INDIAN JOURNAL OF PRACTICAL PEDIATRICS

IJPP

CONTENTS

FROM THE EDITOR'S DESK

The first issue for the year 2009 on "Toxicology", covers some of the common childhood poisonings as topic of interest.

"Poisons and medicine are oftentimes the same substance given with different intents" – Peter Latham [1865].

"Toxicology" is the science of poisons which deals with the nature, effects, detection of poisons and the treatment of poisoning. It is worthy to consider here few general aspects in this field.

Most frequent poisoning we come across include prescribed medications such as salicylates, paracetamol, antiseptics, anticonvulsants as well as non medications like hydrocarbons (kerosene, polish, petrol), cleaning solutions, caustic materials and pesticides.

The reaction to such substances can be a change from a normal state at molecular, cellular. organ systems level or involving entire body system. The changes can be local or systemic, reversible or irreversible, immediate or delayed and graded or quantal. If mortality is the response, the dose that is lethal to 50% of the population is known as LD50,which varies with individual substances.

The toxic effect of a substance on a living organism essentially depends on a) the magnitude of hazard (potential to cause harm), which is an intrinsic property of the substance, b) risk ie, likelihood of harm which is a combination of hazard with probability of exposure and the magnitude and frequency of doses c) exposure (concentration along with duration of contact) and d) dose ie, the amount of chemical that enters the body .

Other important factors which may determine, the toxicity of a substance are: a) Route: Intravenous route is the most dangerous followed by inhalation, intraperitonial, intramuscular, ingestion and topical in that order. b) Absorption, distribution, metabolism and excretion characteristics of the substance. c)Individual's susceptibility where 10-30 fold difference in response can be observed in a population. Individual susceptibility of a population inturn depends on age, nutritional, health status and previous or concurrent exposures (additive, synergistic or antagonistic).

Principles of management include removing poison or the patient from site, initial resuscitation and stabilization, removal of non-absorbed poison,measures for elimination of absorbed poison, specific antidote if any and symptomatic treatment.

Prevention is always better than cure, which holds good for poisoning too. Younger the child more likely the chance that they ingest or come in contact with dangerous material and they should not be left with out supervision. Unintentional or accidental poisoning is usually rare in children more than 5 years of age. Unfortunately, most of the cosmetics and cleaners are distributed in colourful packaging and the children get attracted to them since they look like a candy or toy. It is always better to keep them out of reach of children.

Signs of poisoning are widespread which may be difficulty in breathing or speaking, dizziness, unconsciousness, foaming or burning of mouth, cramps, nausea and vomiting. This should be kept in mind and a high index of suspicion of poisoning is needed in a situation where there is sudden onset of organ disturbance which cannot be explained otherwise.

Dr. K.Nedunchelian,
Editor-in-Chief.

INSTRUCTIONS TO AUTHORS

General

Print the manuscript on one side of standard size A4, white bond paper, with margins of at least 2.5 cm (1") in double space typescript on each side. Use American English using Times New Roman font 12 size. Submit four complete sets of the manuscript.

They are considered for publication on the understanding that they are contributed to this journal solely.

All pages are numbered at the top of the right corner, beginning with the title page.

All manuscripts should be sent to: The Editor-in-Chief, Indian Journal of Practical Pediatrics

Manuscript

1st Page –

Title

Name of the author and affiliation

Institution

Address for correspondence (Email, Phone, Fax if any)

Word count

No. of figures (colour / black and white)

No. of references

Authors contribution

2nd Page –

Abstract (unstructured, not exceeding 100 words) with key words (not exceeding 4)

3rd Page -

Acknowledgement

Points to remember (not more than 5 points)

Text

References

Tables

Figures – should be good quality, 4 copies black & white / colour, (4 x 6 inches – Maxi size) Glossy print. (Each colour image will be charged Rs.1,000/- separately)

Legends

Text

Only generic names should be used

Measurements must be in metric units with System International (SI) Equivalents given in parentheses.

References

Recent and relevant references only

Strictly adhere to Vancouver style

Should be identified in the text by Arabic numerals in parentheses.

Type double-space on separate sheets and number consecutively as they appear in the text.

Defective references will entail rejection of article

Tables

Numbered with Roman numerals and typed on separate sheets.

Title should be centered above the table and explanatory notes below the table.

Figures and legends

Unmounted and with figure number, first author's name and top location indicated on the back of each figure.

Legends typed double-space on separate sheet. No title on figure.

Article Categories

Review article

Article should be informative covering the recent and practical aspects in that field. Main articles can be in 1500 – 2000 words with 12 – 15 recent references and abstract not exceeding 100 words.

Case report (covering practical importance)

250 – 600 words, 8 – 10 recent references

Clinical spotters section

100 – 150 words write up

With 1 or 2 images of clinically recognizable condition

(of which one could be in the form of clinical photograph / specimen photograph / investigation)

Letters to the Editor

200 – 250 words pertaining to the articles published in the journal or practical viewpoints with scientific backing and appropriate references in Vancouver style.

Check List

Covering letter by corresponding author

Declaration (as enclosed) signed by all authors **

Manuscript (4 copies)

Accompanied by a copy in CD / or submit as an email attachment in addition to hard copy.

Failing to comply with the requirement at the time of submission would lead to the rejection of the article.

Author's contribution / Authorship Criteria

All persons designated as authors should qualify for the authorship. Authorship credit should be based on substantial contributions to i) concept and design, or collection of data, and interpretation of data; ii) drafting the article or revising it critically for important intellectual content; and iii) final approval of the version to be published. All conditions i), ii) and iii) must be met.

**Declaration by authors

I/We certify that the manuscript titled '…………………………….' represents valid work and that neither this manuscript nor one with substantially similar content under my/our authorship has been published or is being considered for publication elsewhere. The author(s) undersigned hereby transfer(s), assign(s), or otherwise convey(s) all copyright ownership, including any and all rights incidental thereto, exclusively to the Indian Journal of Practical Pediatrics, in the event that such work is published in Indian Journal of Practical Pediatrics. I / we assume full responsibility for any infringement of copyright or plagiarism.

Authors' name(s) in order of appearance in the manuscript

Signatures (date)

All manuscripts, which are rejected will not be returned to author. Those submitting articles should therefore ensure that they retain at least one copy and the illustrations, if any.

Selection procedures

All articles including invited articles will be peer reviewed by two masked reviewers. The decision of the Editorial Board based on the reviewers' comments is final.

<div style="text-align:center">

TOXICOLOGY

</div>

ORGANOPHOSPHATE, CARBAMATE AND RODENTICIDE POISONING IN CHILDREN

* Rajendiran C
**Ravi G
***Thirumalaikolundu Subramanian P

Abstract : Organophosphate, carbamate and rodenticide poisoining are less common among children. The mode of occurence is usually accidental in children. The pathophysiology, clinical features, diagnosis and treatment of these poisoning are covered in this article.

Key words: *Poisoning, Organophosphate, Organocarbamate, Rodenticide, Children.*

Poisoning is less common among children and takes hundreds of innocent small lives every year. Unfortunately, most of these miseries are accidental and unintentional. Poisonings due to pesticides and rodenticides are relatively less compared to kerosene and drug over dosage in India. But because of their easy availability and accessibility, practitioners should have adequate knowledge about them. There is a need to strengthen the ability to diagnose and treat them.

*   Professor of Medicine

**   Asst. Professor of Medicine

    Poison Control Training & Research Center,
    Institute of Internal Medicine,
    Madras Medical College, Chennai.

***   Director (Retd), Institute of Internal Medicine,
    Madras Medical College, Chennai.

ORGANOPHOSPHATE AND CARBAMATE POISONING

Epidemiology

In the absence of national registers or reliable hospital based data, one looks forward to tertiary hospital for data. Accordingly organophosphate (OP) and carbamate poisonings comprise less than one percent of total poisonings. Rodenticide poisoning is far less than pesticides.

The incidence of pesticide poisoning tends to be higher among children from lower socio-economic class of society due to poor storage facility and parental negligence. Inexperience, lack of maturity, illiteracy and inability to assess the risk make them prone for accidental ingestion.

Older children and adolescents may be directly exposed as field workers, while younger children may be brought into treated fields to accompany their parents. Work clothes often carry pesticide residues, exposing both workers and family members.

Stress factors for poisoning are grouped as family stress (death of a parent, mental illness in a parent, financial problems, conflicts among parents, parental alcoholism, divorce, separation etc.), parent stress (punitive parent, conflict with parents etc.) and school stress (poor academic achievement, examination failures, change of school, teacher stress, etc).

Pathophysiology

Organophosphorous compounds (OPC) and carbamates bind to one of the active sites of

acetylcholinesterase (AChE)[1] and inhibit the functionality of this enzyme by means of stearic inhibition. Carbamylation of esters are quickly reversible than phosphorylation of the esters. Phosphorylation of the esters in AChE will undergo "ageing" process. Aging means loss of one alkyl or alkoxy group leading to stable mono alkyl or mono alkoxy phosphoryl AChE occuring over a period of 48 hours after exposure. Spontaneous regeneration of phosphorylated AchE requires days to months.

The main function of AChE is to hydrolyze acetylcholine (ACh) to choline and acetic acid. Therefore, the inhibition of AChE causes an excess of ACh in synapses and neuromuscular junctions, resulting in muscarinic and nicotinic symptoms and signs.

The pathophysiology of intermediate syndrome is not well defined. In some individuals, neuropathy target esterase (NTE) is targeted to cause OPC induced delayed polyneuropathy.

Poisoning dosage

Children may die of organo phosphorous compounds (OPC) with very minimal dose of 2mg(0.1mg/kg). Studies showed that young animals were more susceptible than adult of same species and that may be applicable to human beings also. The poisoning dose varies from compound to compound[2]. In general, those available for household use (1-2% as dilute formulation) are less toxic than those used in agriculture (40-50% concentration). Whatever be the situation, the victims should be observed for at least 48 to 72 hours.

Clinical features

Children are more vulnerable than adults due to various risk factors like smaller size, differing metabolism and rapidly growing and developing organ systems. Pediatric patients show predominately CNS depression and severe hypotonia, whereas muscarinic symptoms are infrequent[3].

Pesticides can be rapidly absorbed through the skin, lungs, gastrointestinal tract and mucous membranes. The rate of absorption depends on the route of administration and the type of organophosphate or carbamate. Symptoms usually occur within a few hours after ingestion and appear almost immediately after inhalation. Patients often present with evidence of a cholinergic toxic syndrome or toxidrome. It is useful to remember the toxidrome in terms of the three clinical effects on nerve endings[1,4] and they are nicotinic effects at neuromuscular junctions and autonomic ganglia, CNS effects and muscarinic effects on postganglionic and parasympathetic end organs (Table 1). Nicotinic signs and symptoms include weakness, fasciculation and paralysis. Diaphragmatic weakness may result in respiratory difficulty and respiratory failure. In addition as ACh is the neurotransmitter in pre–ganglionic sympathetic nerves, it may cause stimulation of sympathetic nervous system resulting in mydriasis, tachycardia and hypertension, whereas CNS effects may lead to restlessness, tremors, confusion, seizures and CNS depression. The clinical presentation can be a combination of these effects depending on the receptor activity maximally affected. At low doses muscarinic effect predominates. In more severe intoxication nicotinic and central muscarinic effects predominate. Due to this tachycardia and hypertension (nicotinic effect) may be seen in severe poisoning instead of classical bradycardia. Carbamates have less CNS toxicity.

Respiratory failure[5]: There seems to be two underlying mechanisms for respiratory failure and they are an early acute mixed central and peripheral respiratory failure and a late peripheral failure rather than two distinct clinical syndromes.

Intermediate syndrome

The intermediate syndrome (IMS) occurs in approximately 20% of patients following oral exposure to OP pesticides, with no clear association between the particular OP pesticide involved and the development of the syndrome. It usually develops 2 to 4 days after exposure when the symptoms and signs of the acute cholinergic syndrome (e.g. muscle fasciculations, muscarinic signs) are no longer obvious. The characteristic features of the IMS are weakness of the muscles of respiration (diaphragm, intercostal muscles and accessory muscles including neck muscles) and of proximal limb muscles. Accompanying features often include weakness of muscles innervated by some cranial nerves. It has been commonly associated with OPCs like diazinon, dimethoate, methylparathion, methamidaphos, monocrotophos, fenthion and ethylparathion.[3,4]

Organophosphate induced delayed neuropathy (OPIDN) sets in after a period of 7 to 21 days of exposure and causes significant morbidity. The earliest symptoms to be seen are paresthaesia and calf pain. Weakness appears initially in the distal leg muscles causing foot drop, followed by small muscles of the hands. Later it may extend proximally and even involve the truncal muscles. Gait ataxia is disproportionate to the motor and sensory loss. The cranial nerves and the autonomic nervous system are not involved. Deep tendon jerks are absent.

Chronic organophosphate induced neuropsychiatric disorder (COPIND)

Follow-up studies of individuals who have been exposed to high levels of organophosphate compounds revealed development of certain neurobehavioural changes in some of them, which have been termed together as COPIND. These effects include, drowsiness, confusion, lethargy, anxiety, emotional lability, depression, fatigue and irritability.

The effects of dithiocarbamate compounds are currently suspected not only for neurotoxicity, but also as endocrine-disrupting chemicals. Although dithiocarbamates showed weak neurotoxicity in adult animals, more attention needs to be paid to developmental neurotoxicity.[3]

Table 1. Symptoms and signs of organophosphate compound poisoning

SLUDGE/BBB	DUMBELS
S = Salivation	D = Diarrhea and diaphoresis
L = Lacrimation	U = Urination
U = Urination	M = Miosis
D = Defecation	B = Bronchorrhea, bronchospasm, and bradycardia
G = GI symptoms	E = Emesis
E = Emesis	L = Lacrimation
B = Bronchorrhea	S = Salivation
B = Bronchospasm	
B= Bradycardia	

Over all the clinical features of carbamate ingestion are similar to those of OP poisoning and the presenting symptoms include both muscarinic and nicotinic features. However, central nervous system features are not very prominent in carbamate poisoning due to the poor permeability of these compounds across the blood-brain barrier.

OPC and carbamates are also known for their pancreatic toxicity. They may also cause cardiac arrhythmias and ECG disturbances.[6]

Diagnosis and laboratory investigations

The OPC and carbamate poisoning can be confirmed by measuring RBC or plasma cholinesterases. RBC cholinesterase is more accurate and well correlated with neurotoxicity, but the test is costlier and not easily available. Normal value for plasma cholinesterase is 4000-10,000 IU/L. It is otherwise called as butryl cholinesterase (BuChE) or pseudocholinesterase. These cholinesterase levels have no therapeutic as well as prognostic significance. One should remember that measuring enzymatic activity to arrive at a diagnosis of carbamate poisoning may be misleading due to a transient anticholinesterase effect.

Besides routine blood investigations, serum has to be collected for amylase, pancreatic lipase and liver function test. Some patients may have hyperamylasemia, hyperglycemia and increased liver enzymes.

ECG : The common ECG findings are ST-T wave changes and low voltage complexes which are present in severe poisoning. Other less common occurrences are prolonged QT intervals, ectopic beats and conduction block.

Electrophysiological studies following OP poisoning have revealed three characteristic phenomena: (i) repetitive firing following a single stimulus; (ii) gradual reduction in twitch height or compound muscle action potential followed by an increase with repetitive stimulation (the 'decrement-increment response') and (iii) continued reduction in twitch height or compound muscle action potential with repetitive simulation ('decrementing response'). Of these, the decrementing response is the most frequent finding during the IMS, whilst repetitive firing is observed during the acute cholinergic syndrome.

Makhaeva, et al showed that neuropathy target esterase (NTE) assay for whole blood could serve as a biomarker of exposure to neuropathic OP compounds as well as a predictor of OPIDN and an adjunct to its early diagnosis.[7]

Treatment[8-14]

Like any other emergency care, maintaining airway, breathing and circulation is the first and foremost important aspect.

Decontamination[9,13,14] plays a vital role in the outcome of any poisoning. It includes thorough whole body wash with soap and water, washing of eyes with clean tap water and replacing the clothes worn by the patient with fresh ones. Special attention should be given to washing of skin creases, around the ears and external auditory canals, around the umbilicus and genitalia and under the nails. Health care givers should take precautions while decontaminating, like wearing masks with eye shields and water resistant gloves.

Treating OPC poisoned children is a great task as they won't cooperate for gut decontamination and copious ongoing vomiting also interferes with gut decontamination measures. Gut decontamination can be achieved by gastric lavage. If it is done within an hour, the maximum benefit can be attained. 50-100ml of warm saline can be used at a time and it should be repeated till the aspirate becomes clear.

Activated charcoal is of limited value because these highly lipid soluble agents are rapidly absorbed.

Antidotes

1. Atropine

Children with both OPC and carbamate poisoning will be benefitted by atropine. Atropine antagonises the central and muscarinic cholinergic effects and acts by blocking the muscarinic receptors. It will not reverse the muscle weakness caused by the effect on nicotinic receptors. The dose of atropine is 0.05mg/kg IV every five minutes till the signs of atropinisation appear ie. dryness of mouth, no bronchial secretions and no bradycardia. Miosis cannot be taken as a sole indicator of atropine need. The maintenance doses can be repeated whenever it is warranted. After adequate atropinisation is established, maintenance doses are given to keep tracheobronchial tree dry for 24 hours. After this atropine dose can be tapered gradually to prevent rebound effects. One should be cautious in using atropine in children with Down's syndrome and in those with brain damage, as it may precipitate hyperactive response.

2. Glycopyrrolate

It is a quarternary ammonium compound. However, it does not cross blood brain barrier. So it will not alleviate the central effects of the poison. Some investigators recommend this as an alternative to atropine, since adverse effects are less.

3. Pralidoxime

It neutralises the nicotinic effects of OPC. Although there are controversies regarding beneficial effects of pralidoxime in OPC poisoning, WHO recommends 25 to 50mg/kg in normal saline over 30 minutes followed by 10 to 20mg/kg/hr. Even though there are no randomized controlled trials for the duration of continuous infusion in children, in adults it has been given for maximum of seven days. Because diethyl-OP–inhibited AChEs reactivate and age notably slower than the dimethyl analogs, they generally require prolonged oxime treatment. CNS effects and muscarinic effects do not respond to pralidoxime, hence atropine therapy needs to be continued along with this.

Pralidoxime exerts nucleophilic attack on the phosphorus and a phosphoryloxime is formed, leaving the regenerated enzyme. However, high dose of pralidoxime themselves can cause neuromuscular blockade and inhibition of AChE. The side effects are mild weakness, blurred vision, diplopia, dizziness, headache, nausea and tachycardia if given more than 500mg/minute. Pralidoxime is generally not indicated for carbamate poisoning.

4. Newer therapeutic agents

Various trials are being conducted to increase the acetylcholinesterase levels by using Forskolin (cAMP inducer), transcriptional inducers and Trichostatin (histone acetylase inhibitor). Other therapeutic agents such as sodium bicarbonate infusion, magnesium, clonidine and fluoride have been suggested to have a role in OP poisoning but their use is not universally recommended due to a lack of good clinical evidence.[11]

Supportive measures

1. Benzodiazepines: The seizures can be treated successfully with anyone of the benzo diazepines. Phenytoin has to be avoided as it may precipitate cardiac arrhythmias. Diazepam can be used in all patients showing aggressiveness as it relieves the anxiety and counteracts the cholinergic effects on CNS.

2. Respiratory support: Respiratory failure is one of the important complications in delayed

presentation. Children with respiratory compromise have to be dealt with intubation and mechanical ventilation. Frequent suctioning should be done as the secretions block the airway.

3. Other modalities: Fresh frozen plasma has also been tried with fruitful outcome in some of the studies, but adequate clinical trials should be conducted before putting them into the guidelines.

Drugs to be avoided are[12]: Methyl xanthines which antagonises PAM, aminoglycosides which can aggravate muscle weakness and drugs metabolized by plasmacholinesterase like opioids, succinylcholine, mivacurium and esmolol. Avoid phenytoin for controlling seizures as its effect on Na^+ channel may suppress cardiac activity and physiologic autonomic response. Haloperidol should be avoided for sedating the agitated patients due to atropine toxicity as it is non-sedating, but also associated with disturbance of central thermoregulation, prolongation of QT interval and pro-convulsant.

Prevention

Pediatricians should work for primary prevention of poisoning, not only from their offices but also in the community, by supporting efforts at educating parents about properly storing and disposing toxic substances. The farmers who have come from the field should not carry the children without washing their body and changing the clothes.

Community education in the rural areas where small or large-scale farming is practiced is very important.[15] Prevention is better than cure.

Prehospital care

As in most poisoning situations, it is best to "scoop and run;" very little can be done in the field. Always look for a container so that the specific product can be determined. Deconta-mination may be necessary for situations in which patients and their garments may be contaminated with the pesticide.

RODENTICIDE POISONING[10,11,13,14]

Rodenticides are not leading agents for severe poisoning. Children obtain the rodenticide from the site at which it had been laid, as in the kitchen, lounge room or laundry, inside cupboards or wardrobes. Rodenticides are used in two forms to kill rodents and they are single dose or multiple dose type.

Ingredients

The components of rodenticide are usually aluminum phosphide, zinc phosphide, arsenic, thallium, barium compounds, warfarins and super warfarins group. Super warfarins include bromadiolone, brodifacoum, difenacoum and diaphacinone. Among them commonly used ones are warfarin group.

Pathophysiology

The anticoagulant effects of warfarins are secondary to inhibition of vitamin K 2,3-epoxide reductase and vitamin K quinone reductase. The inhibition of these enzymes prevents the activation of vitamin K and subsequent activation of clotting factors II, VII, IX, and X. Superwarfarins are more potent than warfarins and have a longer duration of action. Prolongation of prothrombin time can be demonstrated after 36-48 hours and may persist for long periods.

The phosphide groups can release phosphine gas which is lethal. So the gaseous nature of phosphine poses a potential risk to healthcare providers doing gastric decontamination; this fact should be borne in mind while undertaking the activity. Even 'offgassing' in a patient's exhaled breath may lead to contamination of healthcare staff.

Clinical features

The phosphide groups can release phosgene gas which is lethal. The symptoms may vary from chest pain, hypotension, vomiting to unconsciousness. Finally, they may develop liver and kidney failure. Reversible myocardial injury due to aluminium phosphide poisoning has been reported. Thallium causes GI disturbances, seizures and confused behavior, strange movements of arms and legs and kidney damage.

Warfarin like substances disturb coagulation cascade causing various bleeding manifestations like hematuria, hemoptysis and bleeding gums. A careful search should be done for petechial hemorrhages, and occult blood in the stools. Rarely, the patients may present with intracerebral bleeding and hemarthrosis.

Poisoning dosage

It varies from compound to compound. As the concentration of these substances are very low in rodenticide, severe toxicity is rare.

Investigations

Prothrombin time at the time of admission and 48 to 72 hours after the poisoning helps to assess the coagulation status. Partial thromboplastin time, bleeding time and clotting time are also helpful. Liver function and renal function tests help to assess the organ status. ECG may be taken to find out myocardial damage (various ST, T wave changes). Complete blood count is needed for evaluation of bleeding tendency. Plain x-ray of abdomen may be helpful to detect metal rodenticide because these metals are radio-opaque. The silver nitrate test on the gastric analysate is used for diagnosis of aluminum phosphide poisoning. Also a variant of the gastric test is the breath test.

Management

Like any other poisoning, priority is given for "ABC" and decontamination techniques including gastric lavage with activated charcoal. Routine cleansing with mild soap and water for dermal exposures is warranted.

Patients with unintentional ingestion and who are asymptomatic should be evaluated according to the nature of the compound and observed if required for 48 to 72 hours after exposure.

In an emergency room, in addition to above said procedures, the pediatrician or practitioner should administer specific antidotes for a known compound. Otherwise, it is routine to administer Vit.K in all rodenticide poisoning if the victim has bleeding tendencies or prolonged prothrombin time. Fresh frozen plasma(FFP) could save the life.

Specific antidote for thallium is potassium ferricyano ferrate (Prussian blue). It is administered as 250mg/kg/day in four divided doses until the concentration of thallium in the urine is less than 0.5mg over 24 hour period.

Aluminum phosphide poisoning requires only supportive measures as there is no specific antidote[11]. However absorption of poison from the gut is reduced by gastric decontamination using potassium permanganate in 1:10000 dilution for gastric lavage. Shock should be managed by infusing a large amount of saline. Magnesium sulphate has been shown to stabilize cell membranes and reduce the incidence of arrhythmias. N-acetylcysteine and magnesium have been suggested as potential therapies for the management of poisoning but no effective treatment has been found. Coconut oil has been reported to prevent rapid absorption of unabsorbed phosphine from the gut, but the strength of evidence is at best weak.

Conclusion

Treating doctors and health care workers are reminded of the following golden rules. while treating poison cases.

1. Many cases of poisoning will recover with simple supportive measures and hence all of them do not require tertiary care.

2. Alleviate anxiety of the patient and the family members. Encourage the family member(s) / friend(s) or accompanying attendants to bring the remaining materials of the poison consumed / tablet taken and any other note left by the patient for identification of the poisonous agent(s) in order to decide on appropriate antidote(s).

3. Preserve the first gastric lavage and the materials brought by the patient or care givers for chemical analysis.

4. Never be carried away just because vital signs are stable at the time of presentation, since the toxic manifestations may appear later.

5. Assess the condition of the patient frequently.

6. It is ideal to observe the patients for 24 to 48 hours before discharge.

7. Each patient with poisoning is different from others.

8. Stabilise immediate life threatening problems. "ABC' Airway, Breathing and Circulation".

9. Identifying the causative agent should not delay the emergency treatment based on clinical signs.

10. Medical management of poisoning is difficult at times in view of various biological factors and chemicals consumed.

11. Some times patients will die no matter how well managed.

12. Inform police if death occurs, and the body should be sent for postmortem examination.

Points to Remember

• *Early recognition, careful resuscitation, appropriate use of antidotes, close monitoring and good supportive care should minimise the morbidity and mortality in organophosphate and carbamate poisoning.*

References

1. Ganapathy N.Organophosphorous compound poisoning- a review. Indian J Trauma Anaesth Crit Care 2005; 6 : 432-447.

2. Rexy J, Ramakrishnan TV, Janardhan V. Surveillance and compendium preparation for common agricultural poison. Indian J Trauma Anaesth Crit Care 2002;3 :157-166

3. Lifshitz M, Shahak E, Sofer S. Carbamate and organophosphate poisoning in young children. Pediatr Emerg Care 1999;15: 102-103.

4. Singh S, Sharma N. Neurological syndromes following organophosphate poisoning. Neurol India 2000;48:308-313.

5. Eddleston M, Mohamed F, Davies JOJ, et al. Respiratory failure in acute organophosphorous pesticide self-poisoning. Q J Med 2006;99:513-522.

6. Dalvi CP, Abraham PP, Iyer SS. Correlation of electrocardiographic changes with prognosis in organophosphorus poisoning. J Postgrad Med 1986;32:115-119.

7. Makhaeva GF, Sigolaeva LV, Zhuravleva LV, et al. Biosensor detection of neuropathy target esterase in whole blood as a biomarker of exposure to neuropathic organophosphorus compounds. J Toxicol Environ Health A 2003; 66 :599-610.

8. Eddleston M, Dawsaon A, Karalliedde L, et al. Early management after poisoning with an organophosphorous or carbamate pesticide - a treatment protocol for junior doctors. Crit Care 2004;8 : R391-R396.

9. Pillai VV. Organophosphate/carbamate pesticide poisoning – a primer for physicians. The proceedings of Toxocons-3 Mangalore, 7 & 8 April 2007 & International reference sources. 2007;1-29.

10. Pillai VV. (Ed) Modern Toxicology. 3rd edn, Jaypee Brothers Medical Publication (P) Ltd, New Delhi 2005; pp66-69.

11. Goel A, Aggarwal P. Pesticide poisioning. National Medical India 2007; 20 : 182 -191.

12. Shivakumar S. Principles of management of organophosphorus compound poisoning. (Personal communication).

13. Basic Emergency services for poisoning. Training module for staff nurse and auxillary nurse midwife. State Health Mission, Health and Family Welfare, Government of TamilNadu, Chennai. 2007.

14. Henry J, Wiseman H (Eds). Management of Poisoning: a hand book for heaalth care workers. First Edition: World Health Organisation Geneva, Switzerland, Europe. A.I.T.S. Publishers and distributors (Regd), Delhi , 2002.

