However, ethanol is sometimes technically difficult to manage because of its fast and unimimligible metabolic rate (Jacobsen and McMartin, 1986). A loading dose is needed, followed by titular supportive therapy. Proposed dosing regimen: Oral intravenous dose of 1 ml/kg 95% ethanol diluted 10 ml/kg ethanol in 5% dextrose for 30 minutes Supporting a dose of 0.1 - 0.2 ml/kg/hour 95% ethanol diluted 1-2 ml/kg 10% ethanol in 5% dextrose for 30 minutes Notes: In an emergency, the equivalent amount of any alcoholic beverage can be administered orally. Dosing service should be adjusted according to the concentration of ethanol in the blood, ideally measured hourly, to maintain concentrations of zgt;100 mg/dL. Prolonged ethanol administration can cause hypoglycemia, especially in children, and frequent blood glucose determinations are mandatory (Goldfrank et al., 1986; Bayer et al., 1984). At the erosaialysis, the infusion of ethanol should be increased, as described in section 10.5. (ii) Fomepisol is easily administered intravenously as a loading dose of 15 mg/kg, followed by doses of 10 mg/kg bolus every 12 hours. After 48 hours, the bolus dose should be increased to 15 mg/kg every 12 hours due to induced metabolism over time. The same dose can be administered orally. No side effects have been reported with this dosage regimen and the effectiveness is clearly demonstrated (Brent et al, 2001). If dialysis is performed, the dose of fomepisol should be increased as fomepisol is eliminated at the same rate as urea. 10.5.2 Children Although there have been fewer reports of ethanol therapy in children, comparable doses can be used. Ethanol is more common in children's hypoglycemia (Bayer et al., 1984). Ethanolol (or phomepisol) itself may be the only treatment in minor or suspected cases hospitalized at a very early stage. Ethanol should be administered as soon as possible after exposure, ideally before the onset of clinical and laboratory studies that indicate extensive methanol metabolism. Continuous and accurate control of ethanol levels is rarely achieved even in intensive care units, especially for long periods of time (Litovitz, 1986; Osterloh et al., 1986). In patients who have a history of severe exposure and taking almost lethal amounts, as well as in patients with high levels of methanol in the blood, early hemodialysis is a must to reduce the body's toxic burden quickly. In the late stages or in cases where repeated exposure to low doses or concentrations of methanol ethanol is of dubious value. When laboratory results indicate the absence of permanent methanol and the accumulation of toxic metabolites (very low or absent methanol in the blood, high levels of emate in the blood and urine), ethanol is probably useless. However, hemodialysis can still be beneficial, as both methanol and formate are dialysis substances. Folic acid or associated ethanol folates and 4-MPs prolong the elimination of methanol, impeding its metabolism. A more effective treatment would be to increase toxic metabolites (formic acids) by increasing their metabolism. Primates are sensitive to poisoning because they do not oxidize formate as easily as rodents due to a relative deficiency in the function of the folic system (Eells et al., 1982; Jacobsen and McMartin, 1986). Processing with folic acid in monkeys, even if it started as early as 10 hours after methanol, prevents the accumulation of formate (Noker et al., 1980). In a recent study, four patients poisoned with methanol were treated with intravenous folic acid and ethanol, in combination with two cases of hemodialysis (Osterloh et al., l986). There was a clear reduction in the half-readiness for their fellow inmates. Folate treatment is safe and seems appropriate since many alcoholics have folic acid deficiency (Osterloh et al., 1986; Saxena et al., 1987). Intravenous folate 1 mg/kg (50 to 70 mg) should be taken intravenously every 4 hours for the first 24 hours, for a total of 6 doses (Osterloh et al., 1986; Jacobsen and McMartin, 1986). Two children's cases reported by Wentzle (1968) and Kahn and Blum (1979) are described in section 7.2.1.2. Widespread poisoning of adulterated methanol wine occurred in Italy in l986 (Bozza-Marrubini, 1987), when a law was passed abolishing high state taxes and fiscal control over methanol. Methanol then became cheaper than ethanol as a result of its use to falsify wine. In two days (March 12-13, 1986) three cases with striking clinical features of the general were transferred to the Milany poisonous department: visual blur, vomiting, headache, metabolic acidosis, followed in two cases by a deep coma with enlarged inactive pupils. Summary of 415 cases observed (176) or follow-up through the Poison Unit Information Service (239), March 13-April 30, 1986 (Bozza-Marrubini, 1987) 381 cases of Formate's 100 mg/l.'s symptoms: none, or very mild.' discharged, no treatment of 34 cases q formate' in urine'gt; in urine 100 mg/L (up to 12,000 mg/L). Hospitalized (11 in Milano P.U., 23 in other hospitals). 5 cases of clinical signs: no, or very mild. Good recovery, no sequels. 16 cases of visual impairment, from one scotoma to total blindness. 14, good recovery; 2, irreversible damage to vision. 13 cases of Comatose. 4, good recovery; Nine deaths. It was necessary to quickly create reliable and fast sorting methods to determine the amount of formate in the urine. Patients, zlt;100 mg/l'of formate' in their urine, even if the mild symptoms were present, received no treatment and were discharged.' even if they were imptomatic, were hospitalized and treated with a forced alkaline diuretic, which was very effective in accelerating the elimination of mine acid. Patients with severe clinical signs were in the intensive care units of various hospitals and were treated only with forced alkaline diuresis or ethanol and/or hemodialysis, depending on the level of methanol and the format found in the blood and urine. Some of the features of methanol wine syndrome were different from the one that was different from that of the zlt;100.- Acute pure methanol poisoning and indicated cumulative effects of relatively small but repetitive doses: the hidden period was extended from at least 2 to 3 days. When the concentration of methanol in the blood was received, the concentration of methanol was usually absent or was low; in patients with severe symptoms, blood methanol never exceeded 200 mg/L, while the content of mimata in plasma and urine was consistently high. Some patients had a benign and even imptomatic course, despite high levels of urine. They were probably protected by the fact that the falsified wine contained both methanol and ethanol. Therefore, the toxic metabolite increased very slowly. After a long period, when the disease has moved to full toxic syndrome (blindness, coma, metabolic acidosis), very high mortality (70%) observed despite intensive treatment. The definition of formate in urine was a fast and reliable diagnostic and screening tool. The value adopted by a priori as a toxic threshold (100 mg/L) was significantly higher than the generally accepted normal level (17-30 mg/L) (Baselt, 1982; Schaller and Tribeg, 1985). A retrospective comparison of clinical and laboratory data showed that the actual toxic threshold was even higher, as no patient with urine-cancer below 200 mg/L had no true symptoms or objective clinical signs. Store the goods in appropriate labeled containers, out of reach of children. Add dyes to methanol to distinguish it from ethanol. Provide relevant information on methanol toxicity in professional settings and for potential users. There are no data. Advisory Group (1985) Effects of toxic chemicals on the reproductive system. Prepared by the Advisory Group of the Council on Reproductive Dangers in the Workplace. American Medical Association, Chicago, Illinois. Aquilonius S.M., Asmark H et al(1978). Computerized tomography for severe methanol intoxication. Br Med J 2: 929-930 Baselt RC (1982a). Recycling toxic drugs and chemicals in humans. 2nd ed. Biomedical Publ. Davis, California: 492. Baselt RC (1982b). 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