15. Safer Access to Pesticides Community Interventions. World Health Organisation, Geneva, Switzerland. 2006.

CLIPPINGS

Continuous distending pressure for respiratory distress in preterm infants

Some benefits found in using continuous distending pressure (CDP) for respiratory distress syndrome in preterm babies. Respiratory distress syndrome (RDS) is the most common cause of disease and death in babies born before 34 weeks gestation. Intermittent positive pressure ventilation (IPPV) is the standard way of helping these babies breathe. A simpler method of assisting breathing is to provide a continuous lung distending pressure - either no continuous positive pressure to the airway or continuous negative pressure (partial vacuum). The review of trials found that continuous distending pressure (CDP) reduces the rate of death or the need for assisted ventilation and reduced the need for IPPV. The small and mostly dated trials also found that CDP can increase the rate of pneumothorax (air outside the lung in the chest cavity). In preterm infants with respiratory distress the application of CDP either as CPAP or CNP is associated with reduced respiratory failure and reduced mortality. CDP is associated with an increased rate of pneumothorax. Four out of six of these trials were done in the 1970's. Therefore, the applicability of these results to current practice is difficult to assess. Where resources are limited, such as in developing countries, CPAP for RDS may have a clinical role. Further research is required to determine the best mode of administration and the role of CDP in modern intensive care settings

Ho JJ, Subramaniam P, Henderson-Smart DJ, Davis PG. Continuous distending pressure for respiratory distress in preterm infants. *Cochrane Database of Systematic Reviews* **2002, Issue 2. Art. No.: CD002271. DOI: 10.1002/14651858.CD002271. This version first published online: July 24. 2000 Last assessed as up-to-date: May 24. 2008.**

<div style="text-align:center">**TOXICOLOGY**</div>

HYDROCARBON AND RELATED COMPOUNDS POISONING

*** Utpal Kant Singh**
**** Prasad R**
***** Gaurav A**

Abstract : *In Indian children hydrocarbon (kerosene) is the commonest poison consumed. The clinical manifestations depend on the viscosity and amount of hydrocarbon consumed. Pulmonary toxicity represents the most common complication of hydrocarbon ingestion and accounts for the majority of fatalities. Management is principally conservative but few children require mechanical ventilation.*

Key points: *Hydrocarbon, Kerosene, Viscosity and Pneumonia.*

Poisoning in children is the twelfth most common cause of admission to the pediatric ward.[1,2] It constitutes 0.23 to 3.3% of total poisoning cases and the case fatality rates range from 0.64 to 11.6%.[3] Accidental poisoning commonly involves children below 5 years of age and hydrocarbon(kerosene) is the commonest orally consumed poison in Indian children.[4,5] This is not surprising in view of the fact that hydrocarbon-based products are commonly found in home. Children have access to kerosene during

* Prof. and Head, Dept. of Pediatrics, Nalanda Medical College, Patna

** Lecturer, Institute of Medical Sciences, BHU, Varanasi

*** Senior Resident, JIPMER, Pondicherry.

winter months and charcoal lighter fluid in summer season. Often, the products are inappropriately stored in drinking glasses, water bottles or unlabeled containers, and they may be attractive and pleasant-smelling, like furniture polishes.

Hydrocarbons represent a diverse group of substances and occasionally the terms "hydrocarbon" and "petroleum distillate" are used interchangeably. In fact, petroleum distillate refers to a type of hydrocarbon which results from the processing of crude oil and may be aliphatic or aromatic. Turpentine, on the other hand, is a hydrocarbon that is not a petroleum distillate since it is made from pine oil. The most useful means of classifying hydrocarbons is with respect to their clinical effects and are mentioned below.

Classification of hydrocarbons

A. Based on their chemical and clinical properties

1. Aliphatic hydrocarbons(easily aspirated following ingestion, poorly absorbed from GI tract and minimal systemic effects): kerosene, mineral spirits, gasoline, naphtha and mineral oil, lubricating oil, etc.

2. Halogenated hydrocarbons(minimal aspiration following ingestion, readily absorbed from GI tract and produces systemic toxicity): trichloroethane, methylene bromide, chlordane, lindane.

3. Aromatic hydrocarbons(commonly used for inhalation): toluene, xylene and benzene

Table 1. Classification of hydrocarbons based on viscosity.

Viscosity	Example
1. Very low	Mineral seal oil (furniture polish)
2. Low	Benzene, toluene, aniline, nitrobenzene pine oil, camphor, chlorinated hydrocarbons, pesticides with hydrocarbon
3. Middle	Gasoline, kerosene, lighter oil
4. High	Lubricating greases and oils, motor oil, petroleum jelly, paraffin wax .

B. Based on viscosity

Hydrocarbons are classsified as very low, low, middle and high viscosity hydrocarbons (Table 1).

Halogenated hydrocarbons, such as the solvent trichloroethane and methylene chloride, can produce liver and renal toxicity following chronic exposure, as well as central nervous system (CNS) effects with acute exposure. Toluene, xylene, and benzene belong to the cyclic, aromatic group of hydrocarbons. The solvents toluene and xylene are commonly abused for the euphoric effects produced by inhalation through "huffing" or "bagging." Cardiac arrhythmias may occur due to sensitization of the heart to catecholamines. Chronic exposure can cause peripheral neuropathies, electrolyte abnormalities and renal toxicity. Chronic exposure to benzene has been implicated in the development of aplastic anemia and leukemia.[2] Hydrocarbons may also be used as vehicles for highly toxic ingredients such as camphor, heavy metals and organophosphate insecticides.

Pathophysiology of hydrocarbon poisoning

The physical properties of the hydrocarbons contribute to their ability to produce pulmonary manifestations. The risk for aspiration is directly correlated with viscosity, which is measured in Saybolt Seconds Universal (SSU), the time required for a liquid to flow through a calibrated orifice. Products with a low viscosity (less than 60 SSU) are associated with a high aspiration potential e.g. gasoline, kerosene naphtha. In conjunction with decreased viscosity, the physical properties of low surface tension and high volatility contribute to respiratory injury. Low surface tension enhances spreading of the liquid on lung tissue, while high volatility displaces alveolar gas and interferes with ventilation when aspiration has occurred. Aspiration of mineral seal oil, with a viscosity of 47 SSU, can result in severe pulmonary complications. This may in part be attributable to the ability of mineral seal oil to cause a lipoid pneumonia in addition to chemical pneumonitis.[4] Hydrocarbons with a viscosity of more than 100 SSU, such as fuel oil, lubricating oil and mineral oil, present a low aspiration hazard.

Pulmonary toxicity[5,6] is the result of hydrocarbon aspiration. The lower the viscosity and higher the volatility, the greater is the risk of pulmonary aspiration. The hydrophobic nature of hydrocarbons allows them to penetrate deep into the tracheobronchial tree, producing inflammation. Bronchiolar exudates containing primarily

polymorphonuclear leukocytes may be found within hours of aspiration. This may clinically manifest as bronchospasm, cough, rales and radiographic changes. Another postulated mechanism of pulmonary damage is the loss of surfactant with resultant increase in alveolar surface tension. The volatile chemical may displace alveolar oxygen, leading to hypoxia. Direct contact with alveolar membranes may lead to hemorrhage, hyperemia, edema, surfactant inactivation, leukocyte infiltration and vascular thrombosis. The result is poor oxygen exchange, atelectasis and pneumonitis. Pneumatoceles following hydrocarbon ingestion generally occur in the areas of lung, where densest infiltrates are seen. The two postulated mechanisms for pneumatocele formation are necrosis of pulmonary tissue and/or local obstruction leading to over distension and rupture of alveoli. Clinical manifestations generally begin in the first few hours after exposure and usually resolve in 2-8 days. Complications include hypoxia, barotrauma due to mechanical ventilation and acute respiratory distress syndrome (ARDS). Prolonged hypoxia may result in encephalopathy, seizures and death.

Hydrocarbon ingestion causes gastrointestinal irritation and manifests with throat and abdominal pain, nausea and vomiting. Vomiting increases the likelihood of pulmonary aspiration.

Hydrocarbon toxicity produces various CNS effects, which include disinhibition, depression and euphoria initially as observed in patients with alcohol or narcotic intoxication. Eventually, lethargy, headache, obtundation and coma may follow. Seizures are uncommon and are due to hypoxia. The CNS depression is related to anesthetic property of certain hydrocarbons and other CNS manifestations are secondary to hypoxia.[7]

Dysrhythmias are a major concern. The causes of dysrhythmias include hypoxia,

acidosis, the presence of toxic substances in hydrocarbon base, myocardial sensitization to catecholamine and direct myocardial damage. Sudden death has been reported as a result of coronary vasospasm due to hydrocarbon inhalation.

Hydrocarbons are reported to cause bone marrow toxicity and hemolysis. Chlorinated hydrocarbon toxicity may cause hepatic and renal failure and toluene toxicity may lead to renal tubular acidosis. Direct contact with the skin and mucous membranes may cause effects ranging from local irritation to extensive chemical burns.

Clinical manifestations

Clinical manifestations of hydrocarbon ingestion, in the absence of toxic substituents, are confined to the gastrointestinal tract and the respiratory tract. Local effects include a burning sensation in the mouth and pharynx, nausea, gastric irritation, belching, abdominal pain and diarrhea. These rarely require treatment and are considered fairly innocuous.[2-6] Pulmonary effects, when they do occur, are the result of aspiration. A severe necrotizing pneumonitis, with direct tissue destruction, can occur. Aspiration can occur at the time of ingestion or during vomiting or gastric lavage. Pulmonary toxicity represents the most common complication of hydrocarbon ingestion and accounts for the majority of fatalities. When aspiration occurs, the patient may initially experience coughing, choking, gagging or grunting respirations. Dyspnea and cyanosis may occur. Rales, rhonchi and decreased breath sounds may be present on auscultation. Fever and leukocytosis may also be present but are not thought to correlate with an infectious process.[2,3] This usually subsides after 24-48 hours. The breath, vomitus and urine have peculiar odor. Hydrocarbons may also result in lethargy, tremors and rarely, convulsions or coma. The pupils are first constricted but become dilated later when coma supervenes. These effects are more likely

Table 2. Clinical manifestations of hydrocarbon and related compounds

Respiratory	Coughing, choking, tachypnea, grunting, cyanosis, rales, wheezing
Gastrointestinal	Nausea ,vomiting ,abdominal pain, diarrhea and rarely bleeding
Cardiac	Arrhythmia, congestive heart failure
CNS	Headache , dizziness ,lethargy, ataxia, seizures, coma
Cutaneous	Mucosal irritation, chemical burns
Miscellaneous	Renal and hepatic damage, leukocytosis

due to severe pulmonary injury or hypoxia. Salient clinical manifestations of hydrocarbon are mentioned in Table 2.

On the basis of clinical manifestations, Gupta, et al[8] devised a scoring system to determine outcome and severity of hydrocarbon (kerosene) poisoning. They have taken account of four parameters and scored as in Table 3.

Table 3. Scoring system for hydro-carbon poisoning

Parameter	Absent	Present	Others
Fever	0	1	-
Severe malnutrition	0	1	-
Respiratory distress	0	2	4 (presence of cyanosis)
Neurological symptoms	0	2	4 (presence of convulsion)

The score may range from 0 to 10 in a particular patient. If score is 4 or more; significant risk and patients should be treated in a hospital with facility for advanced life support. Children with a score of 7 or less are likely to survive, whereas with a score 8 or more the risk of death is several fold higher. The predictive value of this scoring system is about 85%.

Admission criteria[9] following hydrocarbon ingestion

1. Admit immediately, if the patient has significant respiratory symptoms or an abnormal chest radiograph.

2. Admit, if patient has significant CNS depression, severe gastrointestinal symptoms or has ingested a significant amount of hydrocarbon.

3. Admit after observation if respiratory symptoms are worsening or if the chest radiograph is becoming progressively worse.

Imaging studies

A chest radiograph must be obtained in all symptomatic patients. Initially, the chest radiographic results may be normal, but findings are usually significant at two to eight hours after ingestion. Common findings include fine perihilar opacities, bibasilar infiltrates and atelectasis. Following aspiration, deterioration of the patient may occur over the first 24-72 hours, with resolution of symptoms in three to six days.[3,5] The course may be prolonged with mineral seal oil exposure.[2] Reported radiographic

complications of hydrocarbon aspiration include pneumatoceles, pleural effusion, empyema and pneumothorax.[10] Repeat CXR is recommended if acute change in the patient's respiratory status occurs because of pneumothorax or pneumomediastinum. If discharge is being considered for an asymptomatic patient, a chest radiograph should be done 6 hours after the ingestion to document the negative findings.

ABG analysis is useful in documenting hypoxemia in severely affected patients. Hypercarbia may be observed in patients with respiratory depression and decreased gas exchange. An increased anion gap may indicate co-ingestion of another toxin.

Pulse oximetry is useful in the emergency room because hypoxia is a direct result of hydrocarbon aspiration. ECG should be done if cardiac arrhythmia is a concern.

Management

Stabilization of the airway is always the first priority of treatment. Supplemental oxygen should be given to all patients with face mask or oxygen hood and monitored on the bedside with pulse oximeter. Early intubation, mechanical ventilation and use of positive end-expiratory pressure may be indicated in a patient in whom oxygenation is inadequate or who has severe respiratory distress or a decreased level of consciousness. A trial of bronchodilators may prove useful in patients with suspected bronchospasm.

The skin is decontaminated as soon as possible by removing the involved clothing and thoroughly washing the skin with soap and water. Vapor inhalation and cutaneous absorption may occur long after the exposure. Regardless of the amount involved, gastric emptying is not indicated for accidental ingestion of a hydrocarbon lacking systemic toxicity. This represents the majority of cases. The risk of aspiration during vomiting or lavage far outweighs any benefit from removal of the substance. The frequently cited amount of more than 1ml/kg as the indication for gastric emptying is not supported by animal studies.[1,2,4]

In the case of ingestion of a hydrocarbon capable of causing systemic toxicity or when coingestion is suspected, gastrointestinal (GI) decontamination would be warranted of toxic hydrocarbons i.e. camphorated, halogenated, aromatic, hydro carbon, co-injection of heavy metals and pesticides. Gastric emptying is not without risk. Both ipecac-induced emesis and emesis from insertion of a lavage tube can increase the risk of aspiration. In addition, aspiration may occur as the result of re-exposure of the larynx to hydrocarbon from the tip of the tube during removal. A cuffed endotracheal tube is not protective against aspiration.[2] GI decontamination should be done provided the patient has a gag reflex, is alert, and is likely to remain so, and provided the substance is not expected to cause seizures.[2,10]

Activated charcoal does not effectively adsorb hydrocarbons and in the absence of co-ingestants, has no role in therapy. Oils, such as mineral or olive oil, once advocated to increase the viscosity of the hydrocarbon, are no longer recommended because of the risk for lipoid pneumonia.[8]

If hydrocarbon aspiration occurs, oxygen and aggressive respiratory support are indicated. With severe pulmonary complications, CPAP or PEEP may be required. Steroids have not been shown to be useful, and antibiotics should be reserved for documented infection. Antibiotics should only be used, when there are signs of pneumonia, in debilitated children and if there are signs of acute infection. Routine prophylaxis with antibiotics is not necessary. A β_2 selective agonist can be given for bronchospasm, while epinephrine should be avoided as it may precipitate dysrhythmias.

Complications

Aspiration pneumonitis is the most common complication of hydrocarbon ingestion, followed by CNS and cardiovascular complications. The major respiratory complications are aspiration and lung injury secondary to pneumonitis. Pneumothorax and barotrauma are potential complications of mechanical ventilation. Most patients improve after 24 hours and symptoms resolve within one week. CNS complications include seizures, encephalopathy and memory loss. These sequelae are usually believed to be secondary to a hypoxic insult. Myocarditis and cardiomyopathy are reported cardiovascular complications of hydrocarbon toxicity. Cardiomyopathy, cerebellar atrophy, dementia, cognitive deficits and peripheral neuropathy have been reported with long-term hydrocarbon inhalant abuse. Sudden death may occur as a result of coronary vasospasm due to hydrocarbon inhalation.[11]

Prevention

Patient education is crucial in the prevention of accidental exposure. Parents should teach young children about the dangers of poisons, beginning at an early age. Advise the parents about the proper storage and labeling of harmful chemicals. Parents should be informed about common household products that may be dangerous and recommend steps that they can take to minimize the possibility of an accidental exposure including safe storage of hydrocarbon. Educate parents about supervision of their children, when they are in high-risk areas (eg, kitchen, garage, laundry room) where toxic substances may be present. Inhalant abuse occurs in adolescents and should be discouraged. Hydrocarbons may be inhaled for recreation and as part of suicidal gestures and attempts. Treatment of the underlying causes of these behaviors might help in preventing hydrocarbon use.

Points to Remember

- *Inducing emesis, gastric lavage and activated charcoal are not indicated in most hydrocarbon ingestion.*

- *If children remains asymptomatic even six hours after ingestion, they can be discharged.*

- *If symptomatic, do chest x-ray and measure oxygen saturation. Administer oxygen to maintain saturation >94%.*

- *If stable but symptomatic, admit in general medical ward.*

- *If there is increasing O_2 requirement, worsening respiratory distress or altered level of consciousness admit in I.C.U. and consider ventilatory support.*

References

1. Datta AK, Seth A, Goyal PK, et al. Poisoning in children: Indian scenario. Indian J Pediatr 1998; 65: 365-370.

2. Litovitz TL, Schmitz BF, Holm KC. 1988 annual report of the American Association of Poison Control Centers National Data Collection System. Am J Emerg Med 1989 ;7:495-545.

3. Litovitz T. Hydrocarbon ingestions. Entechnology 1983; 62:142-147.

4. Arena JM. Hydrocarbon poisoning—current management. Pediatr Ann 1987;16:879-883.

5. Dice WH, Ward G, Kelley J, Kilpatrick WR. Pulmonary toxicity following gastrointestinal ingestion of kerosene. Ann Emerg Med 1982; 11:138-142.

6. Eade NR, Taussig LM, Marks MI. Hydrocarbon pneumonitis. Pediatrics. 1974;54: 351- 357.

7. Karlson KH Jr. Hydrocarbon poisoning in children. South Med J 1982;75(7):839-840.

8. Gupta P, Singh RP, Murali MV, Bhargava SK, Sharma P. Kerosene poisoning-a childhood menace. Indian Pediatrics 1992; 29: 979-984.

9. Anas N, Namasonthi V, Ginsburg CM. Criteria for hospitalizing children who have ingested products containing hydrocarbons. JAMA 1981;246:840-843.

10. Khan, Awais J , Akhtar, Raja P, Faruqui, Zia S .Turpentine Oil Inhalation Leading to Lung Necrosis and Empyema in a Toddler. Pediatric Emergency Care. 2006;22:355-357.

11. Beamon RF, Siegel CJ, Landers G, Green V. Hydrocarbon ingestion in children: a six-year retrospective study. JACEP 1976;5:771-775.

CLIPPINGS

Methods of milk expression for lactating women

The World Health Organization recommends that infants be fed exclusively on human milk from birth to six months of age. Children who do not receive human milk are more likely to suffer health problems. Not all babies are able to feed at the breast because of prematurity, illness, abnormalities or separation from their mothers; these babies need expressed human milk. Mothers may also express milk for their own comfort if they have sore nipples or engorgement; to increase milk supply; or to leave milk if away from their baby. Possible adverse effects from expressing milk include injury to the mother and bacterial contamination that may affect the baby. This review included 12 studies and six of these had data that could be used in the analyses. All the mothers in these six studies were mothers of infants in neonatal units in the USA, UK, Malaysia, Kenya and Nigeria. In one study, using the electric or foot-operated pump provided a greater mean volume of milk than hand expression during a six-day period in the first two weeks after birth. Simultaneous pumping of both breasts and sequential pumping gave similar volumes, though the time taken was different. In one study, mothers given a relaxation tape were more likely to produce a greater volume of milk at one expression. One small study found that hand-expressed and pump-expressed milk had a similar incidence of milk contamination. All studies were small and results may not apply to pumps other than those tested. No study asked mothers if they had achieved their own goals for expressing milk. None of the studies examined costs involved with different methods. Eight of the 10 studies that evaluated pumps or other products had support from the manufacturers. The available evidence indicates that low cost measures such as relaxation, breast massage, frequency of expressing or pumping, and simultaneous pumping, if acceptable to mothers, may be effective in assisting mothers to provide expressed milk. Not all the studies mentioned if basic supports were provided, particularly for mothers with hospitalised children, including access to food and fluid, a place to rest near their baby, and knowledgeable health workers. Whatever method of expression is used, mothers need to feel valued and supported.

Authors' conclusions

Mothers appear to obtain greater total volumes of milk in six days after birth using the electric or foot powered pump tested compared to hand expression, and a greater volume at one expression during the second week when provided with a relaxation tape. Simultaneous pumping takes less time compared to sequential pumping. Further research with larger numbers and more comprehensive reporting is needed, and mothers' reasons for expressing linked to their evaluation of effectiveness rather than market-led research on equipment performance.

Becker GE, McCormick FM, Renfrew MJ. Methods of milk expression for lactating women. *Cochrane Database of Systematic Reviews* 2008, Issue 4. Art. No.: CD006170. DOI: 10.1002/14651858.CD006170.pub2. This version first published online: October 08. 2008

<div align="center">TOXICOLOGY</div>

COMMON DRUG POISONING

Suresh Gupta

Abstract: *Poisonings due to drug ingestion are becoming more frequent. Acetaminophen is the most commonly used antipyretic drug. When significant toxic dose is ingested, N-acetylcysteine is a specific antidote. Poisoning due to sedative-hypnotics can result in cardiorespiratory depression. Good supportive care can save most of the patients. Anticonvulsants can result in toxicity due to overdose, idiosyncrasy or drug interactions. Ingestion of cardiovascular drugs like antiarrhythmics and antihypertensives are relatively less common but the toxicity can be associated with significant morbidity and mortality. Iron ingestion is becoming more common due to increasing use of prenatal iron. Vomiting is the most prominent clinical feature of iron toxicity. Older generation anti-histamines can produce substantial toxicity due to anticholinergic and sedative effects. Most of the beta agonist ingestions generate only insignificant clinical problems.*

Key words: *Poisoning, Acetaminophen, Sedative-Hypnotics, Antihypertensives, Antiarrhythmics, Iron, Antihistamines and β agonists.*

Poisoning is one of the common emergencies in children presenting to emergency room.

* Consultant
Pediatric Emergency Medicine
Center for Child Health,
Sir Ganga Ram Hospital, New Delhi

Most of the poisoning in children are accidental and trivial. But at times it can be life threatening particularly in adolescents with suicidal tendencies. With urbanization, the types of poisoning are changing particularly in metropolitan cities. With increasing use of prescription drugs in adults drug poisoning is becoming increasingly common in children. The commonly available drugs in households include antipyretic-analgesics (acetaminophen, non-steroidal anti-inflammatory drugs), sedative-hypnotics (benzodiazepines, opioids, barbiturates, triclofos), anti-convulsants (older and newer anticonvulsants), hematinics (multivitamins and iron preparations), cardiovascular drugs (anti-arrhythmics and anti-hypertensives), anti-histaminics (older and newer anti-histaminics), anti-asthmatic drugs (salbutamol, theophylline). There is a huge list of drugs which can result in accidental ingestion and poisoning but only accidental ingestion of common drugs in children will be discussed here.

ACETAMINOPHEN

Core facts and pathophysiology[1]

Acetaminophen (paracetamol, N-acetyl-para-aminophenol) is the most widely used antipyretic and analgesic medication in children. The recommended therapeutic dose is 10-15 mg/kg every 4 hours (max. 60 mg/kg/day or 4 g/day). Peak plasma concentrations after a single therapeutic dose occurs in 30 – 120 minutes, with therapeutic levels between 10–30 µg/mL. A level of 150 µg/mL at 4 hours after ingestion is hepatotoxic in 25% of cases. The toxic dose is 140–150 mg/kg, although prepubertal children may be less susceptible to acetaminophen toxicity

than adults due to a more active sulfation pathway; therefore, as much as 250 mg/kg in a single acute ingestion may be needed to develop hepatotoxicity.

Peak levels occur within 4 hours, even in large overdoses. Approximately 95% of acetaminophen is metabolized by the liver to non-toxic glucoronide and sulphate conjugates. Less than 5% is metabolized by the cytochrome P450 system to N-acetyl-parabenzo-quinone-imine (NAPQI), which is further conjugated by glutathione to non-toxic mercapturates. In overdose situations, glutathione is depleted, and the excess NAPQI is toxic to hepatocytes, causing centrilobular necrosis. Acetaminophen level should be obtained in the acute, single ingestion in the first 24 hours post-ingestion. The Rumack-Matthew nomogram (Fig.1) predicts the risk of liver damage for a single, acute ingestion of acetaminophen. Serial levels may be helpful when there is a) an unclear time course of ingestion, b) any chronicity to the ingestion, or c) ingestions involving extended release tablets. N-acetylcysteine (NAC) acts as a substitute for glutathione, and binds NAPQI, therefore blocking hepatocellular toxicity if initiated within 8–12 hours of ingestion. It may be effective even in delayed presentations greater than 24 hours. In this case, it is believed to work as an antioxidant and improves hepatic microcirculation.

Clinical features

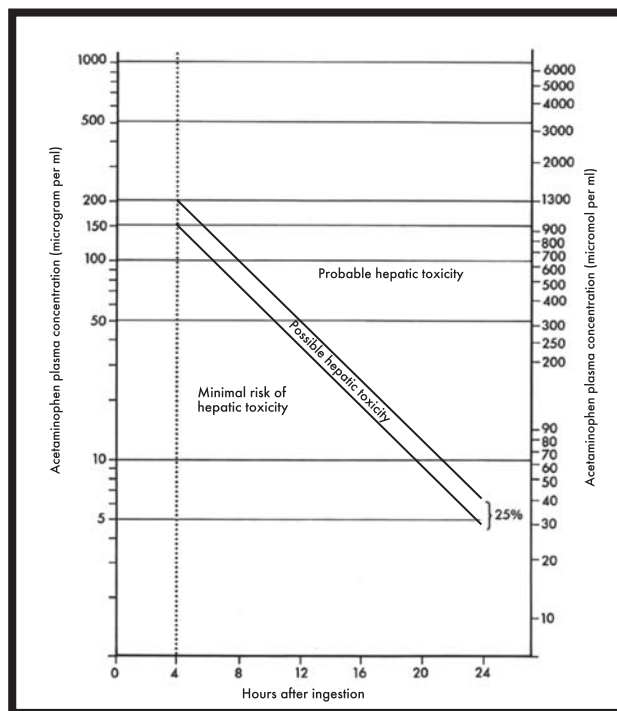Acetaminophen toxicity is divided into four stages[2]

Figure 1. The Rumack-Matthew Nomogram

1. Stage 1 (0 – 24 hours): Asymptomatic or mild GI upset with anorexia, nausea, vomiting, malaise, pallor, and diaphoresis.

2. Stage 2 (24 – 48 hours): Resolution of initial GI symptoms with development of right upper quadrant pain, jaundice, subclinical elevation of transaminases and prothrombin time.

3. Stage 3 (72 – 96 hours): Peak liver dysfunction and possible multi-organ failure, hepatic encephalopathy and coagulopathy.

4. Stage 4 (days to weeks): Resolution of liver abnormalities or progressive liver failure and occasionally death.

Complications: Approximately 2 – 5% of toxic ingestions (in adults and adolescents) go on to develop fulminant hepatic failure requiring transplantation or resulting in death. Renal failure occurs in about 25% of hepatotoxicity cases. Complications are very rare in prepubertal children due to altered metabolism and relatively smaller quantities ingested.

Investigations

Aspartate aminotransferase and alanine aminotransferase levels (AST and ALT), bilirubin, and prothrombin time (PT) elevation indicates liver inflammation and injury. These can be helpful in patients with ingestion of multiple doses or if the time course is unreliable. Baseline electrolytes and glucose are recommended if the acetaminophen level is high enough to warrant treatment with NAC.

Blood Levels: The Rumack-Matthew nomogram is used to interpret blood levels of acetaminophen. Acetaminophen level should be done in the first 24 hours for an estimated ingested dose of more than150 mg/kg or if unknown. Serial acetamino-phen levels may help calculate the half-life to estimate the total amount ingested or pick up a late peak in an extended release preparation.

Management

Potentially toxic ingestions are defined as: 1) a level above the "possible toxicity" nomogram line, 2) the ingestion that is complicated by multiple doses, or 3) the time course is not defined. If reliable, a history of less than 150 mg/kg of acetaminophen ingested in a single acute episode can be managed at home.

Decontamination: GI decontamination is indicated in the first 1 – 2 hours after potentially toxic ingestions or 3 – 6 hours if there has been co-ingestion of substances that delay gastric emptying, e.g., anticholinergics. Acetaminophen has a high affinity for activated charcoal (AC). Early decontamination eliminates the need for gastric lavage and its potential complications. A single dose of AC 1g/kg orally or through nasogastric tube is administered. Lavage is indicated for multiple drug ingestions. There is no role for enhanced elimination such as hemodialysis/hemoperfusion or forced diuresis.

Antidote therapy: N-acetylcysteine (NAC) is indicated in any potentially toxic ingestion or with evidence of hepatic injury (elevated AST/ALT, PT). NAC is most effective in the first 24 hours post-ingestion, even if activated charcoal has been given. NAC is administered orally or through nasogastric tube in 140 mg/kg initial loading dose, then 70 mg/kg q 4 hours for 18 total doses. One can use 10% - 20% NAC solution (10g or 20g/100ml) which is diluted to a 5% solution with water, soda or juice to make it less noxious. If any dose is vomited within an hour it should be repeated in full. Emesis control with antiemetics like ondansetron or phenothiazine is often required to improve the tolerance. Intravenous NAC may also be considered in patients with severe vomiting or ileus or with late presentation of acetaminophen toxicity.[3, 4, 5]

Liver transplantation: Indications for a liver transplant include increasing PT on day 4,

pH <7.30, PT >100 seconds, creatinine >3.4 mg/dl or hepatic encephalopathy at any time.

Supportive: Supportive treatment is an integral part of managing any child with poisoning. Rehydration and maintenance fluids are indicated for the severely vomiting and/or anorectic patient. Even non-toxic ingestions from a suicide attempt or gesture in adolescents should be admitted for mental health evaluation and treatment.

SEDATIVES, HYPNOTICS

The common sedative-hypnotic agents include barbiturates, benzodiazepines, chloral hydrate, opioids, carbromal, buspirone and glutethimide. In pediatric ingestions first four drugs are more commonly involved than others.

Core facts and pathophysiology

All the sedative-hypnotic drugs decrease activity, produce calmness and facilitate sleep. Agents include barbiturates, benzodiazepines, chloral hydrate, buspirone, ethchlorvynol, meprobamate, carbromal, methyprylon and glutethimide[6,7]. Opioid produces analgesia, euphoria and sedation. These agents produce variable degrees of CNS depression after acute ingestion. Some have direct toxic effects on other organs like the liver. A mixed ingestion with more than one agent increases the toxicity and mortality risk. Chronic use of these agents may produce tolerance to the sedative effects but not the toxic effects. Toxic effects generally occur at 10–15 times the therapeutic dose, although individual variation is common.

Barbiturates: Inhibit neurotransmission at synapses, causing generalized depression of neuronal activity. Large doses produce hypotension secondary to decreased central sympathetic tone and direct depression of myocardial contractility. Barbiturates are divided into groups based on the duration of action. Shorter-acting barbiturates are highly lipid-soluble and are more toxic than the long-acting compounds. The significant renal excretion of phenobarbital and its relatively low pKa are the rationale for the use of forced alkaline diuresis. Trichloroethanol has a structure similar to halothane, and may sensitize myocardium to catecholamines and can lead to arrhythmias.

Clinical features

Poisoning may either result from cumulative toxicity of anticonvulsant medication (like phenobarbital) or due to accidental single drug ingestions. Adolescents with suicidal tendencies may have poly-pharmacy ingestion.

CNS Depression: All agents produce similar CNS depression. Onset of symptoms depends on the drug and route of intoxication. Drowsiness is usually the first sign of intoxication. Paradoxical excitation occurs in some children. Mild to moderate toxicity presents with slurred speech, nystagmus and ataxia. More severe toxicity presents as stupor or coma and can progress to respiratory arrest, hypotension and cardio-vascular collapse from decreased myocardial contractility and decreased sympathetic vasomotor tone. Patients in deep coma may have absent reflexes and hypothermia. Initially pupils may be small, but with deeper coma they may become dilated and non-reactive. Mixed ingestions, especially ethanol, potentiate CNS depression and other toxic effects.

Bullous skin lesions may be seen in patients with barbiturate, ethchlorvynol, meprobamate, glutethimide and benzodiazepine intoxication. Typically, the lesions are seen on the hands, buttocks or knees but may appear on other areas of the body.

Opioid: Acute ingestion causes a triad of coma, pinpoint pupils and absent bowel sounds. Respiratory depression, bradycardia, hypotension and depressed sensorium may also occur. Orthostatic hypotension may result from significant histamine release. IV opiate abusers

have needle tracks and are at risk for cutaneous abscesses, endocarditis, hepatitis, vasculitis, extreme constipation and HIV infection.

Benzodiazepines: Most obtunded patients can be aroused within 12 – 36 hours. Hypotension or hypothermia is rare. Respiratory depression is usually not significant with oral ingestion and deaths are seen only in patients with combined ingestion.

Chloral hydrate: Acute poisoning produces stupor and coma about 30 minutes after ingestion. Skin and mucous membrane irritation can result. Nausea, vomiting and gastritis can occur which can become hemorrhagic and lead to perforation. Direct hepatic toxicity with jaundice is also seen. Cardiac dysrhythmias (atrial and ventricular) are common. Persistent ventricular dysrhythmias are common terminal events.

Complications of sedative - hypnotic ingestion: Death or hypoxic-ischemic injury may occur after cardiopulmonary arrest. Dysrhythmias are seen with meprobamate and chloral hydrate. Chloral hydrate can produce gastritis, esophagitis or intestinal perforation and esophageal stricture. Seizures are provoked by overdose of morphine, meperidine and propoxyphene. They are also seen in patients recovering from glutethimide and methyprylon ingestion.

Investigations

Serum electrolytes, glucose, BUN and creatinine, are done to rule out metabolic causes of altered mental status. Barbiturate levels do not correlate with clinical status of patients, especially in those who are tolerant to the drug. Serum therapeutic range of phenobarbital is 15 – 40 µg/mL. Levels in the range of 60 – 80 µg/mL are toxic. Diagnostically, serum phenobarbital levels are helpful, as alkaline diuresis is a therapeutic option. Short-acting barbiturate with serum levels of >20–30 µg/mL are generally associated with

coma. Serial levels of other agents may be useful in patients with clinical deterioration despite aggressive therapy. Rising levels in these patients may indicate prolonged absorption from a concretion. Abdominal x-rays may be useful to demonstrate radio-opaque pill fragments or suspension in phenobarbital ingestion or chloral hydrate tablet ingestion. Atrial, ventricular, and conduction arrhythmias are seen in chloral hydrate or meprobamate ingestion. Evidence of concurrent tricyclic antidepressant overdose includes prolongation of the QRS complex, prolonged QT interval or torsades de pointes.

Management

Therapy is directed towards supporting vital organ functions and enhancing elimination of ingested medications.

Attend to ABCs: Intubation and/or assisted ventilation may be required if protective reflexes are depressed. Myocardial depressant effects of single or multiple-drug ingestion may cause hypotension, arrhythmias or diminished contractility. IV fluids, inotropic agents or antiarrhythmics should be used as guided by protocols.

Decontamination/Elimination: Consider gastric lavage if child is brought within 4 - 8 hours of ingestion. Intubation for airway protection may be indicated, especially in glutethimide ingestion. Administer activated charcoal, 1 g/kg through nasogastric tube or per oral route. Repeat charcoal doses of 0.5 g/kg should be given every 2 - 4 hours until the mental status improves. Hemodialysis or charcoal hemoperfusion to enhance elimination are indicated for extremely large ingestion of medication, failure to respond to aggressive supportive therapy or coma. Urine alkalinization is useful for phenobarbital poisoning but not for other barbiturates. For urine alkalinization use sodium bicarbonate:

1–2 mEq/kg IV initially, then 50–100 mEq/L of IV fluid to maintain a serum pH 7.45–7.50 and urine pH 7–8.

Antidote/Supportive therapy

1. Supportive therapy for hypotension and poor cardiac output: Inotropic support of cardiac output and blood pressure may be required. Excessive fluids should be avoided to prevent pulmonary edema.

2. Naloxone is a narcotic antagonist used for known or suspected opioid overdose. Dose: i) 0.01 mg/kg, im or iv repeated every 3-10 minutes if no response occurs.

3. Flumazenil has been used to treat isolated benzodiazepine overdose[8]. Flumazenil is not indicated for comatose patients with an unknown ingestion. It is not a substitute for basic emergency care (ABCs), although in some patients it may prevent the need for endotracheal intubation. It is given in dose of 0.01 mg/kg, IV over 30 seconds and repeated as necessary every 30 seconds to a maximum dose of 1 mg in children. As duration of action is 30 – 60 minutes, one should monitor for re-sedation. Flumazenil may precipitate: a) arrhythmias in patients with cyclic antidepressant or chloral hydrate ingestion, b) seizures in patients who were brought with seizures, twitching or a history of seizures, c) acute withdrawal, including seizures and autonomic instability, in patients tolerant to benzodiazepines.

4. Propranolol or esmolol is useful for treatment of ventricular arrhythmias in chloral hydrate and meprobamate ingestion. Standard antiarrhythmics are less effective.

5. In chloral hydrate intoxication, adequate glucose must be provided to prevent hypoglycemia associated with liver injury.

6. Continuous cardiopulmonary and oxygen saturation monitoring are to be carried out for all significant ingestions. Arrhythmias may develop with chloral hydrate and meprobamate. Frequent blood pressure determination is essential especially for meprobamate ingestion where profound hypotension may develop unexpectedly.

ANTICONVULSANTS

Phenobarbital, phenytoin, carbamazepine, valproic acid, felbamate, gabapentin and lamotrigine are the anticonvulsants commonly used in both children and adults.

Core facts and pathophysiology[9]

Toxic manifestations of anticonvulsants can be caused by accidental or intentional overdose, drug interactions, idiosyncratic reactions and hypersensitivity reactions. Consider co-ingestions in all overdoses.

Phenobarbital: It is a CNS depressant (inhibition of neurotransmitters) with a long half-life of more than 48 hours. The half life may get extended in overdose up to 7 days. Renal excretion is the main route for elimination.

Phenytoin: It is structurally related to barbiturates and has dose dependent kinetics with increased half-life in overdose. The half-life is more than 8 hours. Metabolism occurs mainly in the liver.

Carbamazepine: It is structurally related to antidepressants. Anticonvulsant properties are related to inhibition of sodium channels and interference with noradrenaline and glutamate metabolism. Oral absorption is slow and erratic and has a half life of 8 – 10 hours.

Valproic acid: It acts by increasing concentration of GABA or inhibition of reuptake. The half-life is 6 – 16 hours with mainly hepatic metabolism.

Felbamate: It is a dicarbamate derivative. It acts as glycine antagonist and is partially metabolized in liver or excreted unchanged in urine. It has a half-life of more than 20 hours. Felbamate has been withdrawn by the FDA.

Gabapentin and Vigabatrin: These are chemical analogues of GABA and inhibit GABA synapses by irreversible binding. It is excreted unchanged in urine. Half-life is 5 – 7 hours.

Lamotrigine: Lamotrigine is unrelated to other anticonvulsant drugs. It blocks sodium channels, limiting release of glutamate and aspartate, thus stabilizing neuronal membranes. It is metabolized by the liver and has very long half-life of more than 14 – 24 hours.

Clinical features

Toxic manifestations of phenobarbital, phenytoin, carbamazepine and valproic acid are as follows :-

- Neurotoxicity includes lethargy, nystagmus, ataxia, dystonia, dyskinesias, seizures and coma. Respiratory depression and apnoea as well as cardiotoxic effects such as arrhythmias and myocardial depression[10,11] are also seen.

- Idiosyncratic reactions include liver failure, hematopoietic toxicity and hypersensitivity skin reactions such as erythema multiforme and Stevens-Johnson syndrome.

- Hypothermia and a vesicular rash occur with phenobarbital overdose.

- Anticholinergic effects (fever, dryness, agitation, flushing) occur with carbamazepine overdose.

Phenytoin sodium settles in the bottle in the suspension form. An unshaken bottle may give low levels at the top and toxic levels at the bottom.

Newer anticonvulsants: (Felbamate, gabapentin, vigabatrin, lamotrigine)

- There are few reports of over dosage and these drugs seem to have a high therapeutic index. Somnolence, ataxia, nausea and vomiting can be expected with these newer drugs and have been seen at therapeutic doses[12,13].

- Aplastic anemia, an idiosyncratic effect has been reported in some patients receiving felbamate and resulted in withdrawal of felbamate by the FDA. Stevens-Johnson syndrome has been reported with felbamate and lamotrigine but not with gabapentin or vigabatrin.

- A lamotrigine overdose may cause mild ataxia and nystagmus. A slightly prolonged QRS may occur on EKG but no arrhythmias are reported.

- Under or overdosage may cause status epilepticus, especially if the patient is on another medication which may affect metabolism of the anticonvulsant. Co-ingestion of other CNS depressants, especially alcohol and benzodiazepines exacerbate respiratory depression and somnolence and increases morbidity and mortality of ingestions. Supportive care usually results in recovery in 24 – 48 hours without significant consequences in most cases.

Investigations

ABG should be done if sedation or respiratory depression is present. Gastric lavage should be cautiously done with airway protection in the presence of respiratory depression. Other investigations which needs to be done include CBC, electrolytes, urinalysis, hepatic enzymes and CPK. Serial levels of ingested anticonvulsants should be followed.

- Phenobarbital: Therapeutic levels range from 15 to 40 µg/mL: Serum levels may not correlate with level of sedation, particularly in those on long-term therapy, as tolerance develops. Sedation to coma is common above 70 µg/mL level. Reversible "flat line" EEG may be seen over 120 µg/mL.

- Phenytoin sodium: Therapeutic levels: 10 – 20 µg/mL. Ataxia and nystagmus occur at >30 µg/mL.

- Carbamazepine: Therapeutic levels: 4-12 µg/mL. Confusion, dizziness and ataxia occur at >14 µg/mL, while there are chances of arrhythmias at >40 µg/mL.

- Valproic acid: Therapeutic levels: 50–100 µg/mL.

Management

Decontamination: Gastric lavage is indicated for recent ingestions. Lavage should be done until returns are clear and one must ensure protection of airway during lavage. Single dose charcoal is indicated for all; multidose charcoal is effective in phenobarbital, phenytoin and carbamazepine overdoses. The first dose should be given in the dose 1g/kg NG or P.O. Repeat charcoal doses of 0.5g/kg once in every 2-4 hours. Extracorporeal elimination is useful for many anticonvulsants. In phenobarbital, carbamazepine and valproate overdose hemodialysis, hemo-perfusion and plasmapheresis can help to decrease serum drug levels. These measures are reserved for seriously ill patients in whom supportive measures are inadequate. Urine alkalinization will enhance phenobarbital excretion. Hyperventilation may achieve the same results in intubated patients. Naloxone may be effective in valproic acid overdose.

Supportive treatment: Supportive care with supplemental O_2 should be done as necessary and airway protection/intubation may be necessary in patients with CNS depression. Seizures should be treated with benzodiazepines. Avoid the use of anticonvulsants suspected in overdose. Continuous cardiorespiratory and pulse oximetry monitoring is necessary for any patient with CNS sedation, respiratory depression or arrhythmias. Rewarming and frequent temperature checks should be done for barbiturate

ingestion. One should consider social service and psychiatric intervention for children with repeated ingestions or teenagers with suicidal psychopathology.

IRON

Core facts and pathophysiology[14]

Iron ingestion is one of the leading causes of non-intentional ingestion deaths in children. Iron is readily available to children and frequently has a bright-colored sugar coating. Often it is not felt to be harmful by family members, and is used by expectant mothers with other small children in the household. The majority of toxic ingestions occur with prenatal vitamins (20% elemental iron) or iron-only preparations. Ingestion of more than 20 mg/kg of elemental iron is toxic. Lethal ingestions occur with 180 – 300 mg/kg of elemental iron. Normal excretion of iron is limited to 1-2 mg/day from the GI tract, urine and desquamated skin.

Iron toxicity occurs via two mechanisms

1. Direct caustic effects on the gastrointestinal mucosa: Mucosal ulceration along the stomach and proximal small bowel causes intramural hemorrhage and iron deposition. Segmental infarction occurs along the distal small bowel and may present late as gastric outlet and small intestine strictures. The damage to the mucosa allows bacterial invasion of the gut wall.

2. Iron also has a direct cytotoxic effect on several tissues and organs, principally the liver, heart and lungs. Iron can uncouple oxidative phosphorylation in the mitochondria and generate oxygen-free radicals. In acute oral ingestion, iron is absorbed in the duodenum and jejunum where it is bound to transferrin. Once the total iron binding capacity of transferrin is exceeded the potential for toxicity exists. Free circulating iron causes vasodilation, venous pooling and increased

capillary permeability. This results in cellular damage to both the liver and the myocardium along with metabolic acidosis and impaired glucose tolerance.

3. Toxicity of iron depends on the elemental iron ingested. The elemental iron varies from preparation to preparation. (Table 1 and Table 2). Example: Ingestion of 20 tabs of 325 mg ferrous sulfate in a 15 kg child = 20 X [325 X 0.2 mg] = 1300 mg elemental Fe which is equal to 87 mg/kg.

Clinical features

Vomiting is the most sensitive predictor of serious iron ingestion. Absence of vomiting at 6 hours means patient is unlikely to have ingested a toxic amount. The classic clinical presentation has four stages[15]:

1. First phase (0 – 6 hours): GI irritation including vomiting, (bloody) diarrhoea, nausea and abdominal pain. Severe ingestions may result in fever, hyperglycaemia, hypotension, tachycardia, poor peripheral perfusion, metabolic acidosis, lethargy and coma.

2. Second phase (6 – 24 hours): Latent phase. This may or may not be present. The patient stabilizes during uptake of free iron by the reticuloendothelial system.

3. Third phase (12 – 24 hours): Systemic toxicity. A minority of patients progress to this stage. GI symptoms recur with profound hypotension, acidosis and pulmonary hemorrhage, hepatic necrosis manifests as hypoglycemia and coagulation defect, oliguria, seizures, lethargy and coma. Sepsis with fever occurs because of bacterial invasion of the gut wall.

4. Fourth phase (2 – 6 weeks): Late complications. Gastric or bowel obstruction occurs secondary to progressive strictures from gut injury at the time of ingestion.

Table 1. Iron composition of common iron compounds

Iron compound	Elemental Fe
Ferrous sulphate	20%
Ferrous gluconate	12%
Ferrous fumarate	33%
Ferric phosphate	37%
Ferric pyrophosphate	12%
Ferroglycine sulfate	16%

Table 2. Toxicity of iron by blood level

Serum Iron (mg/dL)	Level of Toxicity
50 – 150 mg/dL	Normal serum iron concentration
<300	Non-toxic
300 – 500	Mild
500 – 1000	Moderate: Highly associated with toxicity
>1000	Severe: Death if untreated

Complications of severe iron intoxication include:

- Gastrointestinal: Bowel perforation with subsequent peritonitis, stomach or small bowel obstruction and hepatic/pancreatic necrosis.

- Coagulopathy frequently occurs late in severe intoxication and is mostly due to liver dysfunction, but may also occur early due to iron's effect on thrombin, independent of hepatocellular dysfunction.

- Cardiopulmonary: Myocardial dysfunction is mostly due to hypovolemia and shock, but

there is evidence that iron causes direct myocardial toxicity. Respiratory compromise is due to physiologic derangements, but acute respiratory distress syndrome (ARDS) frequently occurs late and is associated with high-dose deferoxamine treatment (15 mg/kg/day or more for more than 24 hours.).

- CNS manifestations are usually associated with the presence of hypovolemia, metabolic acidosis and liver dysfunction.

Investigations

CBC, glucose, serum iron and TIBC may be all that is necessary in an asymptomatic to mild intoxication or with an unknown quantity of ingestion. Total leucocyte count more than 15,000 a serum glucose more than 150 mg/dL is considered a positive predictor of a serum iron more than 300 mg/dl. Bicarbonate establishes the severity of the metabolic acidosis. Coagulation studies and liver function tests define the degree of hepatic involvement.

Total Iron Binding Capacity (TIBC) varies widely and currently has limited value in the evaluation of iron toxicity[16]. Emphasis should be placed on the absolute serum Fe levels as serum iron levels are more important. A serum iron concentration at 2 - 4 hours post-ingestion is the best estimate of risk of toxicity. A level done greater than 6 hours post-ingestion under estimates the toxicity because of tissue accumulation. Plain abdominal radiograph obtained within 2 hours of ingestion may demonstrate radiopaque material consistent with iron. 60% of patients in one study with a positive radiograph had an iron concentration >300 mg/dL. Serial films may be used to assess the efficacy of gastric decontamination. Absence of opaque fragments does not eliminate the possibility of toxicity.

Management

Ingestions of less than 20 mg/kg without symptoms may not require ED treatment. Any patient who is symptomatic requires evaluation in a health care facility.

Decontamination/Elimination: Gastric lavage should be performed on patients where vomiting has not occurred or where retained iron is visible on abdominal radiograph or who exhibit signs of increasing toxicity. Pill fragments are usually large so the largest orogastric tube possible should be utilized. Activated charcoal does not bind iron. Whole bowel irrigation is contraindicated with severe GI haemorrhage or perforation. Hemodialysis is not effective for free iron. Exchange transfusion increases the removal rate 30-fold compared to deferoxamine alone.

Antidote/Specific Therapy: Deferoxamine is an iron chelating agent[17]. Treatment is based on symptoms and the serum iron level:

- Serum iron levels less than 300 mg/dL usually do not warrant therapy.

- A symptomatic patient with serum iron 300 – 500 µg/dL, needs chelation therapy.

- A level more than 500 mg/dL should be chelated even if asymptomatic.

The IV dose is 15 mg/kg/hour for 4 – 6 hours or until the patient stabilizes, then 6 mg/kg/hour.

Side effects include nausea, hypotension, rash, and anaphylaxis. Hypotension is usually responsive to slowing the rate of infusion of desferoxamine, fluids and vasopressor. Administration for more than 15 mg/kg/hr and more than 24 hours is associated with the development of adult respiratory distress syndrome (ARDS).

Supportive therapy: Fluid resuscitation with Ringer lactate or normal saline (20ml/kg) is important

for poor peripheral perfusion, tachycardia, or hypotension. Vasopressors may be required to maintain an adequate blood pressure and end organ perfusion with severe toxicity. Severe iron ingestions may require oxygen therapy or mechanical ventilation if pulmonary oedema or haemorrhage develops, or altered neurological status in late-stage of ingestion. It is essential to do continuous cardiorespiratory and oxygen saturation monitoring for ingestions more than 40 mg/kg.

Admission criteria: All symptomatic patients should be hospitalized and receive chelation therapy. Patients with serum iron levels more than 300 mg/dL should be admitted and receive chelation therapy. If serum iron levels are not available, patients who have a WBC count more than 15,000/mm³ and a serum glucose more than 150 mg/dL should also be admitted.

Antiarrhythmic and antihypertensive cardiovascular drugs

A sudden onset of toxicity is common with antiarrhythmic drug poisoning. Sustained-release preparations may have a delay of 1–2 days before onset of symptoms, especially if decontamination with activated charcoal or whole bowel irrigation is not performed. Antiarrhythmic drug ingestions are rare occurrences in terms of number of ingestions per year, but may represent a disproportionate number of deaths and severe toxicity following prescription drug poisoning.

Core facts and pathophysiology

1. Drugs that slow heart rate and may block electrical conductance through the AV node:

- Class Ib (Lidocaine, phenytoin, tocainide, mexiletine): Toxic effects include lethargy, confusion, coma, seizures, and apnea/ respiratory arrest. QRS and QT intervals usually remain normal. Brady arrhythmias including asystole occur. Rapid infusion of

phenytoin (>1 mg/kg/min, or 50 mg/min) has resulted in sudden asystole, possibly related to the propylene glycol diluent in the IV preparation.

- Class II: ß-adrenergic blockers: Toxic effects include decreased cardiac contractility, centrally mediated coma, seizures, or apnea (especially propranolol). Bradycardia with AV block and hypotension are common[18]. Ventricular dysrhythmias, including torsades de pointes, may occur after sotalol poisoning. Some ß-blockers (pindolol, alprenolol, and oxyprenolol) have intrinsic sympathomimetic activity that in low doses counteracts the effect on rate and rhythm; this effect is lost with large overdoses. Hypoglycemia and bronchospasm occur rarely.

2. Drugs that cause QRS widening and ventricular dysrhythmias (phase 0 fast Na+-channel blockade). (Class Ia: Quinidine, disopyramide, procainamide, Class Ic: Antidysrhythmic agents: Encainide, flecainide, Class III: Amiodarone)

- Ventricular dysrhythmias, hypotension, sudden onset of pulselessness may occur after ingestion or overdose. Anticholinergic findings such as dilated pupils, dry mouth, and delirium may follow quinidine or disopyramide ingestion. Quinidine often causes vomiting and diarrhea. Propafenone and encainide overdoses are associated with status epilepticus.

3. Drugs that cause QT interval prolongation and ventricular tachycardia/torsades de pointes (phase 3 inwardly-rectifying K+-channel blockade): Quinidine, procainamide, encainide, flecainide, sotalol, amiodarone.

4. Calcium channel blockers are Class IV antidysrhythmics: Toxicity produces decreased cardiac contractility, peripheral vasodilatation with

hypotension in varying degrees, depending on the specific drug ingested[19].

- Bradycardia, AV block and hypotension are seen with verapamil and diltiazem. Sudden onsets of coma, apnea or seizures often occur with verapamil poisoning.

- Bradycardia without AV block and hypotension are common with nifedipine and newer calcium channel blockers, e.g., nimodipine.

- Hyperglycaemia may occur due to inhibition of insulin release with ingestion of any calcium channel blocker.

- Diltiazem and verapamil are available as long-acting preparations.

5. Clonidine: It is a central and peripheral α_2 adrenergic agonist that is rapidly absorbed.

- CNS α_2 stimulation causes opioid-like effects, and decreases heart rate and vascular tone, resulting in hypotension[20].

- Peripheral α_2 stimulation may cause brief, paradoxical hypertension.

- Symptoms of overdose include altered mental status, hypertension and hypotension, respiratory depression and miosis. Onset of symptoms occurs within 4 hours of ingestion and rarely last beyond 24 hours.

Investigations

Electrolytes and renal function: Hypokalemia and hypocalcemia may predispose to dysrhythmias after antiarrythmic overdose. Renal functions tests can help to assess potential for decreased renal clearance after overdose, as well as indicate possible prerenal azotemia from hypoperfusion.

Imaging and EKG: EKG changes depend on the type of drug ingested. For example:

a) ß-adrenergic blockers: Bradycardia with AV block, decreased cardiac contractility, ventricular dysrhythmias, including torsades de pointes, b) Digitalis preparations: Bradycardia with heart block, other dysrhythmias, c) Type Ib agents: Bradyarrythmias, including asystole, d) Quinidine, procainamide, disopyramide, encainide, flecainide (Type Ic agents), sotalol and amiodarone: Ventricular dysrhythmias, an R wave in aVR and prolongation of the QTc interval.

Management

Decontamination/Elimination: Activated charcoal should be used in all patients. Multi-dose charcoal may be considered with nadolol, atenolol, sotalol, and sustained-release preparations. Whole bowel irrigation is recommended for ingestion of sustained-release preparations after an initial dose of activated charcoal. Endpoint is passage of clear rectal effluent with improving clinical status.

Antidote/Specific therapy

- For ß-adrenergic blocker medications, antidote therapy include (from most efficacious to least efficacious) i) Glucagon, 50–100 µg/kg IV (up to 1 mg) followed by infusion of 70 µg/kg/hr. (ii) Epinephrine, 10 µg/kg IV (0.1ml/kg of 1:10,000) bolus followed by infusion of 0.1–1µg/kg/min. iii) Atropine 20 µg/kg IV (upto 1 mg) every 5–10 minutes until total dose of 2 mg delivered, iv) Isoproterenol dose is 0.1-1 µg/kg/min IV but it may worsen hypotension due to ß$_2$ agonism causing peripheral vasodilation or v) Transvenous pacemaker if no response to medications. In addition to these, the hypotension will need fluid resuscitation and inotropic support.

- Drugs causing prolonged QRS and ventricular dysrhythmias: The management include i) Sodium bicarbonate 1 – 2 mEq/L rapid infusion which may be repeated as necessary to keep blood pH 7.45 – 7.50.

ii) Lidocaine 1 mg/kg IV, repeat up to 2 doses iii) Phenytoin 15 – 20 mg/kg IV at a rate not to exceed 1 mg/kg/min iv) Correct potassium, calcium, and magnesium abnormalities[21].

- Drugs causing prolonged QTc and ventricular dysrhythmias: i) Magnesium sulfate 30-60 mg/kg rapid IV infusion (up to 2 gms) which may be repeated once. Monitor serum calcium and magnesium levels.

- Calcium Channel Blockers: For bradycardia the recommended treatment in order of preference are i) Calcium infusion (calcium gluconate or calcium chloride) IV which may be repeated along with monitoring of serum calcium and avoid hypercalcemia, ii) epinephrine infusion, iii) glucagon, iv) atropine and v) consider transvenous pacing if above medications fail.

- Clonidine: For hypotension, IV bolus fluids are generally adequate. On the other hand hypertension is generally transient and does not need treatment. For bradycardia atropine may be used. Lethargy and apnoea, due to opioid effects, may respond to naloxone which may not be effective against bradycardia or hypotension[22].

Supportive therapy: Patient should be monitored closely for potential respiratory compromise and all equipment and medications for rapid sequence intubation should be immediately available. Continuous cardiorespiratory monitoring and oxygen saturation by pulse oximetry should be done for at least the first 6 hours after ingestion in every case. Further monitoring depends on the severity of condition.

ANTIHISTAMINES

Core facts and pathophysiology

First generation antihistamines include diphenhydramine, hydroxyzine, chlorpheniramine and many others. Second generation antihistamines include terfenadine, astemizole, loratadine, cetirizine and fexofenadine

Antihistamines are competitive inhibitors of the H1 receptor (H1 antagonists). Second generation antihistamines act selectively on peripheral H1 receptors because they do not cross the blood brain barrier or do so in such low concentrations that blockade of central histamine and cholinergic receptors does not occur, accounting for their "non-sedating" properties. CNS depression occurs at therapeutic doses of first generation antihistamines; over-dosage may result in CNS stimulation in children and young adults. A single dose of 20 – 40 mg/kg has been reported to be a lethal dose in adults. Seizures have been reported with as little as 150 mg in an 18-month-old child. Children seem to be more sensitive to toxic effects[23].

Clinical features

1. Anticholinergic effects like fixed, dilated pupils, hyperpyrexia, facial flushing, excitation, tremors and hallucinations are seen in overdose of first generation drugs. In severe cases even generalized seizures, arrhythmias and coma can occur. Seizures occur much more commonly in children than adults.

2. Second generation antihistamine over-dose (terfenadine and astemizole) causes QT prolongation and ventricular arrhythmias such as torsades de pointes[24]. CNS sedation and seizures have also been noted. Erythromycin and ketoconazole increase the risk of arrhythmia.

3. Antihistamines are widely available combined with other medications in over-the-counter for common cold preparations, particularly acetaminophen and phenyl-propanolamine; therefore, co-ingestion of other medications may also require intervention. Many of these are available as sustained-release preparations, prolonging the period required for observation or treatment.

Management

Decontamination: Gastric lavage is indicated for recent ingestions with potential for altered mental status. Activated charcoal is used as single dose for non-sustained release preparations and multi-dose charcoal for slowed gastric motility or sustained release ingestions.

Supportive management: It includes control of seizures with lorazepam or phenobarbital. Ventricular arrhythmias, torsades de pointes are treated with either magnesium sulphate or phenytoin. Hypertension when occurs is managed with diazoxide or methyldopa. Use of physostigmine for severe anticholinergic toxicity (if seizures, arrhythmias, severe hypertension are unresponsive to above measures) has been reported. Continuous cardiorespiratory and oxygen saturation monitoring are needed for symptomatic patients or those with second generation antihistamine ingestion.

ß–ADRENERGIC AGONISTS

Core facts and pathophysiology

ß-adrenergic agonist toxicity is dose dependent. Ingestion of <1 mg/kg of salbutamol (3–10 times the normal daily dose) is non-toxic. Up to 20 times the normal daily dose of salbutamol has been ingested without serious medical complications or death[25]. All ß-adrenergic agonists are rapidly absorbed, and toxic effects are seen within an hour of ingestion.

$ß_1$-receptors are found on the heart. $β_2$-receptors are found in blood vessels, lungs and pancreas. $ß_1$-effects include tachycardia, increased cardiac contractility, tremor, agitation and vomiting. $ß_2$-effects include peripheral vasodilatation, tachycardia, widened pulse pressure, tremor, hypokalemia and hyperglycemia. Hyperglycemia results from stimulation of glycogenolysis. Hypokalemia results from increased activity in membrane-bound $Na+/K+$ ATPase in skeletal muscle. This reflects $K+$ shift from the extracellular to intracellular space and does not indicate a true deficit of total body potassium. Therefore, potassium replacement is not needed following ß-agonist ingestion. Tremor occurs following ß-agonist poisoning because of differential responses among fast- and slow-twitch muscle groups. Severe CNS effects are rare because most orally administered ß-agonists do not cross the blood-brain barrier in large amounts.

Management

GI decontamination is usually not necessary, definitely not needed if patient has already vomited. Activated charcoal may be used if child arrives early.

Use of ß-adrenergic blockers has been suggested as helpful in patients with severe toxicity. But it is very rare that a child with salbutamol ingestion will ever need ß-blocker administration.

Points to Remember

- *N-acetylcysteine is indicated in any potentially toxic acetaminophen (>150mg/kg) ingestion, and is most effective in the first 24 hours.*

- *A sudden onset of toxicity is common with antiarrhythmic poisoning but with sustained-release preparations symptoms may be delayed up to 1-2 days.*

- *Toxic manifestations of anticonvulsants can be caused by accidental or intentional overdose, drug interactions, idiosyncratic reactions and hypersensitivity reactions.*

- *Ingestion of >20 mg/kg of elemental iron is toxic. Lethal ingestions occur with 180 – 300 mg/kg of elemental iron.*

- *Clonidine toxicity includes altered mental status, hypertension and hypotension, respiratory depression, and miosis. It resembles opioid poisoning.*

References

1. Anker AL, Smilkstein MJ. Acetaminophen: Concepts and controversies. Emerg Med Clin North Am 1994; 12:335–349.

2. Howland MA, Smilkstein MJ, Weisman RS. Acetaminophen. In: Goldfrank LR, ed. Goldfrank's toxicologic emergencies. 5th edn Norwalk, CT: Appleton & Lange, 1994; pp487–497.

3. Howland MA, Smilkstein MJ, Weisman RS. Antidotes in depth: N-acetylcysteine. In: Goldfrank LR, ed. Goldfrank's toxicologic emergencies. 5th edn, Norwalk, CT: Appleton & Lange, 1994;pp498–499.

4. Harrison P, Keays R, Bray G, et al. Improved outcome of paracetamol-induced fulminant hepatic failure by late administration of acetylcysteine. Lancet 1990;335:1572–1573.

5. Keays R, Harrison P, Wendon J, et al. Intravenous acetylcysteine in paracetamol-induced fulminant hepatic failure: A prospective controlled trial. Brit Med J 1991;303:1026–1029.

6. Osborn H, Goldfrank LR. Sedative-hypnotic agents. In: Goldfrank LR, Flomenbaum NE, Lewin NA, Weisman RS, Howland MA, Hoffman RS, eds, Goldfrank's toxicologic emergencies. 5th edn, Norwalk, CT: Appleton & Lange, 1994;pp787–810.

7. Seyffart G. Antihistamines and other sedatives. In: Haddad LM, Winchester JF, eds. Clinical management of poisoning and drug overdose. Philadelphia: W. B. Saunders, 1990;pp820–861.

8. Sugarman JM, Paul RI. Flumazenil: A review. Pediatr Emerg Care 1994;10:37–43.

9. Dodson WE, Bourgeois BFD. Pharmacology and therapeutic aspects of antiepileptic drugs in pediatrics. J Child Neurol 1994;9(Suppl): 2S1–2S7.

10. Macnab AJ, Birch P, Macready J. Carbamazepine poisoning in children. Pediatr Emerg Care 1993;9:195–198.

11. Patsalos PN, Duncan JS. Anti-epileptic drugs: a review of clinically significant drug interactions. Drug Safety 1993;9:156–184.

12. Leach JP, Brodie MJ. New antiepileptic drugs—an explosion of activity. Seizure 1995;4:5–17.

13. Schmidt D, Kramer G. The new anticonvulsant drugs: Implications for avoidance of adverse effects. Drug Safety 1994;11:422–431.

14. Banner W, Tong TG. Iron poisoning. Pediatr Clin North Am 1986;33:393–409.

15. Goldfrank LR. Iron. In: Goldfrank LR, ed. Goldfrank's toxicologic emergencies. 5th edn, Norwalk, CT: Appleton & Lange, 1994; pp 521–531.

16. Henretig FM, Shannon M. Toxicologic emergencies. In: Fleisher GR, Ludwig S, eds. Textbook of pediatric emergency medicine. 3rd edn, Baltimore: Williams & Wilkins, 1993; pp776–779.

17. Howland MA. Deferoxamine. In: Goldfrank LR, ed. Goldfrank's toxicologic emergencies. 5th edn, Norwalk, CT: Appleton & Lange, 1994: pp532–534.

18. Critchley JA, Ungar A. The management of acute poisoning due to beta adrenoceptor antagonists. Med Toxicol 1989;4:32–45.

19. Ramoska EA, Spiller HA, Winter M, Borys D. A one year evaluation of calcium channel blocker overdoses: Toxicity and treatment. Ann Emerg Med 1993; 22:196–200.

20. Fiser DH, Moss MM, Walker W. Critical care for clonidine poisoning in toddlers. Crit Care Med 1990;18:1124–1128.

21. Pentel PR, Benowitz NL. Tricyclic antidepressant poisoning: management of arrhythmias. Med Toxicol 1986;1:101–121.

22. Nichols MH, King WD, James LP. Clonidine poisoning in Jefferson County, Alabama. Ann Emerg Med 1997;29:511–517.

23. Hendes L. Efficacy and safety of antihistamines and expectorants in nonprescription cough and cold preparations. Pharmacotherapy 1993;13:154–158.

24. Wiley JF, Gelber ML, Henretig FM, *et al*. Cardiotoxic effects of astemizole overdose in children. J Pediatr 1992;120:799–802.

25. Wiley JF II, Spiller HA, Krenzelok EP, Borys DJ. Unintentional albuterol ingestion in children. Pediatr Emerg Care 1994;10:193–196.

<div align="center">TOXICOLOGY</div>

CORROSIVE POISONING

* Jayanthi Ramesh

Abstract: *Corrosive ingestion is accidental in children. Though it forms a small group, it causes considerable morbidity and mortality. Corrosives are of 2 types, acids and alkalis. Corrosives produce coagulative necrosis and this depends on the concentration of the ingested material. Acutely, they present with intense pain, hemetemesis, respiratory distress, drooling, stridor and locally may cause burn injuries. Child may require acute care management of the airway, breathing and circulation. Steroids are given to prevent esophageal stricture if the child presents within 48 hours of ingestion. Endosopy is advised within 24 hours. Late complications like esophageal stricture has to be managed by periodic dilatation and surgical intervention as required. Prognosis with corrosive ingestion is guarded.*

Key words: Corrosive poisoning, Acids and Alkalis, Glottic edema, Esophageal stricture, Endoscopy.

Corrosives are widely used for cleaning metals in industries and for domestic purposes. Most of the household cleaning agents contain corrosives which include both acids and alkalies. Children, especially toddlers are more prone for accidental ingestion, whereas in adolescents and adults it is homicidal or suicidal. Corrosives may be thrown on the face or body deliberately (vitriolage) to cause disfigurement or blindness.

Corrosives are classified into four categories: (1) Acids which include, mineral acids such as sulphuric acid, nitric acid and hydrochloric acid, (2) Organic acids like oxalic acid, carbolic acid (phenol), acetic acid, and salicylic acid, (3) Vegetable acid like hydrocyanic acid, and (4) Alkalis which include, sodium hydroxide, potassium hydroxide and ammonium hydroxide.

Side effects of corrosives

It affects the skin (exposed part), mouth, throat, upper gastrointestinal tract and the respiratory system. Initial effects are burning pain, tingling sensation, blood stained vomiting, reduction in voice volume due to laryngeal edema. The late effects are pulmonary edema, broncho-pneumonia and oesophageal and stomach perforation. Laryngeal and oesophageal strictures and stricture at the pyloric junction occur as delayed complications.

Mineral acids are used commonly in automobile industry as battery fluids, in laboratories and as domestic cleansing agents.

Pathophysiology

Corrosive acids cause extraction of water from the tissues, destroy the tissue protein and convert the cellular protein to acid albuminates. Hemoglobin is converted into acid hematin and is precipitated. Due to the intense stimulation caused by the acid, the vascular tone is lost. This causes local irritation, bleeding and sloughing of mucous membrane and skin. In severe cases edema and

* Consultant Pediatrician,
Kanchi Kamakoti CHILDS Trust Hospital,
Chennai.

necrosis of the deeper tissues are seen. The most common area affected is the oesophageal and pyloric junction. It may lead on to perforation and stricture formation.

Clinical features

It depends on the mode, amount and concentration of the acid ingested, contact duration and the age of the child. In acute poisoning there is a severe burning pain in the mouth, pharynx and abdomen followed by vomiting, drooling, stridor, difficulty in breathing, hematemesis, fever and oral burns. Presence of stridor and drooling indicate injury to larynx and pharynx. Child may be in a state of cardio respiratory failure due to hypoxia following glottic oedema. Profound shock may ensue. Occasionally severe metabolic acidosis and multiorgan dysfunction results. If perforation occurs, it may lead to mediastinitis and peritonitis.

Management

History has to be noted and depending upon the clinical features treatment has to be instituted. Airway patency should be maintained and if necessary intubation, cricothyrotomy or tracheostomy is performed. In case of pulmonary edema, positive pressure ventilation is given. The presence of oropharyngeal ulcers indicate that there is increased risk of visceral injuries. Endosopy has to be performed within 24 hours from the time of injury. Hypotension if present should be corrected with normal saline. If the patient is able to swallow saliva, oral feeding can be allowed. In patients who are unable to swallow hydration and nutrition are maintained through IV fluids or through gastrostomy. Steroids are recommended within 48 hours if endosopy cannot be performed or if circumferential burns are identified during endosopy. Antacids can be used for burns in the stomach. Antibiotic may be used in patients with suspected perforation of the stomach. Otherwise use of antibiotics has to be reserved for specific signs of infection.

Gastric lavage, emesis, charcoal and cathartics are contraindicated in corrosive poisoning.

Treatment of sequelae : Esophageal stricture and gastric outlet obstruction require frequent dilatation once the healing is complete, which takes 4 to 6 weeks. Retrograde dilatation may be required in some if it is impossible to dilate from above. This is possible because the lower end of oesophagus is conical as opposed to the proximal end where the opening is eccentrically placed and may be difficult to define.

Surgical treatment is indicated for failure of dilatation to produce an adequate lumen, non compliance of patients with bougienage, complete stenosis and fistula formation. Surgeries which can be done include local excision of stricture if it is short, high oesophagogastrostomy, cervical oesophagogastrostomy, colon or jejunal interposition.

PHENOL (CARBOLIC ACID)

Phenol or its related compounds like resorcinol, hexachlorophene, cresol and hydroquinone are used as antiseptics, germicides, caustics and preservatives. In children poisoning is usually accidental while in adolescents it is suicidal and very rarely homicidal.

Pathophysiology

It is a protoplasmic poison and it causes denaturation of proteins thereby killing cells. Locally it causes anaesthesia by stimulating the nerve endings causing paralysis. Capillary damage result in thrombus formation in superficial vessels. It affects the heart, kidneys and also the central nervous system. It stimulates respiratory centre leading to respiratory alkalosis.

Clinical features

In the acute phase : Intense pain, hematemesis, bloody diarrhea, shock, laboured breathing,

hyperpnoea followed by metabolic acidosis, stupor, coma, convulsions and pulmonary oedema occur. If not attended to it can cause death. If the children survive the acute phase, they may develop renal failure and/or hepatic dysfunction. Urine colour is dark smoky green on exposure to air. Paralysis of respiratory and cardiac centre leads to death.

Lab investigations

Few drops of ferric chloride is added to urine. The colour of urine in the presence of carbolic acid changes to violet or blue.

Treatment

Airway management by intubation is the priority. Gastric lavage using plain water or 10% glycerine (only condition where gastric lavage advocated) is done through a soft nasogastric tube till no phenolic odour is present in the effluent. White of the egg can be given. Supportive management should be given. If the child develops renal failure, it is managed by fluid and salt restriction followed by peritoneal or haemodialysis as required. Apply castor oil for surface burns.

HYDROCYANIC ACID AND ITS SALTS

They are used in industries and for fumigating the homes, photography and silver polishes. Inhalation of these substances may cause cyanide poisoning. Some fruits like cherry, plum, peach, apricot, etc contain amygdaline which on ingestion can release cyanides.

Pathophysiology

They act on the cytochrome oxidase by inhibiting the system of electron transport and hence oxygen utilisation leading to cellular dysfunction and death. Death occurs within 10 minutes after consuming the poison.

Clinical features

It depends upon the mode of intoxication. A large dose leads to death in a minute. Bitter almond odour and hyperventilation are observed.

CNS toxicity include headache, dizziness, nausea, dilated pupils, convulsions and coma. Hypotension and dyspnoea can also be present.

Treatment

Objective of the treatment is methemoglobin production which competes with the cytochrome oxidase cyanide complex and dissociation occurs resulting in restoration of cellular and respiratory function. Oxygen through non-rebreathing mask has to be administered. Specific antidote capsule containing amyl nitrite is broken and inhaled over 30 seconds till sodium nitrite solution is prepared and given IV in a dose of 10mg/kg (max dose 30mg/kg). 25% Sodium thiosulphate solution at a dose of 1.65ml/kg is administered next. Hydroxy cobalamin is another specific antidote (not freely available). Supportive measures to correct hypotension, shock, and metabolic acidosis are used wherever needed. Death results due to respiratory paralysis.

ALKALIS

Potassium and sodium hydroxides, sodium phosphate, sodium and potassium carbonates are the examples of alkalis. They are used in soap manufacturing industries and are used in household cleansing agents. Sugar testing tablets contain sodium hydroxide. Button batteries contain sodium and potassium hydroxide. Accidental ingestion is very common due to their easy accessibility.

Pathophysiology

Alkalis combine with protein to form proteinates and fat to form soaps, thus producing soft, necrotic, deep penetrating wounds on

contact with the tissues. Solubility of these agents causes further damage in due course of time.

Clinical features

Acute presentation: Burning pain in the mouth and stomach, nausea, vomiting (vomitus is slimy and blood stained), swelling of mucous membrane of the mouth and airway compromise may occur. Pharyngeal involvement leading to respiratory distress, dysphagia, bloody diarrhoea with tenesmus, board like rigidity of the abdomen, shock followed by collapse ensues.

Late complications are oesophageal stricture and atrophy of the gastric mucosa. Usually button batteries pass through the oesophagus, GIT with little or no damage. If it disintegrates may lead to perforation of bowel and may prove detrimental to the patient.

Lab investigations

RBC count and hematocrit increases.

Ingestion of button batteries-Radiography to be done.

Treatment

Emergency measures : Nil per oral, take care of the airway, if patient presents with shock give supportive therapy.

Within an hour of ingestion, a soft nasogastric tube or Levine tube can be introduced carefully. Hypocalcaemia due to phosphate ingestion should be treated with calcium gluconate.

Button batteries lodged in the oesophagus should be removed using endoscopy immediately. Usually it will be expelled in 2-3 days time if beyond esophagus. Cathartics can be given. If they are lodged in the Meckel's diverticulum surgical intervention is necessary.

Eye contact : It is an emergency as it produces permanent scarring of the cornea. Wash the eyes with running water for 30 minutes. To allay pain analgesics have to be administered.

Ophthalmology consultation to be obtained. Skin is washed with water till the soapy feeling disappears.

Complications : Oesophageal stricture is treated with internal bougienage. Atrophy of gastric mucosa is at high risk of developing gastric carcinoma.

Points to Remember

- *Symptoms and signs should be correlated with lab investigations.*
- *Maintenance of airway breathing and circulation is the priority.*
- *Gastric lavage is not indicated.*
- *Endosopy has to be done within 24 hours of ingestion.*
- *Steroids are administered within 48 hours, preferably within an hour of ingestion when endosopy is not feasible or if circumferential burn is seen in endoscopy.*

Bibliography

1. Dreisbach RH. Corrosives. In : Text book on Childhood Poisoning, 11nd edn, Lange Medical Publication, California, 1983; pp 216-238.

2. Utpal Kant Singh, Leyland FC, Rajniti Prasad, Shivani Singh. Corrosive poisons. In: Poisoning in children, 3rd edn, Jaypee Brothers Medical Publihsing (P) Ltd., New Delhi, 2006;pp33-40.

3. Penner GE, et al. Acid ingestion, toxicology and treatment. Ann Emerg Med 1980; 9, 374-397.

4. Haller JA, Andrews HG, Write JJ, et al. Acute physiology and management of acute corrosive burn of oesophagus, J Paediatr Surg 1971; 6: 578-584.

5. Pratyush Gupta, Sanjay Verma. Unique presentation of epiglottis in corrosive poisoning, A Case report. The Internt Journal of Anaesthesiology 2007;Volume 12 No.2.

6. Anderson KD, Rouse TM, Randolph IG. Controlled trial of corticosteroids in children with corrosive injury of the oesophagus, N Engl J Med 1990;323: 637- 640.

<div style="text-align:center">

TOXICOLOGY

</div>

HOUSE HOLD MATERIAL POISONING

* Shuba S
** Betty Chacko

Abstract : *Poisoning in children may be accidental, non-accidental, iatrogenic or in older children deliberate. In majority of children, poisoning is accidental and is predominantly seen in children under 5 years. Substances taken could be medicines, plants or household products like cleaning agents, cosmetics, insect repellants and agents used for home remedies. Most of them are consumed in small amounts and hence non toxic. In mild cases, symptoms are predominantly gastrointestinal. In severe cases manifestations may be neurological, cardiovascular or respiratory. Most of them recover with supportive care eventhough no specific antidotes are available. Mortality does occur in a small percentage of cases. Generating awareness and educating caregivers for safe keeping of poisonous household materials would be the best strategy for prevention.*

Key words: *Poisoning, Household materials*

Poisoning during childhood is a universal problem. It may be accidental, non accidental and iatrogenic or suicidal. Data from National Poison Information Centre, New Delhi indicate that among the total poisonings, children constituted 36.5%. Accidental mode of poisoning occurred in 79.7% while intentional attempts were noted in 20.2% of children above 12 years of age.[1] Pediatric poisonings constituted 0.23-3.3% of total hospital admissions according to a multicentric study in India. Children below 5 years constituted 50-90% of all cases. The male:female sex ratio was 1.65-2.65:1. Mortality varied from 0.64 to 11.6%.[2] Among the various agents, the largest group of 44.1% was constituted by household products.[1] These agents are heterogenous and include those used for cleaning and for home remedies, cosmetics and insect repellants. Fortunately most of them are consumed in small amounts and hence non toxic. As symptoms are usually nonspecific and may mimic other diseases, a high index of suspicion should be entertained in any unresponsive child.

NAPHTHALENE

Naphthalene is a constituent of coal tar. It is an ingredient of dusting powder, lavatory deodorant discs, wood preservatives, fungicides, moth balls and insecticides, intestinal antiseptics, vermicides, as well as medicaments of pediculosis and scabies.

Lethal dose

Mean lethal dose in adult is between 5–15gms. Among G6PD deficient individuals even miniscule doses induce dangerous reaction. In children absorption occurs rapidly. Ingestion of 2 gm may be fatal. Newborns are more susceptible. Thinner skin and application of baby oil increase dermal absorption.[3]

* Professor, Department of Pediatrics.

** Professor & Head, Department of Pediatrics
Sri Ramachandra Medical College & RI, Chennai.

Toxicity

Toxicity occurs mostly in children who suck or chew moth balls. Transplacental transfer has also been reported. The formation of epoxide metabolite, probably is responsible for hemolysis. Hemolysis occurs in G6PD deficiency due to instability of erythrocyte glutathione. Ocular toxicity occurs due to oxidative stress and lipid peroxidation. Newborns have increased susceptibility due to inability to conjugate both naphthalene and bilirubin resulting in kernicterus. Erythema and dermatitis, hemolysis and jaundice have occurred after dressing infants in clothing stored with naphthalene moth balls.

Acute Toxicity: Acute intravascular hemolysis is the most characteristic sign, particularly in persons with red cell glucose-6-phosphate dehydrogenase deficiency; This is accompanied by fever, jaundice, anemia, leucocytosis, haemoglobinuria, renal insufficiency and sometimes liver dysfunction. Headache, abdominal pain, nausea, vomiting, diarrhea, fever and profuse sweating can occur. Methemoglobinemia and cyanosis may be present. Irritation of the urinary bladder causes urgency, dysuria and passage of brown or black urine with albumin and casts. Optic neuritis and liver necrosis are reported. In severe poisoning, excitement, coma, convulsion and acute renal failure are seen in older children whereas kernicterus occurs in young infants. Inhalation leads on to respiratory failure and pulmonary oedema. Abuse by inhalation has been described. Dermatitis follows industrial exposure.

Chronic abuse can result in peripheral neuropathy and chronic renal failure.[3-6]

Investigations

Hemoglobin, hematocrit, reticulocyte count, RBC count, peripheral smear, serum bilirubin, methemoglobin levels and plasma hemoglobin indicate presence and severity of hemolysis. Urine is tested for hemoglobin and alpha naphthol.

In hemolysis investigations show a rapid fall in RBC count, hemoglobin and hematocrit followed by temporary increase in reticulocyte count and normoblasts in peripheral blood. RBCs contain Heinz bodies and cells may be fragmented showing anisocytosis and poikilocytosis. During hemolytic crisis, the fragility of remaining cells increase.

Management

Contaminated skin or eyes are flushed with lukewarm running water for 20 minutes. In cases of inhalation, the person is removed from the source of contamination. In ingestion, lavage may not be effective after 2 hours. Lavage is to be done with activated charcoal of 1gm/kg upto 50 grams given as a slurry with water. Milk or fatty meals is avoided for 2 -3 hours, as they promote absorption. Supportive care is needed.

Symptomatic treatment: Repeated blood transfusion is given till Hb is 60 – 80% of normal. Corticosteroid is useful in cases of hemolysis. In case of kernicterus, hemodialysis / exchange transfusion is indicated. Convulsions if any are to be controlled with diazepam. Alkaline diuresis is carried out in the form of sodium bicarbonate 5gm orally q4H or as necessary to maintain alkaline urine and iv fluids are administered at15ml/kg/hr with frusemide 1mg/kg. In cases of methemoglobinemia of >30%, intravenous methylene blue is indicated.[3]

CAMPHOR

Camphor may be naturally produced or synthetic. It is obtained from wood of camphor tree (Cinnamonum camphora).

Uses

Camphor is used as rubefacient, counter-irritant and antipruritic, as moth repellant,

preservative, in dentistry with para chlorophenol for antibacterial activity, as carminative to relieve griping and as mild expectorant.[7]

Toxicity

Lethal dose for children is 0.5 – 1gm and for infants 70mg / kg.[8]

Clinical effects

Camphor is readily absorbed from skin, GIT and respiratory tract. Odour of camphor can be observed in breath. Onset of symptoms is seen within 5 – 90 min after ingestion. Oral and epigastric burning sensation, nausea, vomiting and feeling of warmth can be seen. Mydriasis and impairment of vision are noted. Headache, confusion, vertigo, excitement, restlessness, delirium, hallucinations, increased muscular excitability, tremors and jerky movements can occur. Epileptiform convulsions which may be severe can be followed by depression and coma. Inhalation above 2 PPM causes irritation to nose and throat. Chronic ingestion has symptoms of viral illness and Reye syndrome like illness with neurological deterioration, liver injury, prolonged prothrombin time and hypoglycemia. Camphor crosses placenta and has been implicated in fetal and neonatal death.[7-11]

Course and prognosis

If patient survives for 24 hours recovery is likely. Death is from respiratory failure, status epilepticus or circulatory collapse. Autopsy shows hemorrhage and brain cell degeneration

Management

If 10mg/kg has been ingested and asymptomatic by 4 hours, hospitalization is not indicated. If 30mg/kg ingested, patient is to be admitted. Convulsive state may be life threatening. Convulsion is treated with diazepam before attempting emesis or gastric lavage. Gastric lavage is done with warm water (38^0-40^0C) only after airway protection. Cathartics like sodium sulphate 250mg/kg and activated charcoal of 15-30gms are administered in children. In case of inhalation, patient is removed from exposure and administered oxygen. For external contact, skin is washed thoroughly with soap and water. Eye exposure is managed by flushing with large amount of water. Lipid hemodialysis and resin hemoperfusion may be helpful. There is no specific anti dote.[7-10]

EUCALYPTUS OIL

Eucalyptus oil is obtained from leaves of various species of eucalyptus. Major active ingredient is cineole. Medicinal eucalyptus oil contains not less than 70% w/w/ of cineole.

Uses

It is not recommended in children. It is used by inhalation as decongestant, orally for catarrh and cough, applied as rubefacient (0.5-3%), flavouring agent and cleaning solvent.

Toxic dose

Toxicity is seen with 0.05 – 0.5 ml / kg dose. It is well absorbed orally. Minor depression occurs with ingestion of 2-3ml and severe depression with 5ml.[1]

Toxicity

Toxic effects are rapid in onset and extensive. GI symptoms like abdominal pain, vomiting, diarrhea occur initially followed by CNS symptoms of loss of consciousness, hypoventilation, depression of reflexes and convulsions. Onset of coma occurs within several minutes to 2 hours. Coma lasts for half an hour to 30 days. Convulsions may be prominent in children. Miosis or mydriasis (miosis more common) occurs. Muscle weakness and ataxia are observed.

Respiratory involvement in the form of respiratory depression, dysphonia, pneumonitis, bronchospasm, aspiration pneumonia following vomiting and pneumonia after inhalation may occur. Tachycardia, weak irregular pulse and irritation to skin and eyes may be seen. Nephritis and prolonged prothrombin time rarely occur.

Management

Close observation is required for minor or moderate poisoning. Asymptomatic patient is to be observed for 6 hours and x-ray to be taken after 6 hours. ABC and neurological status are monitored and symptomatic and supportive care given. Attempts to induce vomiting and aggressive GI decontamination are to be avoided. Lavage and instillation of charcoal are to be done only after ET tube is in situ. Routine use of peritoneal dialysis or hemodialysis not established to be useful. No specific antidote is available.[12-15]

Prognosis

Most recover within 24 hours. Prominent sequelae are not reported but death may occur.

NEEM OIL / MARGOSA OIL

Neem oil is obtained from the tree Azadirachta indica. It contains neutral oils such as palmitic and stearic acids. Active ingredients are terpenoids such as azadirachtin, nimbin, picrin and sialin. It also contains aflatoxin in very low concentrations. Seed kernels comprise primarily of glyceride azadirachtin which is the most active insecticidal component of neem.

Uses

Neem oil is used as insecticide and insect repellent, oral dentifrice, in traditional medicine to treat malaria, diabetes, helminthiasis, CVS and skin diseases and as a contraceptive, anti ulcer, antisecretory and fungicidal agent and home remedy for respiratory infection.

Toxicity

Toxin may be a long chain monosaturated free fatty acid. Toxic dose is not known but symptoms seem to be dose related. Toxic encephalopathy in the form of Reye like illness may result.

Neem oil ingestion can give rise to vomiting, metabolic acidosis, tachypnoea, recurrent seizures, drowsiness, coma and cerebral edema. Polymorphonuclear leucocytosis is observed. Liver enzymes may be elevated but hepatic failure is not seen. Fatty infiltrate of liver and proximal renal tubules is seen. In animal models neem oil acts rapidly within 30 minutes on nuclei of hepatocytes, followed by mitochondrial injury, loss of ribosomes, loss of liver glycogen and presence of lipid droplets in the hyaloplasm.[16-18]

Treatment

Gastric lavage is not recommended. Convulsions are treated with diazepam. Supportive management is most important.

Prognosis

Prognosis is good in patients with mild vomiting and gastrointestinal features but fatalities and neurological deficits are reported in patients with CNS symptoms.

MOSQUITO REPELLANT POISONING

Mosquito repellants are based either on synthetic chemicals or natural ingredients. Major method of dispersion includes sprays, burning mosquito repellant sticks or liquids, or application as skin cream. Synthetic repellants contain chemicals like DEET (N, N – diethyl – m-toluamide), PMD (P-menthane – 3, 8 – diol), icaridin, pyrethroid compounds as permethrin. The major plant product is extract of lemon eucalyptus tree and citronella oil

DEET

DEET is one of the most potent mosquito repellants but cannot be used on damaged skin.

Products are available in varying concentration from 7.5%–95%. Only products containing lower concentration of DEET ($<15\%$) formulated with ethyl or isopropyl alcohol should be used in children

Toxicity

DEET is generally well tolerated on external application. About 50ml of 100% DEET may be potentially lethal, though even at doses as low as 21mg/kg/day children have developed toxic encephalopathy. DEET is efficiently absorbed through the skin and gut. Ingestion of small amounts produces nausea, vomiting, diarrhoea and abdominal pain. Large ingestion gives rise to coma, hypotension, abnormal hypertonic movements, tremors and convulsions within 0.5 to 6 hours. Toxic encephalitis is rarely seen but extremely severe and is characterized by irritation, altered behaviour, restlessness, convulsions, clonic movements, CNS depression, abnormal CSF (lymphocytic pleocytosis) and altered EEG. A Reye syndrome like finding with severe hyperammonemia can occur and it may be associated with ornithyl-carbamoyl transferase deficiency. Eye exposure causes irritative conjunctivitis and skin contact can produce mild tingling. Dermatitis with erythema and bullous reaction or urticaria may occur after prolonged or repeated skin exposure to highly concentrated formulations.

Treatment

In minor ingestion, induction of vomiting is avoided. In major ingestion, gastric lavage is done after airway protection. Stomach should be aspirated, and a slurry of activated charcoal administered, followed by sorbitol or saline cathartics.

In case of cutaneous exposure, skin is washed with non-irritant soap and water. For eye contamination, prolonged flushing of eyes with copious amount of water is carried out. For dermatitis, topical steroids and oral antihistamines will help. Seizures are controlled with anticonvulsants. Haemodialysis and charcoal haemoperfusion have been tried.

Prognosis

Recovery following DEET poisoning is usually within 36 hours but death has been reported in children with ornithyl-carbarmoyl transferase deficiency.[19,20]

PYRETHROIDS

Pyrethroid compounds are widely used as insecticides both at home and in agriculture. Two types of pyrethroids are in existence, Type II is more commonly used as agricultural insecticides. Some of the pyrethroid compounds such as Allethrin are used as mosquito repellants. Pyrethroids are primarily sodium channel toxins, readily prolonging excitation. The major site of action of all pyrethroids has been shown to be the voltage-dependent sodium channel.

Type I Pyrethroids: Bioallethrin, Cismethrin, Permethrin, Pyrethrins.

Type II Pyrethroids: Cyhalothrin, Cyper-methrin, Deltamethrin, Fenvalerate.

Toxicity

Symptoms occur when exposure is large. Two basic poisoning syndromes are seen depending on the type of pyrethroids.

Signs of pyrethroid poisoning

Type I Poisoning: Severe fine tremor, marked reflex hyperexcitability, sympathetic activation, paresthesia (dermal exposure)

Type II Poisoning: Profuse watery salivation, coarse tremor and seizures, increased extensor tone, moderate reflex hyperexcitability, sympathetic activation, choreoathetosis, paresthesia (dermal exposure). Pyrethroid ingestion gives rise to a sore throat, nausea, vomiting and abdominal pain within minutes. Systemic effects occur 4–48 hours after exposure.There may be mouth ulceration, increased secretions and/or dysphagia. Dizziness, headache and fatigue are common, and palpitations, chest tightness and blurred vision are less frequent. Coma and convulsions are the principal life-threatening features. Most patients recover within 6 days, although there were seven fatalities among 573 cases in one series and one among 48 cases in another.Paresthesiae usually resolves in 12-24 hours

ALLETHRIN

It is a synthetic pyrethroid and has chemical properties similar to pyrethrin

Dermal exposure gives rise to tingling, pruritis, blotchy erythema. Inhalation leads to respiratory tract irritation with cough, mild dyspnea, sneezing and rhinorrhea. Ingestion is associated with nausea, vomiting, abdominal pain, headache, dizziness, anorexia and hypersalivation. Severe poisoning is characterized by impaired consciousness, convulsions, muscle fasciculation which take several days or weeks to recover, and rarely non-cardiogenic pulmonary oedema.

Management

Immediate decontamination of the skin with soap and water is essential first aid.

Topical Vitamin E (Tocopherol Acetate) reduces skin irritation and paresthesia. The mechanism of action may in part be due to sequestration of pyrethroid into the vitamin E or to a membrane interaction. In ocular exposure, irrigation with lukewarm water or 0.9% saline for at least 10minutes is carried out and topical anesthetic may be required for pain relief. Lavage is not undertaken because of the associated solvents in case of ingestion. Treatment is mainly symptomatic. Fasciculations may be treated with atropine In experimental animals, ivermectin, a chloride channel agonist has been useful to reverse the peripheral signs of deltamerin poisoning, while pentobarbitone reduced the motor signs but was not effective in Type I pyrethroid toxicity. Diazepam or phenytoin is used for seizures.[21-24]

BUTTON BATTERY INGESTION

Small foreign bodies that are swallowed generally pass down the gut without any problem. Passage usually takes 2-6 days but occasionally may take 2-4 weeks. Most foreign bodies that cause trouble do so in the oesophagus. Button batteries are used to power digital watches, hand held calculators, hearing aids and photographic equipments. Although these cells are sealed they contain corrosive and toxic chemicals. There are four main types of button cells - mercury, silver, alkaline manganese and lithium.

Lithium cells are mostly used in watches where replacement is mostly by a specialist, thereby limiting access to children. Lithium cells are more resistant to corrosion than others. Their thin shape may facilitate gut transit. Silver cells are nontoxic when swallowed. Used batteries are potentially far less toxic than new ones as discharged cells are less liable to leak or cause tissue injury. In discharged mercury cells the mercuric oxide is largely converted to elemental mercury which is not absorbed.

When undischarged cells are swallowed the electric current produced by the battery causes a rise in the pH at the anode surface. It is this (possibly with the short circuit current through the tissues) and not leakage from the cell that can cause tissue burns.

2009; 11(1) : 47

Lodgement in the esophagus can lead to mucosal damage, tracheoesophageal fistula. Exposure to gastric acid is associated with remote risk of leakage of the cell contents.

The hazard following disassembly of the cells is confined to mercury cell. This can lead to toxic levels of mercury in the blood depending upon the size and state of discharge of the cell.

Management

Identify the type of cell swallowed. Obtain radiograph of the chest and abdomen. Five percent of those who have ingested would have swallowed more than one cell. Lodgement in the nose and esophagus are indications for immediate removal by endoscopy. Virtually all cells that have reached the stomach will be passed out spontaneously. Unless the cell is too large to negotiate the pylorus, endoscopic or surgical removal is not required. Daily abdominal radiograph should be obtained to show passage from the stomach or show cell disassembly. If it has crossed the pylorus, radiograph once in 4 days is suggested. Endoscopy is indicated if the cell is in the esophagus, or if it remains fixed to the stomach or gut mucosa for a prolonged period or if there are signs of peritonitis. Endoscopic removal may be helped by a Foley catheter or a magnet. Induction of vomiting should not be attempted as it does not work and there is a theoretical risk of fatal airway obstruction. Oral antacids may reduce corrosion of the cell. Metaclopramide to enhance gastric emptying and laxatives to speed up intestinal transit can be tried.Patient should be observed for fever, abdominal pain, vomiting, tarry or bloody stools, or decreased appetite and passage of the cell in the stools.[25-26]

DEODORANT

Deodorants are a wide range of products and include aerosol as body deodorants and antiperspirants, room fresheners, etc. while deodorant blocks are used in toilets. Aerosol sprays, sometimes called pressure packs, are metal cans containing chemicals under pressure which form a cloud of tiny droplets when released from the can. Aerosol abuse is common in some countries as it causes a feeling of euphoria. The composition of deodorants are variable. Chemicals such as butane, propane or chlorofluorocarbons are used as propellants to carry the active chemicals out of the can and others are used as the active ingredients. The toxicity may be due to one or more of these chemicals. The toxicity of a few of the chemicals are listed below.

Para-dichlorobenzene

This is used in solid air fresheners and deodorant blocks.Liquid air fresheners contain water perfume and detergent rather than para-dichlorobenzene. The amount of para-dichlorobenzene likely to be eaten by children would probably not cause serious poisoning. It causes irritation to the gut causing nausea, vomiting, diarrhoea and abdominal pain along with irritation and redness of the eyes. Erythema and irritation of the skin can occur on contact.Hepatic and neurologic toxicity are also observed.

Management

Following ingestion if the patient is awake, water should be given. Milk and fatty foods should be avoided for 2-3 hours. In case of contact with skin or eyes, it should be washed thoroughly with soap and water preferably under running water for about 15 to 20 minutes. Vomiting is induced if ingestion occurred less than 4 hours ago. Supportive care is important. Seizures can be controlled with benzodiazepines.

BUTANE

Butane is a simple asphyxiant on inhalation with explosive and flammable potential. It is also a widely used substance of abuse. The main target

organs are in the central nervous and cardiovascular systems.

Initial effects: Euphoria, excitation, blurred vision, diplopia, slurred speech, nausea, vomiting, coughing, sneezing and increased salivation occur initially.

As dose increases, Disinhibition, confusion, perceptual distortion, hallucinations (ecstatic or terrifying), delusions (which may lead to aggressive or risk taking behaviour), tinnitus and ataxia follow.

Large doses: This may produce nystagmus, dysarthria, tachycardia, CNS depression, drowsiness, coma and sudden death which may result from anoxia, vagal inhibition of the heart, respiratory depression, cardiac arrhythmias or trauma.

Management

Supportive and symptomatic care are essential. ECG monitoring is done for at least 4 hours. It is better to avoid stimulants (eg. adrenaline or noradrenaline, except for resuscitation). Arrhythmias may respond well to β blockers (eg. atenolol). Vagal inhibition of the heart can lead to bradycardia or cardiac arrest. Recovery normally occurs quickly once exposure has ceased but support of the cardiovascular and respiratory systems may be needed. Seizures are controlled with anticonvulsants.

TRICLOSAN *(5 CHLORO 2 PHENOL)*

Triclosan is a phenol derivative used in soaps, mouth washes, tooth paste, handwashes and cosmetics for its antibacterial property.

Toxicity

Local skin irritation blisters on local contact noticed. Internally small amount can be lethal. Cold sweat, circulatory collapse, convulsion, coma, noncardiogenic pulmonary oedema, respiratory paralysis and death can occur. Long term exposure may cause drug resistant bacteria and may be carcinogenic

Treatment

Symptomatic care[27,28]

DETERGENTS

Poisoning usually occurs through ingestion. Detergents fall into three main categories—non-ionic, anionic and cationic. Non-ionic and anionic detergents are of low toxicity. Only observation is required if respiratory symptoms, suggestive of foam aspiration, are present. Cationic detergents, such as benzalkonium chloride and cetrimide, are less frequently encountered in domestic cleaners. They may produce corrosive effects if a concentrated solution is consumed. Oral fluids should be encouraged and asymptomatic children may be discharged after a short period of observation.

Dishwasher powders, liquids, and tablets are strongly alkaline. Accidental ingestion can produce severe corrosive injury, although this is usually confined to the oral mucosa, lips, and tongue. Abdominal pain, vomiting, hematemesis, oseophageal ulcer, melena and oesophageal stricture may result. Respiratory distress, laryngeal oedema, hypotension, collapse, irritation, burns, skin necrosis and metabolic acidosis are the other serious effects.

Management

At presentation any remaining product should be washed from the skin and oral mucosa. Oral fluids should be encouraged. Attempts at neutralisation are dangerous. Further treatment, where required, is supportive. Asymptomatic children can be discharged. Oesophageal damage can occur in the absence of oral burns and parents should be advised accordingly. Follow up is recommended.[29-31]

Washing powders contain mixtures of enzymes, perfumes, softeners, and anionic and non-ionic

detergents. They are of low toxicity and specific treatment is not required.

NAIL POLISH

Ingredients

Toulene, Bertyl acetates, Ethyl acetates, Dileutyl phthalate.

Toxicity

Poisoning from nail polish is either from swallowing or breathing it. Nail polish usually comes in small bottles and so serious poisoning is unlikely. Increased frequency of micturition, irritation to eyes are observed. Breathlessness and slow respiration can be due to respiratory system involvement. GIT manifestations noted are nausea, vomiting, and abdominal pain. Drowsiness, coma, stupor are features of CNS involvement.

Treatment

Stomach wash is given. Antihistamines may be given for allergic reaction. Endoscopy is done for oesophageal erosion. Irrigation of skin and supportive care are carried out.

NAIL POLISH REMOVER

Toxic ingredient : Acetone

Toxicity

Polyuria, polydypsia are observed. Respiratory symptoms of shortness of breath and bronchial irritation may be noted. Nausea, vomiting, abdominal pain and fruity odor may be present. Stupor, drowsiness and coma are the neurological features.

Investigation: Acetone in blood and urine can be measured.

Treatment

Enuresis should not be induced. Gastric lavage with 3 – 5% sodium bicarbonate is useful if done less than 2 hours. Syrup of ipecac may be used and activated charcoal can be tried. Symptomatic treatment is the mainstay. O_2 and aritificial ventilation for hypoventilation and treatment of circulatory collapse are carried out. Hemodialysis may be done in severe cases. No specific antidote is available.

Acetone free nail polish remover has gamma butyrolactone which is readily converted to gamma hydroxy butyrate whose toxicity symptoms include CNS depression, hypotension, bradycardia, shock, mild respiratory acidosis, upper airway obstruction and pneumothorax.

Treatment

Symptomatic care

GLUE-ON NAIL REMOVER

Toxic ingredient: Acetonitrile which gets converted to inorganic cyanide via hepatic microsomal enzymes.

Toxicity

Vomiting, drowsiness, increase in serum osmolality and osmolal gap, pulmonary oedema.

Treatment

Activated charcoal. 5% dextrose. Sodium bicarbonate. Sodium thiosulphate. Hyperbaric O_2. Amyl nitrite by inhalation.[32,33]

MATCH STICK POISONING

Match sticks are usually made of potassium chlorate, sulphur, gum, glass and red phosphorus.

Ingestion of match sticks are usually harmless but potassium chlorate when ingested in large amount (which is usually suicidal) is highly reactive and toxic.

Toxicity

Toxic dose of potassium chlorate in adults is 5 gm. Lethal dose : 15 – 35gm. On ingestion it leads to rapid oxidative destruction of RBCs. It can give rise to methemoglobinemia and

cyanosis and may progress to renal failure. Hypoxic brain injury can occur. MRI shows symmetric hyperintense signals within deep gray matter and medial temporal lobes consistent with hypoxia caused by potassium chlorate, but these findings are non-specific.

Treatment

Gastric lavage with activated charcoal is given. Sodium thiosulphate, alkaline diuresis or methylene blue are used. Exchange transfusion or hemodialysis are done when needed. Hyperbaric oxygen may help. Symptomatic treatment is most useful.[34]

VACHA/VASAMBU/SWEETFLAG

It is the dried rhizome of the plant Acorus calamus commonly used in native medicine

Constituents

Volatile oil, Acorin, a bitter principle acoretin, calamine starch, mucilage.Root is a stimulant and aromatic, expectorant, antispasmodic and nervine sedative. Usual dose is 5 – 20 gms. Toxic dose is not known.

Uses

It is used for diarrhea as an antidote to several poisons, counter irritant and as insecticides. Root is burnt and mixed with coconut oil or castor oil and smeared over the abdomen as antiflatulant.

Side effects

Calamus oil causes hypothermia. Can lead to generalized CNS depression, sedation, hypothermia, hypotension, depression of respiration and diarrhoea.

PREVENTION OF HOUSEHOLD AND CHEMICAL PRODUCTS POISONING

- Use safety locks for all cabinets. Store potential poisons out of reach of small children.

- Store all poisonous household and chemical products out of sight of children.

- If you are using a product and need to answer the telephone or doorbell, take the child with you. Most poisonings occur when the product is in use.

- Store all products in their original containers. DO NOT use food containers such as milk jugs or soda bottles to store household and chemical products.

- Store food and household and chemical products in separate areas. Mistaken identity could cause a serious poisoning. Many poisonous products look alike and come in containers very similar to drinks or food.

- Return household and chemical products to safe storage immediately after use.

- Use extra caution during mealtimes or when the family routine is disrupted. Many poisonings take place at this time.

- Pesticides can be absorbed through the skin and can be extremely toxic. Keep children away from areas that have recently been sprayed. Store these products in a safe place where children cannot reach them.

- Discard old or outdated household and chemical products.

- Take time to teach children about poisonous substances.

Points to Remember

- *Poisoning due to household agents is a global problem in children. They are mainly accidental in those less than 5 years of age and intentional in children above 12 years.*

- *Most of the household agents are taken in small doses and hence do not cause toxicity. In larger doses they exhibit signs*

of poisoning and occasionally may be fatal.

- *Symptoms are usually nonspecific and may mimic other diseases and hence a strong index of suspicion is required in any unresponsive child.*

- *For most agents gastric lavage is avoided unless airway is protected. The mainstay of management is good supportive care, as no specific antidote is available.*

- *Implementation of good safety measures at home will bring down morbidity and mortality due to poisonings.*

References

1. Srivastava A, Peshin SS, Kaleekal T, Gupta SK. An epidemiological study of poisoning cases reported to the National Poisons Information Centre, AIIMS, New Delhi. Hum Exp Toxicol 2005; 24: 485.

2. Dutta A K, Seth A, Goyal P K, et al. Poisoning in children: Indian scenario. Indian J Pediatr 1998; 65: 365-370.

3. Fernando R, Nissanka S. Naphthalene. Chemical Safety Information from Intergovernmental Organizations. Website: http://www.inchem.org

4. Chun T, Perrone J, Osterhoudt K, Ugur S, Henretig F. Mothball blues: confusion in naphthalene toxicities and treatment. Clin Toxicol 1998; 36: 465.

5. Weintraub E, Gandhi D, Robinson C. Medical complications due to mothball abuse. South Med J 2000; 93: 427-429.

6. Santucci K, Shah B. Association of naphthalene with acute hemolytic anemia. Acad Emerg Med 2000; 7: 42-47.

7. Wickstrom E. Camphor. Safety Information from Intergovernmental Organizations Website: http://www.inchem.org Accessed on 24 Dec., 2007.

8. Siegel E, Wason S. Camphor toxicity. Pediatr Clin North Am 1986; 33: 375-379.

9. Jimenez JF, Brown AL, Arnold WC. Chronic camphor ingestion mimicking Reye's syndrome. Gastroenterology 1983; 84: 394-398.

10. Geller RJ, Spyker DA, Garrettson LK, Rogol AD. Camphor toxicity. Development of a triage system. Vet Hum Toxicol 1984; (Suppl 2): 8-10.

11. Manoguerra AS, Erdman AR, Wax PM ,et al. American Association of Poison Control Centers. Camphor Poisoning: an evidence based practice guideline for out-of hospital management. Clin Toxicol 2006; 44: 357-370.

12. Magarey J. Victorian Poison Information Centre. International program on chemical safety. Eucalyptus oil. Website http://www.inchem.org Accessed on 24 Dec., 2007.

13. Hindle RC Eucalyptus oil ingestion. N Z Med J 1994; 185-186.

14. Tibballs J. Clinical effects and management of eucalyptus oil ingestion in infants and young children. Med J Aust 1995; 163: 177-180.

15. Webb NJA, Pitt WR. Eucalyptus oil poisoning in childhood: 41 cases in south-east Queensland. J Paediatr Child Health 1993; 29:368-371.

16. Sinniah D, Baskaran G. Margosa oil poisoning as a cause of Reye's Syndrome. Lancet 1981; 1: 487-489.

17. Sundarvalli N, Raju BB, Krishnamoorthy KA. Neem oil poisoning. Indian J Pediatr 1982; 49: 357-359.

18. Lai SM, Lim KW, Cheng HK. Margosa oil poisoning as a cause of toxic encephalopathy. Singapore Med J. 1990; 31:463-465.

19. Heick HMC, Shipman RI, Norman MG, et al. Reye syndrome associated with use of insect repellent in a presumed heterozygote for ornithine-carbamoyl-transferase deficiency. J Pediatr 1980; 97: 471-473.

20. Tenenbein M. Severe toxic reactions and death following the ingestion of Diethyltoluamide-containing insect repellents. JAMA 1987; 258: 1509-1511.

21. Ray DE, Ray D, Forshaw PJ. Pyrethroid Insecticides: Poisoning Syndromes, Synergies, and Therapy. Clin Toxicol 2000; 38: 95 – 101.

22. Bradberry SM, Cage SA, Proudfoot AT, Vale JA. Poisoning due to pyrethroids. Toxicol Rev. 2005;24:93-106

23. Forshaw PJ, Lister T, Ray DE. The role of voltage-gated chloride channels in type II pyrethroid insecticide poisoning. Toxicol Appl Pharmacol 2000; 163:1-8.

24. Yang PY, Lin JL, Hall AH, Thomas C Y, Tsao, Ming-Shyan Chern. Acute Ingestion Poisoning with Insecticide Formulations Containing the Pyrethroid Permethrin, Xylene, and Surfactant: A Review of 48 Cases. Clin Toxicol 2002; 40: 107 - 113.

25. David TJ, FergusonAP. Management of children who have swallowed button batteries. Arch Dis Child 1986; 61: 321-322.

26. Banerjee R, Rao GV, Sriram PV, Reddy PKS, Reddy DN. Button battery ingestion. Indian J Pediatr 2005; 72: 173-174.

27. Haris D, Mirza Z. Butane encephalopathy. Emerg Med J 2005; 22: 676 –7

28. Kumar PKP, Ebenezer K, Agarwal I. Deodorants-need for caution. Indian J Pediatr. 2007;74: 876.

29. Riordan M, Rylance G, Berry K. Poisoning in children: 4 Household products, plants, and mushrooms. Arch Dis Child 2002; 87:403-406.

30. Einhorn A, Horton L, Altieri M, Ochsenschlager D, Klein B. Serious respiratory consequences of detergent ingestions in children. Pediatrics. 1989; 84: 472-474.

31. Wheeler DS, Bonny AE, Ruddy RM, Jacobs BR. Late-onset respiratory distress after inhalation of laundry detergent Pediatr Pulmonol. 2003; 35: 323-325.

32. Savage T, Khan A, Loftus BG. Acetone-free nail polish remover pads: Toxicity in a 9 month old. Arch Dis Child 2007;92:371.

33. Caravati EM, Litovitz TL. Pediataric cyanide intoxication and death from an aceto nitrile containing cosmetic. JAMA 1988;260:3470-3473.

34. Hakan M, Emir S, Zekai P, et al. Normal MR imaging finding of potassium chlorate intoxication . Am J Neuroradiol 2003; 24: 1396 – 1398.

CLIPPINGS

Dressings for treating superficial and partial thickness burns

Superficial burns are those which involve the epidermal skin layer and partial thickness burns involve deeper damage to structures such as blood vessels and nerves. There are many dressing materials available to treat these burns but none have strong evidence to support their use. Evidence from small trials, many with methodological limitations, suggests that superficial and partial thickness burns may be managed with hydrocolloid, silicon nylon, antimicrobial (containing silver), polyurethane film and biosynthetic dressings. There was no evidence to support the use of silver sulphadiazine. There is a paucity of high quality RCTs on dressings for superficial and partial thickness burn injury. The studies summarised in this review evaluated a variety of interventions, comparators and clinical endpoints. Despite some potentially positive findings, the evidence, which largely derives from trials with methodological shortcomings, is of limited usefulness in aiding clinicians in choosing suitable treatments.

Wasiak J, Cleland H, Campbell F. Dressings for superficial and partial thickness burns. *Cochrane Database of Systematic Reviews* **2008, Issue 4. Art. No.: CD002106. DOI: 10.1002/14651858.CD002106.pub3. This version first published online: October 08. 2008**

<div style="text-align:center">**TOXICOLOGY**</div>

CARDIOTOXINS

Rashmi Kapoor

Abstracat : *Common cardiotoxins which pediatricians come across are oleander, aconite, digitalis, tricyclic antidepressants and antihypertensives. All cases of suspected poisoning with cardiac drugs must be treated vigorously. The presense or absence of underlying heart disease may greatly influence clinical problems. The pathophysiology, symptoms and signs, diagnosis and treatment of these substances are discussed.*

Key words : *Cardiotoxins, Oleander, Aconite, Digitalis, Tricylic antidepressants, Anti-hypertensives.*

Accidental toxic exposures resulting in injury or death is a significant problem before a child reaches health care facility, emergency department and critical care units.

Cardiotoxins are the drugs, over dosage of which affect the heart either directly or through the nervous system. Oleander, aconite, digitalis, tricyclic antidepressants, and antihypertensives are few of the important cardiotoxins we come across as childhood poisoning.

OLEANDER

The oleander plants grow wild in India. Its flowers are used as offerings in the temples. There are two varieties, white (Nerium odorum) and yellow (Cerbera thevetia).

* Consultant Pediatrician,
  Regency Hospital Ltd.,
  Kanpur, Uttar Pradesh.

White Oleander (Nerium odorum, Kaner)

All parts of the plant are poisonous. The active principle is "Nerin", consisting of three glycosides, viz, Neriodorin, Neriodorein and Karabin. The principal action of Neridorin is that of digitalis (see digitalis poisoning), causing death from cardiac failure. Neriodorein causes muscular twitching and tetanic spasms more powerful than strychnine. Karabin acts on the heart like digitalis and on spinal cord like strychnine[1]. It is an evergreen shrub found in India, China and places with Mediterranean climate and is grown as a garden plant[2].

Symptoms and signs: Clinical features include abdominal pain, vomiting and frothy salivation followed by restlessness, bradycardia and tachypnea. There is difficulty in swallowing and muscular twitching of extremities deepening into tetanic spasms. This is followed by exhaustion, drowsiness, coma and death from heart failure.

Fatal dose and fatal period: About 15 grams of root can kill an adult in about 24 hours.

Treatment: Airway, breathing and circulation are to be maintained. The patient is connected to a cardiac monitor and observed frequently. Stomach wash will be useful. For bradycardia with heart rate of less than 40 beats per minute atropine may be useful. Atropine is used at a dose of 0.02mg/kg with a minimum dose of 0.1mg and a maximum single dose of 0.5mg in a child and 1 mg in an adolescent. The dose may be repeated in 5 minutes to a maximum total dose of 1 mg in a child and 2 mg in an adolescent. Sometimes

cardiac pacing may be required. Symptomatic treatment, frequent observation, anticipation of life threatening arrhythmias and their prompt treatment are the key to successful management. Treatment is similar to that of digitalis poisoning.

Yellow oleander (Thevetia, pila kaner)

This plant is highly poisonous. It is a small ornamental tree with bright yellow flowers and fleshy round fruits which are green when unripe and black when ripe. Plant has a milky white sap.

The yellow oleander contains at least eight different cardiac glycosides including thevetin A, thevetin B (cerberoside), thevetoxin, neriifolin, peruvoside and ruvoside. All parts of the plant are dangerous especially the seeds[3]. Ingestion of oleander seeds is a common mode of accidental poisoning in children.

Pathophysiology

The myocardial effects of these compounds are attributable to increased intracellular concentration of Ca^{++} and Na^+ resulting from inhibition of transmembrane Na^+ / K^+ ATPase pump[3].

Signs and symptoms

General: It consists of burning sensation in the mouth with tingling of tongue, dryness of throat, vomiting and diarrhea. In severe toxicity these may be followed by headache, dizziness, dilated pupils, drowsiness, collapse, coma and death.

Cardiac signs: AV node conduction block, sinus node block and ventricular tachycardia may occur. A few may reach the hospital in cardiac failure or arrest. There may be severe hyperkalemia.

Fatal dose and fatal period: 8 to 10 seeds or 15 to 20 grams of root prove fatal to an adult. Death ensues within 24 hours.

Treatment

After maintaining airway, breathing and circulation, the child should be connected to a cardiac monitor. Gastric lavage is done followed by other symptomatic treatment. Hyperkalemia should be taken care of. Cardiac pacing may be required in children having heart rate of less than 40/minute. At some centers anti digoxin fab fragments have been used showing good results[3]. Treatment by and large is similar to that of digoxin toxicity.

ACONITE POISONING

This plant is known as aconitum napellus or monks'hood. It is grown in the Himalayan ranges in India. Aconide alkaloids are present in the roots of this plant. The active principles are aconitine and other C_{19} - diterpenoid alkaloid which are known neurotoxins and cardiotoxins. With increasing popularity of herbal medicines among the general public, herb induced aconite poisoning is seen even in the western countries. The root extract is used for treating rheumatism and wounds[4].

Pathophysiology

Most of the cardiovascular and neurologic features of poisoning with aconitine can be explained on the basis of its actions on voltage-sensitive Na^+ channels in excitable tissues, including myocardium, nerve, and muscle. Aconitine binds with high affinity to the open gate of Na^+ channels at receptor site, causing persistent activation of these channels. This sustained Na^+ influx delays the repolarization phase of the action potential and initiates premature excitation[4].

Symptoms and signs

Patients invariably develop a combination of neurologic, cardiovascular, gastrointestinal, and other signs and symptoms.

CNS: The neurologic features can be sensory, motor, or both. CVS: Cardiovascular features include palpitations, chest tightness, hypotension, ectopics, bradycardia, tachycardia, ventricular arrhythmias and pulmonary edema. Gastrointestinal features include nausea, abdominal pain and diarrhea.

Fatal dose and fatal period: One gram of root, 250 mg of extract, 25 drops of tincture or 4 mg of the alkaloid prove fatal. The latent period between ingestion of aconite roots and onset of symptoms can be as short as 10 minutes suggesting that aconitine and related alkaloids can be rapidly absorbed by the upper gastrointestinal tract. In some patients, symptoms occur only after a longer latent period[4].

Treatment

After maintaining airway, breathing and circulation, the child should be connected to a cardiac monitor. Gastric lavage is effective if patient is brought to the hospital in time. Arrhythmia may be treated by lidocaine or amiodarone. Lidocaine is given at a loading dose of 1mg/kg IV followed by an infusion 20-50 mcg/kg/minute. Refractory arrhythmias may require charcoal hemoperfusion for 4 hours. Patients with severe bradycardia may require atropine or cardiac pacing. The dose of amiodarone is 5mg/kg IV load over 20-60 minutes (maximum dose 300mg) can repeat to maximum daily dose of 15mg/kg (2.2g in adolescents).

DIGITALIS

Digitalis remains one of the most frequently prescribed proprietary drug in the developed countries. However, just as all drugs are therapeutic in one dose but toxic in another, digitalis therapy has always been confounded by a high incidence of inadvertent acute poisonings and chronic intoxications[5]. Digitalis, digoxin and digitoxin are prepared from the foxglove plant Digitalis purpurea. Its roots, leaves, and seeds contain several glycosides of which digitoxin, digitalin, digitalein and digitonin are the most poisonous and have a cumulative action. The glycosides act directly on the heart muscle.

Pathophysiology

Digitalis acts by inhibiting the enzyme sodium – potassium ATPase, leading to increased intracellular sodium and calcium and decreased potassium.

Fatal dose and fatal period: The usual fatal dose is 15- 30 mg of digitalin and 4 mg of digitoxin. Digoxin is slowly absorbed and distributed, serum levels may not correlate with the pharmacologic effects for up to 8 hours. Elimination is primarily by the kidney and the remainder is metabolized by the liver. The half life ranges from 36 hours to 45 hours.

Symptoms and signs

General: Nausea, vomiting, headache and loss of appetite.

Cardiovascular: Sinus arrhythmias, sinus bradycardia, premature ventricular contractions, bigeminy, ventricular tachycardia and fibrillations can occur. Ventricular premature beats, often regularly spaced in the form of bigeminal rhythm and multifocal ventricular ectopics are typical of digitalis toxicity. Further progression of this process, if digitalis is continued, may lead to ventricular tachycardia. Another common manifestation of digitalis toxicity is disturbances of conduction. Mild degrees of A-V block (including Wenckebach phenomenon) and even complete heart block may develop in the course of digitalis therapy, indicating drug overdose. The third cardiotoxic manifestation of digitalis is the production of varieties of junctional (nodal) rhythm. This may emerge as atrioventricular dissociation when sinus rhythm is present or as nodal tachycardia. Finally, evidence of atrial

irritability may be produced by digitalis, causing atrial extrasystoles and atrial tachycardias, including atrial tachycardia with 2:1 block. The rarest of atrial arrhythmias attributed to digitalis are atrial flutter and fibrillation[6].

ECG manifestations: Commonly observed changes are depression of ST segment, inversion of T wave, shortening of Q-T interval and all types of arrhythmias.

Central Nervous system: Dizziness, restlessness, headache, hallucinations, psychosis, depression and visual disorders are commonly seen.

Diagnosis of digitalis intoxication

The proper use of digitalis requires a high index of suspicion regarding the possibility of toxic reaction. Virtually every arrhythmia may be caused by digitalis. It is therefore proper to regard with suspicion every form of rhythm disturbance occurring in a patient taking digitalis, which was not evident before the administration of this drug. The difficulty in the proper interpretation of arrhythmias occurring in digitalized patients is enhanced by the fact that even the most characteristic arrhythmias caused by digitalis toxicity are not specific and often occur in response to factors unrelated to the drug.

Treatment

The management of digitalis intoxication has relied upon good supportive care of the patient, early decontamination to remove the drug before it is absorbed, palliative medications such as atropine and antiarrhythmic drugs, correction of metabolic abnormalities and ventricular pacing for severe conduction disturbances and bradyarrhythmias. As in any type of drug toxicity, the basic approach to digitalis toxicity is the discontinuation of the drug. Active therapy of digitalis intoxication should only be undertaken when the arrhythmia is poorly tolerated (as in the excessively fast or excessively slow rates).

Attention should be paid to the possible presence of potentiating factors, which may need correction, such as hypokalemia or hypoxia. In the presence of hypokalemia or total body potassium depletion, administration of potassium chloride is especially efficacious.

Among antiarrhythmic agents used for the therapy of digitalis intoxication, diphenylhydantoin and propranolol have been most extensively studied. Both agents can be used intravenously for termination of digitalis induced tachyarrhythmias. Lidocaine and procainamide have also been used successfully in such instances[6]. Procainamide is given at a dose of 15mg/kg IV load over 30-60 minutes. Despite best efforts, severely poisoned patients still die, most often from malignant ventricular arrhythmias, asystole or pump failure and cardiogenic shock. However, within the past 15 years, a quiet revolution in the treatment of digitalis intoxication has been taking place. The advent of immunotherapy, digitalis-specific Fab antibody fragments (digibind®), has made it possible to salvage even those moribund patients with advanced symptoms of digitalis toxicity. Fab is now widely available in the United States and many developed countries; its cost, although still quite high, would perhaps be offset, at least theoretically, by a decreased need for prolonged, invasive and expensive monitoring of digitalis-intoxicated patients in the intensive care setting[5].

The approximate dose of Fab fragments (mg) is 80 times the digoxin body burden (mg). If neither the dose ingested nor the plasma digoxin/digitoxin concentration is known, in both adults and children 380 mg of anti-digoxin Fab fragments should be given. Each vial (38 mg) will bind approximately 0.5mg of digoxin. If amount of digitalis ingested is known the required dose can be calculated. The dose for elderly patients or those with renal impairment should be similar to that for those with normal renal function. Fab fragments have a plasma half-life of

12-20 hours, but this can be prolonged in patients with renal impairment. Factors limiting the efficacy of Fab fragments are the dose, the duration of the infusion and any delay in administration. Guidelines for Fab fragment administration in children include (i) dilution to a final Fab concentration of 1mg/ml in either 5% (w/v) dextrose or 0.9% (w/v) sodium chloride; (ii) infusion through a 0.22 micron membrane filter to ensure that no undissolved particulate matter is administered (iii) administration of the total dose over a minimum of 30 minutes; and (iv) avoiding co administration of other drugs and/or electrolyte solutions. Fab fragments are generally well tolerated. Adverse effects attributable to Fab treatment include hypokalemia and exacerbation of congestive cardiac failure; renal function could be impaired in some patients[7].

TRICYCLIC ANTIDEPRESSANTS

The tricyclic antidepressants (TCA) are one of the most common class of antidepressants of toxicologic significance. They, increasingly prescribed for multiple indications in children and adults, are responsible for many pediatric poisonings. They include amitriptyline, nortriptyline and sinequan.

These agents block the neuronal reuptake of norepinephrine, serotonin and dopamine, in both central and peripheral nervous system[8].

Pathophysiology

Tricyclic antidepressants affect the autonomic, central nervous and cardiovascular systems. TCAs have central and peripheral anticholinergic effects. Acting centrally, they inhibit re-uptake of neurotransmitters (the biogenic amines: norepinephrine, serotonin, and dopamine) into presynaptic nerve terminals and inhibit central sympathetic reflexes. Additionally, TCAs block the fast sodium channels of the myocardium, particularly in the distal conducting

system. Based on their effects on the various systems, it is clear how TCAs cause toxicity. First, centrally, the change in neurotransmitters causes delirium, psychosis, lethargy, coma and generalized seizures. The exact mechanism for the seizures is not completely understood. Second, as competitive antagonists of muscarinic acetylcholine receptors and as H1-histamine blockers, TCAs exert central and peripheral anticholinergic effects. Finally, the blockade of sodium channels in the heart causes the most dangerous effects: conduction delays and dysrhythmias. The decreased inward movement of sodium at the fast sodium channels slows phase zero of depolarization in the distal conduction system and the ventricle, thus slowing ventricular depolarization and prolonging the QRS complex. Phase 4 is also affected with slowed repolarization that manifests as QT prolongation. The pathophysiology also comes into play in the development of Brugada Syndrome (the development of ST changes in leads V1 to V3 because of altered sodium channel flow) in TCA overdose. The most common dysrhythmia resulting from TCA overdose is sinus tachycardia secondary to peripheral anticholinergic action; however, wide complex tachycardia is the characteristic cardiac complication. The wide complex tachycardia can be supraventricular tachycardia with aberrancy or actual ventricular tachycardia. Much of TCA overdose evaluation and disposition has come to depend on the patient's electrocardiogram (ECG).

Fatal dose: Ranges from 5 – 20 mg/kg.

Signs and symptoms

Clinical toxicity becomes evident by 6 to 8 hours of an overdose and peaks within 24 hours. The anticholinergic effects initially present as: General: Dry mouth, ileus, dilated pupils, urinary retention and mild sinus tachycardia. CNS: Effects may be seen at any

time post-ingestion and include delirium, agitation, restlessness, hallucinations, convulsions, and CNS depression or coma. Generalized seizures most often develop within 1–2 hours of presentation.

CVS: The most life-threatening toxicity remains cardiac dysrhythmias. In general the symptoms consist of coma, convulsions and cardiac arrhythmias, and in some cases acidosis. A helpful mnemonic to remember the symptoms is TCA or three Cs and an A[9].

ECG changes: In either adults or children, the ECG is not sensitive or specific enough to be used alone to diagnose or predict outcome in TCA overdose. However, the characteristic ECG changes seen with TCAs serve to confirm TCA toxicity. Conduction delays such as QRS and QTc prolongation seem to be associated with seizures. Leonard, et al. showed that with the EKG changes in children, with desipramine and clomipramine included, as in adults, tachycardia, the most common change, along with PR, QRS, and QTc prolongation[10].

Management

Protect the airway, ensure adequate oxygenation and ventilation, and establish continuous ECG monitoring. Treat arrhythmias with sodium bicarbonate only after establishing adequate airway and ventilation. Sodium bicarbonate narrows QRS complex, shortens the QT interval, and increases the myocardial contractility. The goal of sodium bicarbonate therapy is to raise sodium concentration and arterial pH. This can be achieved by administering 1 to 2 mEq/kg bolus infusions until the arterial pH is >7.45. After the bolus administration, sodium bicarbonate may be infused as a solution of 150 mEq $NaHCO_3$ per liter in D_5 W titrated to maintain alkalosis. If hypotension is present administer normal saline boluses (10 ml/kg each)[9].

For treatment of seizures induced by TCA, administer benzodiazepines. Phenobarbital may be preferable to phenytoin in treating seizures refractory to benzodiazepines[9]. Rest of the management is supportive.

CALCIUM CHANNEL BLOCKERS

Calcium channel blockers (CCB) are commonly found in the medicine cabinets of each household. They have increased in popularity since their introduction in the 1960s and are now the most frequently prescribed class of cardiac medications. As a result, these medications are more accessible to the curious toddler than ever before. The frequency of unintentional pediatric ingestions has increased steadily; calcium channel and beta blocker ingestions rank in the top 10 causes of drug-toxin-related deaths in children under 6 years of age.

Most accidental pediatric ingestions are asymptomatic, a small number do result in cardiovascular instability or even death. The dihydropyridines, particularly nifedipine, and the phenylalkylamine, verapamil are most often implicated in symptomatic ingestions. Calcium channel blockers have not been approved for use in the pediatric population; nevertheless, nifedipine, diltiazem, amlodipine, and verapamil are frequently prescribed for hypertensive children[11].

Pathophysiology

The morbidity and mortality of CCB toxicity are due to conduction system delays and blocks, loss of myocardial contractility, and loss of systemic vascular smooth muscle tone. Toxicity of CCBs typically manifests as an exaggeration of the therapeutic response. Verapamil and diltiazem generally exhibit the most cardiac (negative inotropic and chronotropic) effects, and overdoses present with bradycardia, heart block, AV conduction disturbances, and myocardial

dysfunction. In contrast, dihydropyridine overdoses present initially with baroreceptor-mediated tachycardia in response to decreased systemic vascular resistance. However, as receptor selectivity is overwhelmed by the available CCB and all L-type channels are blocked, bradycardia and sustained hypotension may result[11]. Activation of insulin secretion by the pancreatic beta islet cells has been shown to produce hypoglycemia via inhibition of a slow Ca++ channel on the cell membrane.

Signs and symptoms

CVS: Bradycardia and hypotension are the main cardiovascular findings. Systemic: Symptoms and physical findings are related to the physiologic events. The most common physical finding after CCB overdose is hypotension. Systemic hypoperfusion results in a variety of symptoms ranging from mild orthostatic dizziness accompanied by nausea and vomiting, to more severe manifestations including syncope, mental status changes, seizures, cerebrovascular ischemic events, renal failure, intestinal ischemia, and liver infarction. Hypoglycemia and acute pulmonary edema (occurring via an unknown mechanism) have also been reported with CCB overdose.

Fatal dose: Lethal and toxic doses of calcium channel blockers in humans are poorly described. Inferences on toxic doses are made from therapeutic ranges and case reports of toxic ingestions.

Management

The initial approach to therapy for calcium channel blocker overdose is to provide oxygenation and ventilation, continuous ECG monitoring and frequent assessment. Onset of symptoms may be immediate or delayed in cases of sustained release preparations.

The American Academy of Clinical Toxicology states that charcoal administration may be considered in the case of potentially toxic ingestions up to 1 h after ingestion[11]. All patients with significant overdose require close monitoring of blood pressure and hemodynamic status. Intra arterial blood pressure monitoring should be considered. Normal saline bolus in a dose of 5 to 10 ml/ kg is administered if hypotension is present. The fluid bolus is restricted to 5-10ml/kg to prevent pulmonary oedema and careful reassessment is required after each bolus. Intravenous calcium to compete at the channel receptors can be used to support the circulatory system. Use of atropine and transcutaneous pacing to support heart rate, epinephrine and pressors to improve cardiac contractility and maintain vascular tone, heart-lung bypass, extracorporeal membrane oxygenation to augment cardiac function, and glucagon to support cellular metabolism are indicated, although their therapeutic efficacy in the calcium channel blocker overdose patient is variable. High dose insulin combined with supplemental glucose, improve intracellular metabolism and have been associated with improved outcomes[11].

HDIDK (High dose insulin with dextrose and potassium) should be considered if there is an inadequate response to fluid resuscitation. It should be administered with calcium and epinephrine. Calcium should be dosed as 10–20 mL of 10% calcium gluconate via peripherial venous access or 5–10 mL of 10% calcium chloride via central venous access. Epinephrine is given i.v. at a rate of 1 µg (as the hydrochloride) per minute and increased as necessary. Before initiation of insulin therapy, blood glucose and potassium concentrations should be checked. If they are <200 mg/dL and <2.5 mEq/L, respectively, then dextrose 0.25 g/kg of 25% dextrose injection and potassium chloride (2mEq/kg orally or IV) should be administered. Regular insulin is administered as

a 0.1-0.2 unit/kg bolus dose, followed by 0.1–0.2 unit/kg/hr adjusted to clinical response.

Because potential adverse effects of insulin infusion include hypoglycemia and hypokalemia, capillary glucose should be monitored every 20 minutes for the first hour. Next, serum potassium and capillary glucose should be checked hourly. Infusions of dextrose should be started with the insulin bolus dose to maintain adequate blood concentrations.

Administering 10% dextrose and 0.45% sodium chloride injection at a rate equal to 80% of the maintenance rate is appropriate for most patients. Potassium should be readministered if the blood concentration falls below 2.5 mEq/L. The insulin infusion may be tapered off once signs of cardiotoxicity begin to resolve[12].

A very high dose of vasopressors therapy (norepinephrine and epinephrine) may be required for treatment of bradycardia and hypotension.

BETA ADRENERGIC BLOCKERS

There are a wide variety of therapeutic indications for beta-adrenergic antagonists, better known as beta-blockers. They are most commonly used in cardiovascular disease. Other indications include migraine headache, tremor, panic attacks, and as medications to decrease intraocular pressures. In the pediatric population, betablockers are used primarily to treat hypertension, dysrhythmias, thyrotoxicosis, and migraine headache.

Pathophysiology

Beta adrenergic blockers compete with norepinephrine and epinephrine at the beta adrenergic receptor, resulting in bradycardia, and decreased cardiac contractility[9]. Serious morbidity and mortality from beta-blocker overdose is generally the result of cardiovascular

toxicity. In addition, beta-blockers also possess the ability to block fast sodium channels, which is sometimes called membrane stabilizing activity (MSA). Sodium channel blockade is generally believed to be an important pathophysiologic process underlying beta-blocker toxicity. MSA-related myocardial toxicity results in decreased contractility, bradycardia and conduction delays, all of which may contribute to hypotension. High lipid solubility also allows for rapid diffusion of the drug across the blood-brain barrier. The subsequent central nervous system (CNS) toxicity can lead to sedation, delirium and coma. Seizures may result from hypotension or a direct CNS effect. Bronchospasm and hypoglycemia are a direct result of betablockade at the β_2 receptors[13].

Signs and symptoms

CVS: Bradycardia, bradyarrhythmias, conduction delays, and severe hypotension are the main signs of cardiovascular toxicity.

CNS: Sedation, delirium, seizures and coma may occur. Others: Bronchospasm and hypoglycemia may also be seen.

Management of serious beta-blocker overdose

The initial approach to therapy for beta blocker overdose is to provide oxygenation and ventilation, continuous ECG monitoring and frequent assessment. Onset of symptoms may be immediate or delayed in cases of sustained release preparations.

Patients with suspected significant beta-blocker overdose toxicity should be placed on a cardiac monitor, have frequent blood pressure monitoring, a 12-lead electrocardiogram (ECG), and a serum glucose determination. If congestive heart failure is suspected, chest radiograph and oxygen saturation should be obtained.

Pharmacologic distinctions between beta-blockers and CCBs may not be evident upon presentation; therefore, initial treatment efforts should be similar regardless of the type of drug involved based on general overdose treatment guidelines, after ensuring that the airway, breathing, and circulation are intact, GIT decontamination with orogastric lavage, activated charcoal, or whole bowel irrigation should be administered[12].

In addition to decontamination, therapies to support perfusion are often needed in cases of overdose. I.V.fuids (5-10 ml/kg as a bolus dose) should be used as first-line therapy for patients who develop hypotension. Atropine sulfate 0.5–1 mg i.v. is usually the first-line agent for symptomatic bradycardia. In any pediatric beta blocker exposure with the potential for serious toxicity such as those involving a large number of ingested pills, atropine should be given prior to laryngoscopy or gastric cannulation, or in the presence of persistent vomiting.

Current antidotal therapy for beta -blocker poisoning is based on animal studies and case reports. Unfortunately, no prospective human study evaluating optimal therapy has been performed. These therapies include beta agonists, glucagon, and phosphodiesterase inhibitors. Of these agents, glucagon is generally recognized as first-line therapy.

High-dose glucagon is recommended for cardiotoxicity produced by beta-blocker poisoning. Glucagon is thought to activate adenylate cyclase in cardiac tissue by directly stimulating a G protein on the beta-receptor complex.

An initial bolus dose of 50–150 µg/kg should be administered i.v. over one to two minutes. This initial dose will have a transient effect that should occur within approximately five minutes. If a benefit is seen, the initial dose should be followed by a continuous i.v. infusion at a rate of 2–5 mg/hr (maximum: 10 mg/hr) diluted in 5% dextrose injection. The infusion rate can then be tapered downward as the patient improves[12].

Approach to management of Cardiotoxins

General management[14]

Once poisoning is suspected even asymptomatic patients must be admitted for observation. In the symptomatic patient support for cardiac and pulmonary function is essential. The minimum duration of observation should be determined with reference to the drug's half life and the formulation taken (some antiarrhythmics and hypotensive agents are formulated for sustained release) and when practicable should be guided by plasma drug concentrations. If immediate admission to an intensive care unit is not possible or not indicated the ward staff should be fully aware of the risks and the intensive care unit informed that its services may be needed.

A twelve lead electrocardiogram should be obtained as soon as possible, both to assess underlying myocardial disease and as a baseline to measure progress. A chest radiograph, full blood count, and samples for laboratory analysis should also be taken early. If the drugs were ingested as a single dose the stomach should be emptied either by emesis or gastric lavage. Activated charcoal (AC) is an effective adsorbent for all cardiac drugs and should be given orally in a dose at least 10 times the weight of the suspected overdose (General recommended dose of AC is 1g/kg in children upto 1 year of age, 25-50g in children 1-12 years of age and 25-50g in adolescents and adults).

Supportive

1) Treat all suspected cases seriously, 2) support cardiac and pulmonary function, 3) empty stomach and give oral activated charcoal, 4) avoid artiarrhythmic drugs,

5) consider temporary pacemaker for bradycardia, 6) use fluids before vasopressors for hypotension: administer fluid boluses of 5-10ml/kg slowly over 10-20 mins with careful reassessment after each bolus, 7) persist with cardiac massage if output fails.

Whilst supportive treatment is in progress: Measure electrolytes, urea, creatinine and plasma drug concentrations, urgent correction of hyperkalemia, correct hypokalaemia, maintaining potassium in upper normal range, consider other treatments, antibodies for digoxin, haemo-perfusion for disopyramide, glucagon/isoprenaline for beta blocker, calcium for verapamil.

Prevention

Childhood poisoning is usually accidental, which makes it amenable for prevention. Most cardiotoxic drugs are either being consumed by an adult member of the household or by the child himself/herself due to some cardiac lesion. It is important to protect children, because they cannot protect themselves. It is the duty of all members of the household to store these potentially toxic drugs/herbs with following points in mind:

- They should be stored at a place which is beyond the reach of a child.
- They should not be stored in containers that are used to store food.
- Make it a habit to properly close the pill bottles tightly after opening them.
- Explain to the child that the flowers for prayers are not to be consumed.
- Keep the herbs away from the child's reach.

Points to Remember

- *Acute poisoning with cardiac drugs is uncommon. They have a narrow toxic to therapeutic ratio and are the most hazardous drugs in common use.*

- *In general poisoning with cardioactive drugs will produce hypotension and all types of arrhythmias. Extracardiac effects include gastrointestinal symptoms, especially nausea and vomiting, and central nervous system effects with irritability, convulsions, and loss of consciousness.*

- *In the critically ill patient while activated charcoal, continuous renal replacement therapy and specific antidotes may be of benefit, maintenance of the patient's airway, ventilation and circulation still remain the most important aspect of management.*

REFERENCES

1. Parikh C K. Cardiac poisons In: Parikh's text book of Medical Jurisprudence, forensic medicine and toxicology. 6th Edn, CBS Publishers, Mumbai, 1999; pp10:62-10:68.

2. Henry JA, Wiseman HM. Management of poisoning A hand book for health care workers. World Health Organization Geneva 1997; pp277-278.

3. M Eddleston, Warell DA. Management of acute Yellow Oleander Poisoning. Q J Med 1999; 92: 483-485.

4. Chuan LC, Thomas CYK, Fang DJ. Clinical Features and Management of Herb-Induced Aconitine Poisoning. Ann E Med 2004; 43: 574-579.

5. Alan W. Revising the Management of Digitalis Poisoning. Clin Toxicol 31; 2: 275 – 276.

6. Selzer Arthur, Keith CE. Production, Recognition and Treatment of Digitalis Intoxication. Western J Med 113; 4: 1-7

7. Flanagan RJ, Jones AL. Fab antibody fragments: some applications in clinical toxicology. Drug Saf 2004; 27;1115-1133.

8. Rodgers GC, Matyuns J N and Jr. Poisoning In: Nelson Text book of Pediatrics 17th Edn, W.B Saunders Company, Philadelphia pp2362-2375.

9. Hazinski MF, Zritsky AL, Nadkarni VM, Hickey RW, Schexnayder SM, Berg RA eds, PALS Provider Manual. Dallas, Texas: American Heart Association/American Academy of Pediatrics, 2002; pp305-335.

10. Rosenbaum TG, Kou M. Are one or two dangerous? Tricyclic antidepressant exposure in toddlers. J E Med 2005; 28: 169–174.

11. Ranniger C, Roche C. Are one or two dangerous? Calcium channel blocker Exposure in toddlers. J E Med 2007; 33: 145–154.

12. Shepherd G, Clinical reviews cardiovascular drugs. Treatment of poisoning caused by beta-adrenergic and calcium-channel blockers. Am J Health-Syst Pharm 2006; 63: 1828-1835.

13. Love J N, Sikka N. Are 1- 2 tablets dangerous? Beta-blocker exposure in toddlers. J E Med 2004; 26: 309-314.

14. John H, Glyn V. ABC of Poisoning. Br Med J 1984; 289: 1062- 1064.

CLIPPINGS

Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates

More trials are needed to determine whether delivering nutrition into superficial or deep veins is better for newborn infants. Preterm or sick newborn infants are often fed with a special nutrient solution that is delivered directly into the veins. The solutions can either be given into a superficial vein through a standard short (peripheral) cannula or into a large deep vein via a long (central) catheter. This review found limited data from five small randomised controlled trials that compared the effects of using these two different methods of delivering nutrient solutions. There is some evidence from one study that infants who received the solution into a deep vein received more nutrition. The use of central catheters has been thought to increase the risk of bloodstream infection in newborn infants, but this review did not find any evidence that this was the case. More trials are needed to determine which method is better at improving growth and development in newborn infants. Data from one small study suggest that using a percutaneous central venous catheter to deliver parenteral nutrition improves nutrient input. The significance of this in relation to long-term growth and developmental outcomes is unclear. Three studies suggested that the use of a percutaneous central venous catheter decreases the number of catheters/cannulae needed to deliver the nutrition. No evidence was found to suggest that percutaneous central venous catheter use increased the risk of adverse events, particularly systemic infection.

Ainsworth S, Clerihew L, McGuire W. Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates. *Cochrane Database of Systematic Reviews* **2007, Issue 3. Art. No.: CD004219. DOI: 10.1002/ 14651858.CD004219.pub3. This version first published online: April 19. 2004. Last assessed as up-to-date: July 08. 2008**

TOXICOLOGY

NARCOTIC POISONING IN CHILDREN

*** Kala Ebenezer**

Abstract:*Narcotic poisoning is not commonly seen in pediatric practice. They merit particular attention because of the potential mortality they cause when untreated and the relative ease of reversing their effects if recognised.*

Key words: *Narcotics, Poisoning*

Narcotics or more specifically opioids are a group of drugs used for pain relief. They all cause analgesia without loss of consciousness coupled with euphoria, the intensity of which varies with each drug.

Most narcotics do not produce serious side effects in therapeutic dosage. However, the direct depressant effect on respiration which they all share can be life threaten**in**g when recommended dosages are exceeded.

Narcotics have been abused for their euphoric action and for the feeling of well being that they produce. Tolerance and physical and psychological dependence develop quickly leading to addiction and withdrawal symptoms. Narcotic use and abuse have been reported as increasing in frequency in the past few years, a trend that has been blamed on increasing availability and utilization of narcotics by medical personnel, as well as illicit drug abuse.

---

* Professor and Head, Pediatric Intensive Care Unit, Christian Medical College and Hospital, Vellore, Tamilnadu.

Opium is known to humans since prehistoric times. There are evidences that the poppy plant was cultivated in the ancient civilisations of Persia, Egypt and Mesopotamia. Opium is obtained by lacerating the immature seed pods of the poppy plant and it contains about 25 alkaloids. Many synthetic derivatives are also available for clinical use. Table 1, shows the important opioids classifed according to their action.

Table 1. Shows the important opioids classified according to their action.

Strong agonists	Morphine Pethidine Fentanyl Methadone Heroin Remifentanil Alfentanil Sulfentanil
Moderate agonists	Codeine Oxycodone Propoxyphene
Mixed agonists (partial agonist and antagonists)	Buprenorphine Butorphanol Nalbuphine Pentazocine
Antagonists	Naloxone Naltrexone

The most frequently prescribed opioids in clinical medicine are morphine, pethidine, fentanyl, fortwin (pentazocine), codeine and methadone. Heroin (diacetylmorphine), the most commonly abused narcotic, available only illicitly, is not prescribed in clinical practice.

Opioid receptors

Opioids exert their action through the opioid receptors, the μ (mu) and ê (kappa) receptors in the central and peripheral nervous system, particulary brain stem, substantia nigra of spinal cord, limbic system and hypothalamus. μ receptors found in the brain stem mediate respiration, cough, nausea, vomiting, and maintenance of blood pressure, pupillary size and control of stomach secretions while ê (kappa) receptors in spinal cord and thalamus mediate analgesia.

Narcotic poisoning

Opioid overdosage is not commonly seen. Literature search shows they constitute about 3.8-5.1% of ED presentations in U.S.A. Although opioids constitute a relatively small percentage of pure overdoses encountered in the ED, they merit particular attention because of the potential mortality they cause when untreated and the relative ease of reversing their effects.

Opioids are prescribed often in combination with other analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs) or muscle relaxants. They are frequent ingredients of cough mixtures. Overdosage in children could occur accidentally or intentionally. Drug abuse and inadvertent overdosage by adolescents is a cause for poisoning. Unintentional medical and nursing errors have also been described as a potential source for overdosage.

Clinical presentation

Opiate toxicity should be suspected when the clinical triad of CNS depression, respiratory depression and miosis are present. Respiratory depression is the most predominant cause of mortality in opioid overdosage. Both bradypnea and hypopnea are observed. Rates as slow as 4-6 breaths per minute often are observed with moderate-to-severe intoxication. The body retains the hypoxic drive to breathe but may be overridden by the CNS sedative effects of a severe overdose.

Acute mental changes and euphoria are sometimes seen. Seizures are not common but occur with pethidine, dextromethorphan, propoxyphene, tramadol. Seizures occur most commonly in infants because of CNS excitation. Seizures may also occur in patients with renal dysfunction who receive repeated doses of pethidine owing to accumulation of norpethidine.

Cardiac toxicity, ventricular arrhythmias similar to that seen with tricyclic antidepressants and quinidine can occur particularly with propoxyphene. Noncardiogenic pulmonary edema may occur.

Reliance on miosis to diagnose opioid intoxication can be misleading. If sufficiently severe, hypertension and pupillary dilation may present because of CNS hypoxia. Morphine, pethidine, pentazocine, diphenoxylate/atropine (Lomotil), and propoxyphene sometimes are associated with mydriasis or midpoint pupils.

Mild peripheral vasodilation may occur and result in orthostatic hypotension. However, persistent or severe hypotension should raise the suspicion of co-ingestants and needs prompt reevaluation. Pink frothy sputum, dyspnea and bronchospasm strongly suggest pulmonary edema.

Nausea and vomiting even if present initially are transient. Nightmares, anxiety, agitation, euphoria, dysphoria, depression, paranoia, and hallucinations are encountered infrequently, mainly

with high doses. Pruritus, flushed skin, and urticaria, conjunctival injsetion may arise because of histamine release. Hearing loss has been associated with heroin and alcohol but is generally considered recoverable. Needle marks may be seen indicative of drug abuse.

Table 2. Acute and chronic effects of opioids

Acute	
Analgesia	Vomiting
Respiratory depression	Miosis
Sedation	Constipation
Euphoria	Urinary retention
Cough suppression	Biliary spasm
Chronic	
Tolerance	Physical dependence

Metabolism

Peak effects of opioids generally are reached in 10 minutes with the intravenous route, 10-15 minutes after nasal insufflation (eg, butorphanol, heroin), 30-45 minutes with the intramuscular route, 90 minutes with the oral route, and 2-4 hours after dermal application (ie, fentanyl). Toxic doses may have delayed absorption because of delayed gastric emptying and slowed gut motility.

Most opioids are metabolized by hepatic conjugation to inactive compounds that are excreted readily in the urine. Neonates, owing to their low hepatic glucuronidase activity are predisposed to toxicity and lower doses should be used. All opioids have a prolonged duration of action in patients with liver disease (eg, cirrhosis) because of impaired hepatic metabolism. This may lead to drug accumulation and opioid toxicity.

Opiate metabolites are excreted in the urine, making urine toxicology useful. Renal failure also leads to toxic effects from accumulated drug or active metabolites.

Regardless of the mode of administration, narcotics taken by a pregnant addict readily pass the placental barrier and are capable of producing effects on the infant *in utero* and after birth.

Investigations

Drug screens are most sensitive when performed on urine. Positive results are observed up to 36-48 hours post exposure, but wide variations are possible depending upon test sensitivity, dose, route, and the patient's metabolism. However in uncomplicated patients they rarely alter management.

In patients with moderate-to-severe toxicity, performing baseline studies, including a CBC, comprehensive metabolic panel, and arterial blood gas determinations, is appropriate. Blood glucose should not be forgotten.

Chest radiographs are obtained if pulmonary edema is suspected. Abdominal film may be helpful when evaluating a suspected body stuffer or body pack. An ECG should be obtained on all patients with intentional overdose (possible cardiotoxic co-ingestants) or those with significant toxicity.

Treatment

Emergency and supportive measures:

Emergency management hinges on aggressive airway control, supplemental oxygen and intubation for respiratory depression or in comatose patients.

• Stomach wash may be given if patients present within 2 hours.

• Activated charcoal (1g/Kg) is the GI decontamination method of choice for patients with opiate intoxication following ingestion. Because of impairment of gastric emptying and GI motility produced by opiate

intoxication, activated charcoal still may be effective when patients present late following ingestion.

- Naloxone is the specific antidote. The dose is 2 mg in the adult and 0.1 mg/kg in the child or infant. Doses may be repeated up to a maximum cumulative dose of 10 mg.

- The onset of effect following IV naloxone administration is 1-3 minutes; maximal effect is observed within 5-10 minutes. Clinical reversal occurs within 5-10 minutes and patient quickly awakens.

- A repeat dose is indicated for partial response and can be repeated as often as needed. Repeat doses of 2 mg can be given every 3-5 minutes as needed, up to a total of 10 mg. Reconsider the diagnosis if the patient fails to respond after 10 mg.

- Naloxone can be administered intramuscularly, via endotracheal tube, intraosseously or intralingually.

- Constant infusions are particularly useful for overdoses of long-acting opioids, such as methadone. Larger doses of naloxone may be required for diphenoxylate/atropine (Lomotil), methadone, propoxyphene, pentazocine, and the fentanyl derivatives.

Aggressive airway control must take precedence over pharmacologic reversal because the vast majority of morbidity and mortality result from respiratory depression.

Points to Remember

- *Morphine, pethidine, fentanyl and pentozocine are some of the commonly prescribed opioids for pain relief.*

- *Uncommon overdosage and poisoning do occur occasionally.*

- *The clinical triad of depressed conscious state, respiratory depression and pupillary miosis are characteristic of narcotic overdosage.*

- *Naloxone is the specific antidote.*

Bibliography

1. Way WL, Fields HL, Schumacher MA. Opioid analgesics and antagonists. *In*: Katzung BG, ed. Basic and clinical Pharmacology. NewYork: Lange medical books/McGraw-Hill, 2001; pp512-531.

2. Opioid analgesics and antagonists. *In*: Harvey RA, Champe PC, eds. Lippincott's illustrated reviews: Pharmacology. Baltimore: Lippincott Williams & Wilkins, 2006; pp157-168.

3. Unintentional poisoning deaths - United states.1999-2004. MMWR Morb Mortal Wkly Rep. 2007; 56:93-96.

4. Everett Stephens. Toxicity, Narcotics. http://emedicine.medscape.com/article/815784-overview.

5. Blatman S. Narcotic poisoning of children (1) Through accidental injestion of methadone and (2) in utero. Paediatrics 1974; 54:329-332.

6. Albertson TE. Opiates and opioids. *In:* Olson KR, ed. Poisoning and overdose. California: Prentice Hall International, 1999; pp242-243.

ERRATUM

To read the designation of Dr.Swati Y Bhave as Visiting Consultant, Indraprastha Apollo Hospital, New Delhi. Executive Director, AACCI (Association of Adolescents and Child Care in India) instead of the designation published in 2008; 10(4):347 issue, which is an error, for which we regret.

The Editorial Board, IJPP.

GENERAL ARTICLE

INTRAUTERINE GROWTH RETARDATION: JOURNEY FROM CONCEPTION TO LATE ADULTHOOD

* Neelam Kler
** Naveen Gupta

Abstract:*Understanding of Intrauterine growth retardation (IUGR) gains importance because of significant perinatal morbidity and mortality related to them. It is essential to differentiate fetus that is constitutionally small for gestational age (SGA) and whose growth has been restricted in utero. IUGR represent 23.8% of the newborns in developing countries. Factors affecting fetal growth, pattern of fetal growth, their postnatal growth and development, the relation of fetal origin of adult disease and future perspectives etc are discussed in this article.*

Key words: *IUGR, Factors, Growth and Development, Adult disease.*

Background

Monitoring the well being and growth of the fetus is a major purpose of antenatal care. Many fetuses delivered with a lower than expected birth weight are healthy, thriving infants; whereas others are small because their growth in utero has been impaired and they have increased perinatal morbidity and mortality.

*   Chairperson,

**   DNB Fellow,

Department of Neonatology,
Sir Ganga Ram Hospital

A distinction therefore needs to be made between the fetus that is constitutionally small for gestational age (SGA) and one whose growth has been restricted in utero. A diagnosis of growth restriction implies that a fetus has not achieved its optimal growth potential; a prerequisite for making this assessment is that the expected growth pattern of the fetus could have been predicted. Although ultrasound biometry in second trimester may give some suggestion of expected growth, in practice it is only with serial measurements (either clinically or with ultrasound) that reduced growth velocity can be demonstrated.

In many discussions of linear growth retardation there is a need to address arguably the most important phase of human growth - Growth from conception to term.

Questions that come to mind include: 1) Can children be programmed in utero to be linearly growth retarded after birth? 2) What are the relationships between intrauterine growth retardation (IUGR) and postnatal growth?

Depending on its growth in utero, the newborn baby can be categorized as a healthy full-term (FT) infant within the normal birth weight range; a macrosomic infant above the normal birth weight range; or an infant of low birth weight (ILB). Regarding the latter, WHO estimates are of great interest: they show that approximately two-thirds of all infants of low birth weight born in the developed world are true pre-term (PT) infants and one-third are small-for-gestational-age (SGA). This relationship is reversed in the developing world, where about 75% of ILB are

SGA. The much higher proportion of SGA infants in the Third World seems to be due primarily to malnutrition and infection and should therefore be preventable.

Quantum of problem

At least 13.7 million infants are born every year at term with low birth weight (LBW), representing 11% of all newborns in developing countries. This rate is approximately 6 times higher than in developed countries. LBW, defined as < 2500 g, affects 16.4% of all newborns, or about 20.5 million infants each year. IUGR, defined as birth weight below the 10th percentile of the birth-weight-for-gestational-age reference curve, represents 23.8%, or approximately 30 million newborns per year. Overall, nearly 75% of all affected newborns are born in Asia - mainly in South-central Asia - 20% in Africa and about 5% in Latin America. Although some of these are healthy, small infants who merely represent the lower tail of a fetal growth distribution, in most developing countries a large proportion of newborns suffer from some degree of intrauterine growth retardation. These data demonstrate that many developing countries currently exceed the internationally recommended IUGR (> 20%) and LBW (> 15%) cut-off levels for triggering public health action, and that population-wide interventions aimed at preventing fetal growth retardation are urgently required.

Factors affecting fetal growth

The principal determinants of fetal growth are fetal genotype and in utero environment. Environmental factors include maternal and paternal genetics, maternal size, and the capacity of the placenta to provide nutrients to the fetus. These environmental factors interact with the intrinsic growth pattern of the fetus, yielding a particular rate and composition of fetal growth. Most of the variation in fetal growth in a population is due to variations in environmental factors, not the fetal genome, although a genetically abnormal fetus clearly might not grow as well as a normal fetus if affected genes include those that are important for growth.

Genetic factors: Many genes contribute to fetal growth and birthweight. Techniques in which specific genes can either be deleted ("knockouts") or overexpressed have led to greater under-standing of how some of these genes regulate fetal growth. Such studies have shown that both maternal and paternal influences are present during fetal development and are passed on to the developing fetus by spermatozoa or oogonia by a mechanism called imprinting. Although the maternal genetic composition exerts greater influence than fetal genotype in the overall regulation of fetal growth, both maternal and paternal genomes are important in fetal growth and development.[1] For example, gynogenetic zygotes (two maternal genome copies) lead to underdeveloped extraembryonic tissues but well-developed embryos. The more modest regulation offered by the paternal genotype is essential for trophoblast development. For example, zygote nuclear transfer experiments have shown that androgenetic zygotes (two paternal genome copies) develop extensive trophoblast tissues but contain underdeveloped embryonic tissues.

Although several genes have been described as maternally or paternally imprinted, insulin-like growth factor I (IGF-I) and IGF-II are two protein products of genes that specifically regulate the development of trophoblast cells, which form the placenta. Gestational profiles of IGF-II, IGF-binding proteins, and IGF receptors (types 1 and 2) suggest they are involved in enhancing placental growth.[2] Additionally, IGF-II may regulate placental growth directly, as evidenced by 60% placental and fetal growth restriction in mice lacking IGF-II, which implicates IGF-II in the proliferation of trophoblast cells.

Non genetic maternal factors: Uterine Size:
Under usual conditions, fetal growth follows its genetic potential, unless the mother is unusually small and limits fetal growth by a variety of factors considered collectively to represent "maternal constraint." Maternal constraint results primarily from a limited uterine size and, thus, the capacity to support placental growth and nutrient supply to the fetus, not to any particular genetic factor. A clear example of maternal constraint is the reduced rate of fetal growth of multiple fetuses in humans,[3] who optimally support only one fetus (Fig. 1).

Fetal growth constraint from the maternal environment is a physiologic process that includes the maternal-specific capacity of uterine size, placental implantation surface area of the uterus, and uterine circulation, which together support the growth of the placenta and its function.

Obviously, small fetuses of small parents or large fetuses of large parents do not reflect fetal growth restriction or fetal overgrowth, respectively. Their rates of growth are normal for their genome and for maternal size. Unless maternal constraint is particularly prominent, such fetuses would not grow faster or to a larger size if more nutrients were provided.

Pattern of gestational growth

In most species, fetal weight tends to increase exponentially in the middle part of gestation, but there is considerable interspecies variation. In humans, cross-sectional evaluations of newborn weight versus gestational age tends to produce a typical S-shaped curve, with an apparent slowing of fetal growth rate in the third trimester following the mid-gestational exponential increase in fetal weight.[4] In contrast, more recent ultrasonographic observations show that human fetal growth is linear over the latter third of gestation, with no tendency for slowing of fetal growth that would produce the flattening of the fetal growth curve derived from the cross-sectional studies.[5] The apparent slowing of growth derived from cross-sectional data most likely is due to miscalculation of gestational dates, with inclusion of more preterm infants.
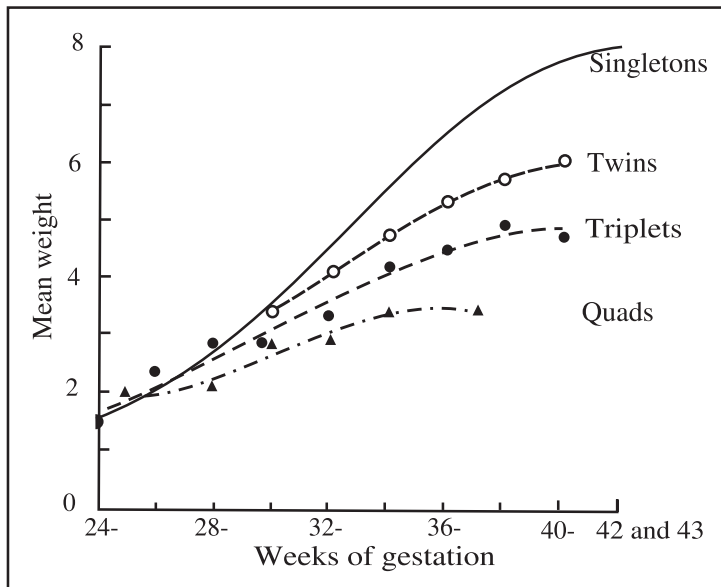
Fig. 1. Mean birth weights of single and multiple fetuses related to duration of gestation.

The length of gestation is more strongly correlated with growth of neural tissue (range, 0.015 to 0.033 $g^{1/3}$/d—a 2.2-fold range) than with growth of the fetal body (range, 0.033 to 0.25 $g^{1/3}$/d—a 7.6-fold range). The physiologic significance of this relationship is not known, but intrauterine development of a large brain/body mass ratio in humans is favored in a single fetus and is made possible by a slow rate of somatic growth. The latter allows a steady increase in fetal cerebral metabolic demand while the total metabolic demands of the conceptus are kept within limits that the mother can easily support without stress on her own metabolism.

Maternal nutrition: Normal variations in maternal nutrition have relatively little effect on fetal growth because they do not markedly alter maternal plasma concentrations of nutrient substrates or the rate of uterine blood flow, the principal determinants of nutrient substrate delivery to and transport by the placenta. Human epidemiologic data from conditions of prolonged starvation as well as nutrition deprivation in experimental animals indicate that even severe restrictions in maternal nutrition only limit fetal growth by 10% to 20%.[6] Calorie and protein intakes must be reduced to less than 50% of normal for a considerable portion of gestation before marked restrictions in fetal growth are observed.[7] Such severe conditions often result in fetal loss before late gestation fetal growth rate and fetal size at birth are affected. Similarly, fetal macrosomia is only common in pregnancies complicated by gestational diabetes mellitus in which maternal plasma hyperglycemia and hypertriglyceridemia combine with fetal hyperinsulinemia to produce excessive fetal adiposity.

The placenta: Endocrine and architectural characteristics of the placenta provide an adequate supply of nutrients for the developing fetus, a site for nutrient uptake and waste removal, and a line of defence against pathogens. Members of the GH/PRL gene family produced only in the placenta include placental lactogen (PL), growth hormone (human (h)GH-V), and prolactin-related proteins (PRP).[8] PL is believed to have a pivotal role in the growth and development of the fetus by coordinating metabolic and nutrient supply from the mother to the developing fetus to promote growth.

The placenta exerts strong control over fetal growth by providing nutrients directly or in metabolically altered forms and amounts. Naturally and experimentally, placental growth precedes fetal growth and failure of the placenta to grow is directly associated with subsequent decline in fetal growth.

Characteristically, therefore, limitations of placental transfer of nutrients to the fetus directly limit fetal growth. A direct relationship between fetal weight and placental weight in humans indicates that large-for-gestational age (LGA), average- or appropriate-for-gestational age (AGA), and small-for-gestational age (SGA) infants are directly associated with LGA, AGA, and SGA placentas (Fig. 2).[9] Clearly, placental size and fetal size are directly interrelated, although functional interrelationships between placenta and fetus also are important to fetal growth and development.

Fetal growth in normal and IUGR baby

Fetal growth restriction can occur during any or all periods of gestation. During the embryonic period, growth occurs primarily by increased cell number (hyperplasia); in the middle of gestation, cell size also increases (hypertrophy) and the rate of cell division stabilizes. In later gestation, the rate of cell division declines, but cell size continues to increase. Thus, insults that limit fetal growth in early gestation result in global reduction in fetal growth. Insults in later gestation usually limit growth of specific tissues, such as adipose tissue
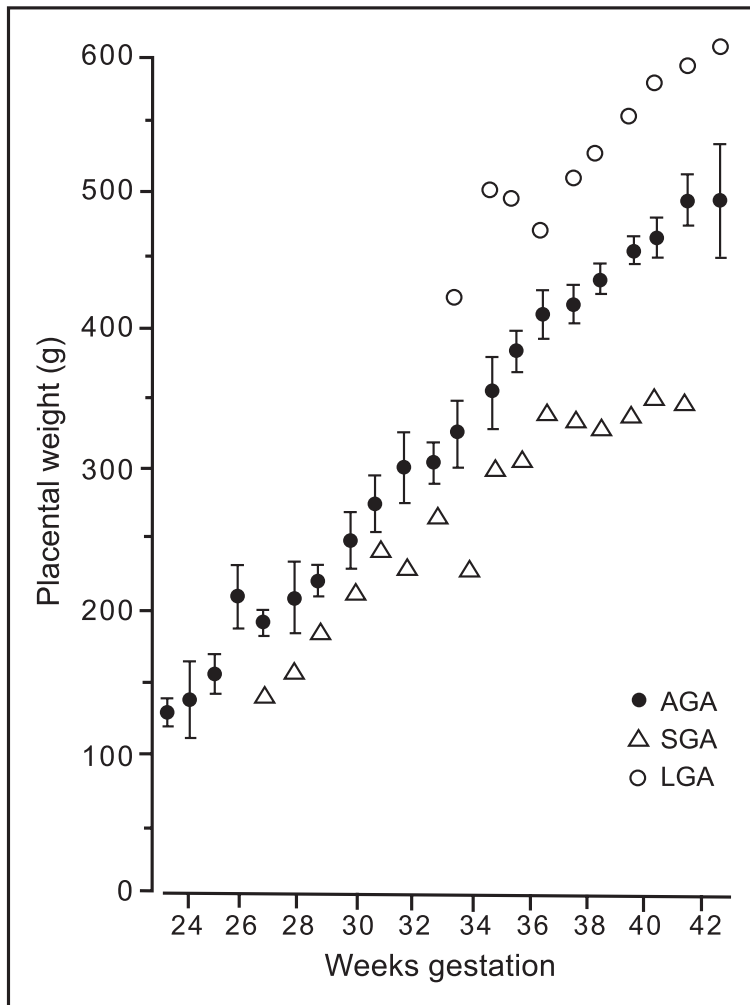
Fig 2. Mean placental weights for large-for-gestational-age (○), average-for-gestational-age (•), and small-for-gestational-age (△) human infants at each gestational age. ± SEM given only for average-for-gestational age infants.

and skeletal muscle, that primarily develop during this period and spare other organs and tissues, such as the brain and heart, whose growth rate already has slowed.

Water: Total body water content in the normal fetus increases over gestation, but fetal total body water content as a fraction of body weight decreases due to relative increases in protein, mineral and fat accretion. Extracellular water also decreases more than intracellular water as gestation advances, primarily because of increasing cell number and size. In fetuses that exhibit mild-to-moderate IUGR, measurements of extracellular fluid are usually normal for gestational age because adipose tissue, skeletal muscle, and mineral accretion all are decreased to about the same extent. In contrast, severe IUGR with markedly decreased fat content

is characterized by higher fractional contents of body water.

Minerals: Mineral content per body mass and bone mass in IUGR fetuses does not differ from that in normally grown fetuses. For example, fetal calcium content in IUGR fetuses increases exponentially with a linear increase in length because bone density, area and circumference increase exponentially in relation to linear growth. Accretion of other minerals varies more directly with body weight and according to the distribution of the minerals into extracellular (eg. sodium) or intracellular (eg. potassium) spaces.

Nitrogen and protein: Data from the very few available chemical composition studies of normal human infants show that nonfat dry weight and nitrogen content (predictors of protein content) have a linear relationship with fetal weight and an exponential relationship with gestational age (Fig. 3).

Approximately 80% of fetal nitrogen content is found in protein; the remainder is in urea, ammonia and free amino acids. Among IUGR infants, nitrogen and protein contents are reduced for body weight, primarily due to deficient muscle growth.
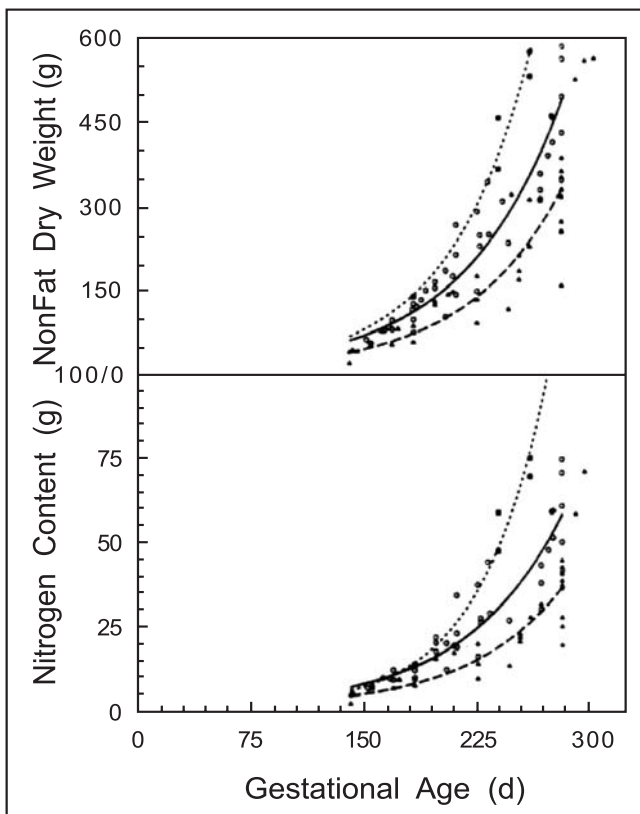
Fig 3. Nonfat dry weight (top) and nitrogen content (bottom) versus gestational age. Large-for-gestational age infants (■); average-for-gestational age infants (•); small-for-gestational age infants (◉).

Glycogen: Glycogen synthetic rates are low in the human fetus, accounting for less than 5% of fetal glucose utilization. Insulin acts synergistically with glucose to increase hepatic glycogen stores, with cortisol, epinephrine and glucagon developing the capacity to promote glycogenolysis and glucose release into the plasma close to term. Most tissues in the fetus, including brain, liver, lung, heart and skeletal muscle, produce glycogen over the second half of gestation. Liver glycogen content, which increases with gestation (Fig.4) is the most important store of carbohydrate for systemic glucose needs because only the liver contains sufficient glucose-6-phosphate for release of glucose into the circulation. Skeletal muscle glycogen content increases during late gestation and forms a ready source of glucose-6-phosphate for glycolysis within the myocytes. Lung glycogen content decreases in late gestation with change in cell type, leading to loss of glycogen-containing alveolar epithelium, development of type II

pneumocytes and onset of surfactant production. Cardiac glycogen concentration decreases with gestation owing to cellular hypertrophy, but cardiac glycogen appears essential for postnatal cardiac energy metabolism and contractile function.

Glycogen content is markedly reduced in IUGR infants, both in the liver and in the skeletal muscles (Fig. 4), due to lower fetal plasma concentrations of glucose and insulin, which are the principal regulators of glycogen synthesis. Repeated episodes of hypoxemia in severe IUGR can stimulate epinephrine secretion, which will deplete glycogen further by activating glycogen phosphorylase and increasing glycogenolysis.

Adipose tissue: The fat content of human newborns at term is about 15% to 20%, which is considerably greater than the 1% to 3% found in most other land mammals (Fig. 5). Human fat accretion begins in the late second to early third trimester of gestation. In the first half of gestation,
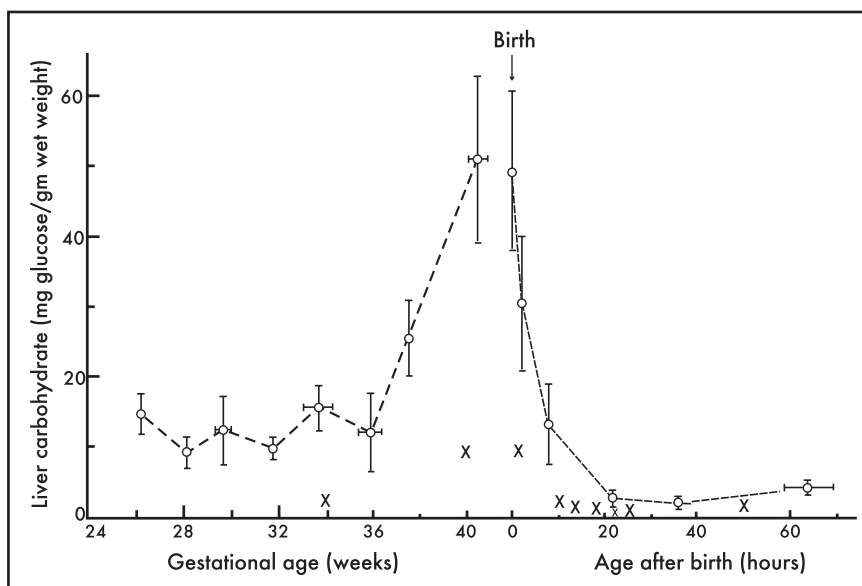
Fig 4. Liver glycogen content (as carbohydrate) in normal human fetuses and newborns with normal birthweights for gestational age (◌ ; mean±SEM) and infants of low birthweight for gestational age (X).

nonfat and fat components contribute equally to the carbon content of the fetal body. Subsequently, fat accumulation exceeds that of the nonfat components such that between 36 and 40 weeks' gestation, the rate of fat accretion is approximately linear and accounts for more than 90% of the carbon accumulated by the fetus.

In human IUGR fetuses at term, fat content may be less than 10% of body weight. Causes include decreased fatty acid, triglyceride and glucose supplies from the smaller placenta as well as a simultaneous insulin deficiency that limits fat synthesis because of decreased stimulation of fatty acid synthase in adipocytes. Because fat has a high energy content of 9.5 kcal/g and a very high carbon content of approximately 78%, decreased fat content in IUGR fetuses leads to large decreases in energy and carbon accretion rates.

Total energy balance and tissue mass

The relative mass of all tissue components, not just fat and glycogen stores, depends on energy supply, particularly for protein deposition. For example, chronic selective restriction of glucose delivery to the fetal sheep leads to increased protein breakdown as well as to lower rates of fetal growth and lipid content. Although most studies suggest that the greatest relative decrease in tissue mass occurs in the fat compartment in human IUGR fetuses, others have shown that muscle mass can be markedly deficient, even more than fat.

Immediate postnatal growth

Infants usually lose some weight immediately after birth, which they regain rapidly later. On average, catch-up growth is greatest in
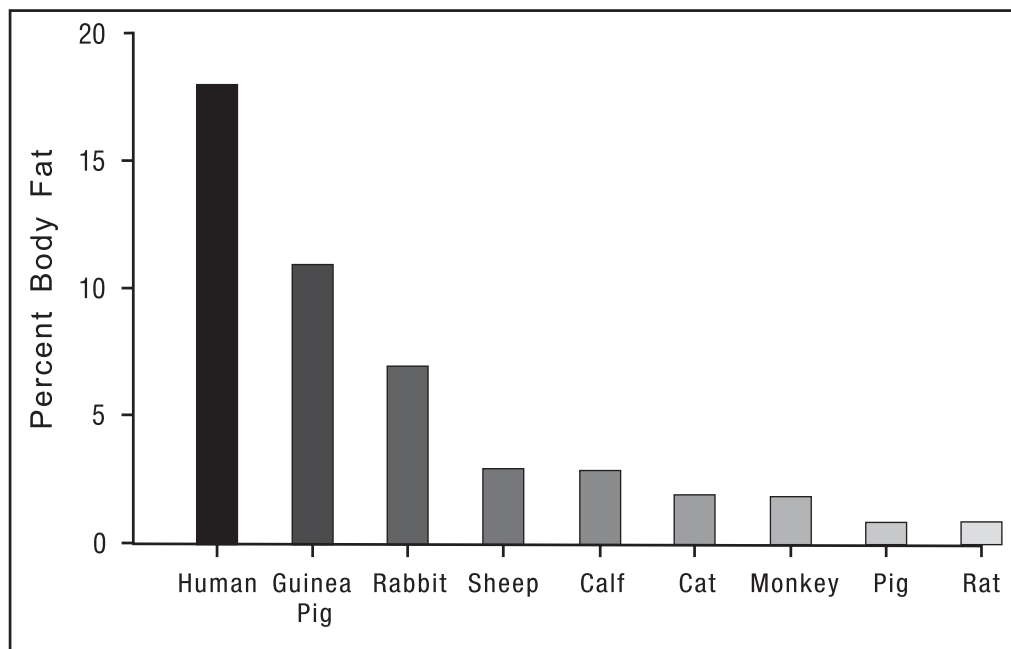
Fig. 5. Fetal fat content at term as a percent of fetal body weight among species. Reproduced with permission from Hay WW Jr. Nutrition and development of the fetus: carbohydrate and lipid

those infants most delayed in utero. As a result, there is a significant negative correlation between birth weight and weight gain in the early postnatal months. The same phenomenon occurs for length; the smaller the infants, the more, on average, they grow in the postnatal period.

Growth and developmental outcome

As noted previously, because most studies of SGA infants have involved a heterogeneous group of babies with the potential for a variety of outcomes, it is difficult to predict outcomes in SGA infants. Some affected infants are small from familial predisposition to small size and, therefore, may be expected to achieve their full growth potential and have normal neuro-development. Infants who have specific chromosomal errors or significant congenital infections are likely to experience severe and unrecoverable failure of growth and development. Most infants have a less defined reason for abnormal in utero growth. The infant who has symmetric growth restriction may have little chance for postnatal catch-up growth after an early, global disruption of growth. However, a neonate who had normal growth in early gestation, but developed growth restriction from limited nutrient availability in later gestation, likely has a reasonable potential for catch-up growth and normal development. Additionally, socio-economic status and environment are among the most important, but difficult to control, variables affecting the growth and development of SGA infants.

Most studies of normal and restricted fetal growth and development support the concept of critical windows of time in human development during which normal growth of certain tissues (eg. fat, muscle, bone) or organs (eg. pancreas, brain) must occur. Insults at such times that limit growth can program persistent, even life-long failures in growth and development.

Only relatively recently have studies of outcomes of IUGR and SGA infants included in the study design the recognition that the etiology of small size at birth carries great prognostic value has been found out. Because head size correlates with brain size, volume, weight and cellularity, head growth at the time of birth and the degree of catch-up growth thereafter are prognostic of future neurodevelopment. Deficient fetal head growth, evidenced by relative microcephaly at birth, whether at term or preterm, is felt to be a poor prognostic indicator because it reflects the severity and duration of in utero growth failure. A lack of head sparing and small head circumference is associated with poor neurologic and psychological outcome. If catch-up head growth has not occurred by 8 months of age, head size is a predictor of lower intelligence test scores at 3 years of age. This correlation seems to be independent of environmental or other risks. Decreased head size when compared with siblings carries significant risks of deficient mental and motor function.

Postnatal physical growth of SGA infants

As with developmental outcome, long-term growth probably depends most on the etiology and severity of fetal growth restriction. Many SGA infants continue to be smaller and relatively underweight for age as they grow older, even through adolescence and early adulthood. These infants more commonly have short stature as teenagers and young adults, indicating lifelong growth deficit.

Differences in patterns of early growth have been observed in SGA infants. Normal infants experience a period of rapid growth during the first 3 years of life. Adult size correlates with the individual growth curve after this time. Moderately affected SGA infants whose reduction in weight occurred primarily in the third

trimester of gestation follow the same pattern of normal neonatal and infant growth, but tend to have an accelerated velocity of growth during the first 6 months of life. This catch-up growth occurs mostly from birth to 6 months of age, with some infants continuing an accelerated rate of growth for the first year. A few of these infants achieve a normal growth percentile and thereafter have a growth rate similar to appropriately grown children. Head circumference parallels growth in length during catch-up and sustained growth periods. After the first year, no difference in the rate of growth has been noted.

Ultimate weight and height are less in SGA children compared with their normal siblings. Interestingly, a subgroup of severely growth-restricted infants (<40% of expected birthweight) showed no difference in weight or height at 6 months of age compared with less-affected SGA peers, adding concern for the growth outcome of even modest degrees of IUGR. Former SGA infants had no delay in bone age, puberty or sexual maturation at adolescence, although they were shorter, lighter and had smaller heads. Muscle mass between the two groups was similar, but adipose tissue development was less in the SGA group.

Postnatal neurodevelopmental outcome of term SGA infants

Neurologic disorders and other morbidities are generally more frequent in SGA infants, occurring 5 to 10 times more often than in AGA infants. However, IUGR may have little impact on behavior or mental ability in adolescence or adulthood among term, mild-to-moderately SGA infants who have normal brain growth, no hypoxic-ischemic injury, and good environmental support. The incidence of major handicap and risk of severe neurologic morbidity in term infants born SGA is not increased; cerebral palsy is infrequent. Findings on routine neurologic examination are

usually normal. Although the absence of gross neurologic outcome in the term SGA infant is reassuring, evidence of minimal brain dysfunction continues to be of concern. Many studies have revealed signs of minor brain damage, including hyperactivity, short attention span, learning problems, poor fine motor coordination and hyperreflexia.

Former term SGA infants more frequently have substandard school performance and display subtle neurologic and behavioral problems despite normal intelligence quotients. Sensorimotor abilities often are affected. Overall, poor early brain growth in infancy is associated with more problems. Measures of cognition at 4 to 6 years correlate well with test results at adolescence, which suggests that cognitive potential is reached early. It seems likely that environmental and socioeconomic factors play a significant role in the learning deficiencies seen in these children. At adolescence, trends toward lower test scores, especially in mathematics and an increased incidence of learning disabilities have been noted. Most believe, however, that the cognitive and academic differences are small and do not significantly affect school performance or ultimate intellectual ability.

Postnatal neurodevelopmental outcome in preterm SGA infants

The prognosis for preterm SGA infants is less clear and is confounded easily by other problems of preterm birth. In general, subnormal intellectual outcomes are more common among preterm SGA infants than term SGA infants. Some authors have shown that infants who suffer the dual insults of preterm birth and growth restriction are at higher risk of neurodevelopmental deficit. Among extremely preterm infants, gestational age (not growth status) has been the most significant predictor of intellectual outcome. Socioeconomic status is independently associated with learning disabilities in these children.

Evidence for fetal origins of adult disease

The importance of the early environment for long-term health has been recognized for many years. Seventy years ago, observations in England, Scotland, and Sweden showed that death rates decreased between 1751 and 1930 due to improved childhood living conditions. Death rates in specific age groups at any time depended more on the date of birth of the individuals than the year under consideration.

In 1986, Barker and Osmond examined mortality rates from stroke and cardiovascular diseases in different areas of England and Wales. They noticed a parallel relationship between neonatal mortality in the 1920s and 1930s and the mortality rates from strokes and cardiovascular diseases in the 1960s and 1970s from the same geographic areas. In the early 20th century, a high neonatal mortality rate was an indication of a high occurrence of low-birthweight babies and of poor nutrition and health of the mothers. Barker and Osmond concluded that the health of the mothers was important in determining the risk of stroke in their offspring and proposed that cardiovascular diseases might originate during fetal life or early childhood.

Low birth weight and adult disease

To follow up these findings, Barker and colleagues examined records of early life measurements from babies born in the 1920s and 1930s. They found a strong relationship between low-weight babies at birth or 1 year of age and ischemic heart disease and hypertension at 50 to 70 years of age. Low-birthweight babies subsequently were shown to have increased risk factors for coronary heart disease, including elevated plasma glucose, insulin and low-density lipoprotein cholesterol.

It is well known that fetal life and early childhood are critical periods for human pancreatic beta cell development. By 1 year of age, almost 50% the adult beta cell population has developed. With this in mind, Hales and Barker investigated whether there was a link between low birthweight and later impaired glucose tolerance and type 2 diabetes. Their initial study focused on men ages 59 to 70 years (mean, 64 y) born in Hertfordshire, United Kingdom. Low birthweight was associated with impaired glucose tolerance and type 2 diabetes. The odds ratio of impaired glucose tolerance was 6.6 times higher in men who had the lowest birthweights and 8.2 times higher in men who had the lowest body weights at 1 year of age. In both cases, these odds fell in a continuous relationship with increasing body weight. They also showed that individuals who were born small, but had a high body mass index (BMI) of more than 28 as adults had the worst glucose tolerances.

Subsequent studies found a relationship between low birthweight and the metabolic syndrome (syndrome X). In the same Hertfordshire cohort, the odds ratio of developing the metabolic syndrome, defined as impaired glucose tolerance, hypertension and hypertriglyceridemia, was 18 times higher in low-birthweight babies. Another study by Phillips and colleagues found that adult insulin resistance was linked to thinness at birth.

A series of epidemiologic studies conducted since the initial studies in Hertfordshire by many groups in numerous populations worldwide and of varied ethnic groups confirm the original findings. Studies have examined men and women in the United Kingdom, Sweden, United States (on Mexican-Americans), India, and Pima Indians as well as on many others. Thus, the relationship between low birthweight and adult disease is widely accepted, although the mechanism is unknown, and the relative roles of genetic and environmental factors are debated.

Fetal insulin hypothesis and MODY genes:
One explanation for the relationship between low birthweight and subsequent risk of type 2 diabetes is the possibility of genes causing both low birthweight and increased risk of type 2 diabetes. Hattersley and associates have suggested that genetically determined defects in insulin secretion or insulin action could result in poor fetal growth, low birthweight and subsequent susceptibility to type 2 diabetes. This fetal insulin hypothesis was supported by data from individuals who had mature onset diabetes of the young (MODY) type 2. These individuals have mutations in the glucokinase gene that result in decreased insulin secretion, reduced fetal growth and MODY2.

Thrifty phenotype hypothesis: An alternative hypothesis to explain the associations between low birthweight and adult disease was put forward by Hales and Barker in 1992. It was termed the "thrifty phenotype" hypothesis, so named to contrast it with the "thrifty genotype" hypothesis proposed by Neel in 1962. Neel had proposed that genes that caused diabetes had been retained through natural selection because they brought some benefit to the individual. It was suggested that the genes resulted in a greater capacity to store fat during times of starvation and undernourishment, which had been the majority of the time. The recent overabundance and overeating of food as well as the onset of obesity due to lack of exercise had caused the genes to become detrimental.

The thrifty phenotype hypothesis suggested that when the intrauterine environment was poor, the fetus adopted a number of strategies to maximize its chances of survival postnatally. A nutritionally restricted fetus would divert nutrients to the brain and away from other organs such as muscle, liver, and pancreas. Metabolic programming occurred at this crucial time based on the environmental conditions, with the fetal metabolism adapting to survive in conditions of
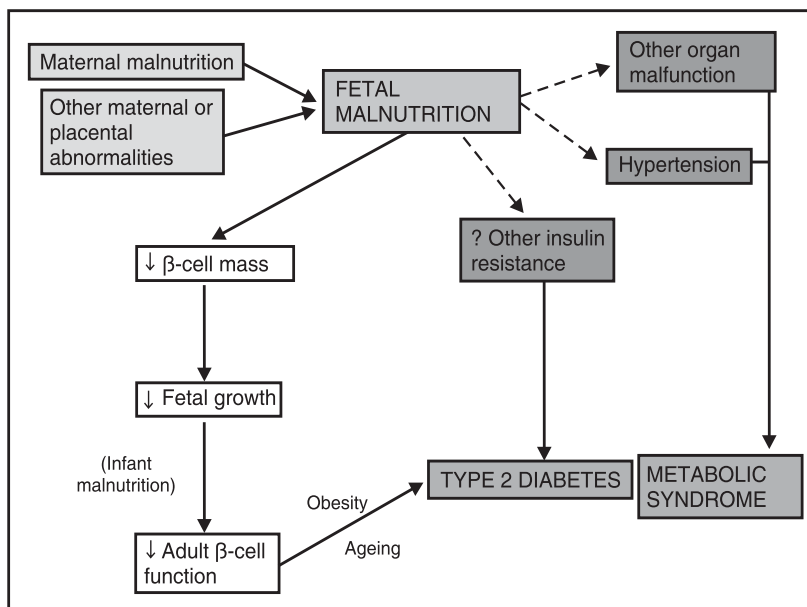
Fig.6. The thrifty phenotype hypothesis as proposed by Hales and Barker (1992).

poor postnatal nutrition. Problems occurred when nutrition during postnatal life was normal or excessive, which conflicted with the earlier programming and led to diseases such as hypertension, ischemic heart disease and type 2 diabetes (Fig.6). Populations that have served as good examples of the detrimental effects of the thrifty phenotype include Ethiopian Jews, who, after relocation to Israel and an adequate diet and lifestyle, had a high prevalence of type 2 diabetes compared with those who remained in Ethiopia, where diet and lifestyle were inadequate. In sub-Saharan Africa, the prevalence of diabetes is very low because poor fetal nutrition is followed by poor postnatal nutrition.

In some populations, such as the Pima Indians, birthweight and adult diabetes are linked by a "U"-shaped curve, with both low- and high-birthweight babies having a higher risk of the disease. This is believed to be due to the high prevalence of gestational diabetes in these populations, which is not seen in the other studies due to the low frequency and survival rate in the early part of the 20th century. The high birthweight, therefore, represents macrosomic offspring of gestational diabetic mothers. It is well established that gestational diabetes leads to an increased risk of diabetes in the offspring.

Future prospects

Research clearly indicates a relationship between the early fetal nutritional environment and later adult disease, although the mechanistic basis of the relationship is not known. Maternal diet restriction leading to intrauterine growth retardation of the fetus leads to type 2 diabetes and the metabolic syndrome in the rat and it has been shown to be associated with programmed changes in protein expression. These proteins are potential markers that would allow prediction of future diseases and a target area of research would be to identify such markers in a clinically accessible human tissue to allow implementation of intervention strategies to prevent future disease.

Points to Remember

- *Fetal growth results from interactions among maternal, placental and fetal factors and a mix of environmental influences through which the fetal genotype is expressed and modulated.*

- *The single most important environmental influence is fetal nutrition and its principal determinant is the size and nutrient transport capacity of the placenta. Placental size is determined by the size of the uterus and thus, the size of the mother. Increased nutrient supply to the fetus subsequently increases fetal tissue and plasma concentrations of anabolic hormones and growth factors.*

- *The variable supply of nutrients, anabolic hormones and growth factors in the fetus modulate the expression and/or action of growth-promoting genes and their gene products, leading to variation in fetal growth.*

- *Deficiencies in any one of these factors can limit fetal growth and produce intrauterine growth restriction.*

References

1. Surani MA, Barton SC, Norris ML. Nuclear transplantation in the mouse: heritable differences between parental genomes after activation of the embryonic genome. Cell. 1986;45:127-136.

2. Hollenberg SM, Sternglanz R, Cheng PF, Weintraub H. Identification of a new family of tissue-specific basic helix-loop-helix proteins with a two-hybrid system. Molec Cell Biol 1995;15:3813-3822.

3. McKeown T, Record RG. Observations on foetal growth in multiple pregnancy in man. J Endocrinol 1952;8:386.

4. Battaglia FC, Meschia G. An Introduction to Fetal Physiology. Orlando, FL: Academic, 1986; pp1-27.

5. Lubchenco LO, Hansman C, Boyd E. Intrauterine growth in length and head circumference as estimated from live births at gestational ages from 26 to 42 weeks. Pediatrics 1966;37:403-408.

6. Ounsted M, Ounsted C. On fetal growth rate. In: Clinics in Developmental Medicine No. 46. Philadelphia, JB Lippincott Co, 1973;p46.

7. Lumey LH. Decreased birthweights in infants after maternal in utero exposure to the Dutch famine of 1944–1945. Paediatr Perinat Epidemiol 1992;6:240-253.

8. Roberts RM, Anthony RV. Molecular biology of trophectoderm and placental hormones. In: Findlay JK, eds. Molecular Biology of the Female Reproductive System. Academic Press San Diego, Calif, 1994;pp395-440.

9. Molteni RA, Stys SJ, Battaglia FC. Relationship of fetal and placental weight in human beings: fetal/placental weight ratios at various gestational ages and birth weight distributions. J Reprod Med 1978;21:327-334.

CLIPPINGS

Fetal fibronectin testing for reducing the risk of preterm birth

Preterm birth before 37 weeks is the main cause of death and sickness for newborn infants. While most women have preterm labor symptoms such as contractions before having a preterm birth, most such women with symptoms deliver at term (greater than or equal to 37 weeks). Fetal fibronectin is a test that can identify the women with symptoms of preterm labor most at risk for preterm birth by measuring the level in secretions from the vagina and/or cervix. This review of five controlled studies that randomised 474 pregnant women did not find enough evidence to support or refute the use of the fetal fibronectin test for the management of women with symptoms of preterm labor. Further research should be encouraged.

Authors' conclusions

Although FFN is commonly used in labor and delivery units to help in the management of women with symptoms of preterm labor, currently there is not sufficient evidence to recommend its use. Since this review found an association between knowledge of FFN results and a lower incidence of preterm birth before 37 weeks, further research should be encouraged.

Berghella V, Hayes E, Visintine J, Baxter JK. Fetal fibronectin testing for reducing the risk of preterm birth. *Cochrane Database of Systematic Reviews* **2008, Issue 4. Art. No.: CD006843. DOI: 10.1002/14651858.CD006843.pub2. This version first published online: October 08. 2008**

GENERAL ARTICLE

CHILD ADOPTION

* **Ganesh R**
* **Suresh N**
** **Eswara Raja T**
*** **Lalitha Janakiraman**
*** **Vasanthi T**

Abstract: *Adoption is the process through which the adopted child is permanently separated from his/her biological parents and becomes the legitimate child of his/her adoptive parents with all the rights, privileges and responsibilities that are attached to the relationship. In-country adoption, process of prospective adoptive parents and its medico legal aspects are discussed in detail.*

Keywords: *Adoption, Prospective adoptive parents.*

"I shall be called by a new name, embraced by a fresh pair of arms, but I shall come and go, the external me"- Rabindranath Tagore.

Adoption is the act of lawfully assuming the parental rights and responsibilities of another person, usually a child under the age of 18.[1] In this era of modernisation, the abandonment of a newborn child is not uncommon. At the same time it is also encouraging to see many persons coming forward to bring up such babies as every child has a right to love and be loved, be grown up in an atmosphere of love and affection. Adoption is reflected as a triad formed between the child, adoptive parents and birth parents, the corners of which are connected by organisations such as adoption agencies, children homes to form a complete circle so as to get a rewarding and satisfying outcome.[2] With the increasing awareness and acceptance of adoption in India, it becomes important for the doctors to be aware of the recommendations, medico legal aspects and the role of Governmental and non-Governmental organizations in the process of adoption. This article outlines the step-by-step approach to the prospective adoptive parents about how a baby is placed for in-country adoption, the rules of adoption and the legal aspects in detail.

Reasons for adoption

The reasons for adopting a child includes a desire to give a home to a child who needs one, as an alternate method of attaining parenthood by a childless couple, desire to have a child of the other sex, advanced age of the parents and due to death of one spouse.

Types of adoption

Adoption may be open or closed. An open adoption involves some exchange of personal information between the biological and adoptive parents. In closed adoption there is no exchange of information or any personal contact between the biological and adoptive parents.[1]

Laws of adoption

In India there are two laws that govern the process of adoption namely hindu adoption and

* Registrar in Pediatrics
** Junior Consultant in Pediatrics
*** Senior consultant Pediatrician
    Kanchi Kamakoti CHILDS Trust Hospital,
    Chennai.

maintenance act (HAMA), 1956 governing all hindus adopting children and the second, the guardians and wards act (GWA) 1890, governing adoptions by parents who are not hindus by religion. Personal laws for muslims, christians, parsees and jews do not recognize complete adoption and hence persons belonging to these communities desirous of adopting a child can do so only in guardianship under the provision of GWA, 1890. This does not provide the child the same status as that of the child born to the family and confers only a guardian ward relationship. In inter country adoptions, children are given for adoption under GWA 1890 in foster care till they are finally adopted according to the law of the country of adoptive parents.[3]

The requisites of valid adoption are:

1. The person adopting has the capacity and also the right to take in adoption

2. The person giving in adoption has the capacity to do so

3. The person adopted is capable of being taken in adoption and

4. The adoption is made in compliance with the laws governing the adoption.

Sources and medico legal aspects of adoption

Now a days adoption in India is no longer the traditional adoption-taking place in the related groups. Hence adoption must always be done through recognized Indian placement agencies, Sishu grehas getting grant in aid from central government and licensed adoption placement agencies (LAPA).[4] In all the states of India there are many orphanages and agencies recognized in this manner by the government for giving adoption. The child to be adopted should be legally free for adoption. Both verbal and written consent to be obtained for children aged above 6 years. Siblings/twins/triplets should not be separated as sibling relationship is associated with less loneliness, fewer behavior problems and enhanced their safety and well being. Prospective adoptive parents can adopt even if they have biological children and a single parent has equal legal status to adopt. If the adoption is by a male and the person to be adopted is a female, the adoptive father should be atleast 21 years older than the person to be adopted. If the adoption is by female and the person to be adopted is male, the adoptive mother should be atleast 21 years older than the person to be adopted. A child once adopted has to break all his/her relations with the biological parents and can never return to them even when he/she opts for this course when grown up.

Adoption process

The steps involved in adoption process are as follows:

1) Prospective adoptive parents should register with the local licensed adoption placement agency or any recognized Indian placement agencies. They should also be equipped with their marriage registration certificate or marriage invitation, age proof certificate and medical certificate regarding their health status etc.

2) The next step is pre adoption counseling that is offered to prospective adoptive parents which is done by the social worker of the agency to allay the fears and apprehensions. Home study report of the prospective adoptive parents is conducted by the trained social worker of the agency, the guidelines of which are available.[5]

3) Submission of the financial and health status of the prospective adoptive parents to the agency. The prospective adoptive parents should have a minimum average monthly income of atleast Rs 3000 per month. However lower income may be considered

taking into account other assets and support system. The couple should be in good health and remain free from communicable diseases and should not be suffering from any health problem which might be physically or mentally debilitating as it will affect their care giving ability.

4) After the home study report has been accepted and approved, a child will be shown to the parents and the agency takes care to match a child meeting the desired description of the parents and if a child is above 6 years of age, both written and verbal consent of the child is obtained.

5) The child undergoes medical screening for fitness, which includes identification data, anthropometry, systemic examination, detection of any gross deficiency disorder, overt or covert anomalies and their correct ability potential. Standard investigations that are performed includes complete hemogram, urine analysis, stool for parasites, chest X-ray, Mantoux test, tests for VDRL, HIV, hepatitis B, TORCH titres and any other indicated tests with special reference to hypothyroidism, hemolytic anemia, chromosomal anomalies and metabolic screening test for mental retardation like phenylketonuria, galactosemia and aminoacidurias.[3] If prospective adoptive parents are willing to adopt a child with disability or health problem, a document stating the same should be obtained.

6) Once a child is successfully matched, filing of a petition by the agency under the relevant act for obtaining the necessary orders in the competent court. If a child cannot be placed in adoption with a suitable Indian family, the child may be transferred to the nearest recognized Indian placement agency with prior permission from the competent authority of the state government.

7) Payment of fees as prescribed by the government to the licensed adoption agency for maintenance and legal cost is to be made.

Table I. Do's and Don'ts in adoption

Do's	Don'ts
Adopt only from a recognized placement agency or Licensed adoption placement agencies (LAPA) or shishu greha	Do not adopt from nursing homes/ hospitals directly or from unrecognized agency/ unrelated persons.
The consent of children above 6 years should be taken for adoption	Do not succumb to the demands for donation and any amount more than the prescribed adoption fee.
The child study report should be signed by both adoptive parents	Take informed decisions based on facts made available to you.
Pay adoption fee as prescribed under guidelines and obtain fee receipt.	
Obtain a copy of the receipt of registration from the adoption agency	

8) The above process is normally completed in 8-12 weeks once the child has been matched with the parents.

9) The last step is the regular follow-up visits and post adoption counseling done by the social worker till the child adjusts in his/her new environment. The follow up should preferably be for a period of one year or as directed by the court /Juvenile Justice Board(JJB) and the copies of these follow up reports should be sent to the district social welfare officer/concerned state Government department and the court/ (JJB) where the order was obtained.

Once a child is adopted, an adopted child shall be deemed to be the child of his/her adoptive father/mother for all purposes with effect from the date of adoption and from such date all the ties of the child in the family of his/her birth shall be deemed to be settled and replaced by those created by the adoption in the adoptive family. Encouraging, insisting and helping the adoptive parents to tell the child about his/her adoption is the most vital post adoptive follow up action to be done usually between the ages of 6 to 10 years (ie), the time by which the child can comprehend the concept of biological and adoptive parenthood in order to avert the future problems.[3]

The Do's and don't's in adoption are shown in Table 1.

Conclusion

The above article outlines the adoption process and its medico legal aspects. However more efforts are needed to bring up a child in the heart and not under the heart when a desire is made to provide a family for a child.

Points to Remember

- *Adopt only from a recognized agency*

- *Early decision by the prospective adoptive parents to adopt a child is preferable (age of one parent should be at least below 35 years)*

References

1. Nair MKC. Adoption. Indian Pediatr 2004; 41: 653-655 .

2. Banerjee SR, Banerjee S. Adoption. In: Banerjee SR, Ed, Community and Social Pediatrics. 1st Edn, New Delhi, Japee, 1995;pp313-324.

3. Potdar RD. Adoption. In: A Parthasarathy, MKC Nair, PSN Menon, eds. IAP Text book of pediatrics. 3rd Edn, New Delhi, Jaypee, 2006; pp190-192.

4. Adoption made simple. Available from URL: http://www.cara.nic.in/Article.htm, Accessed 10 December, 2006.

5. http://www.adoptionindia.nic.in/ guide_incountry_ann_6.htm.

NEWS AND NOTES

GEM (Pediatric Golden Hour Emergency Management) Course,
Hyderabad.
February 14-15, 2009

Contact:
Dr. Dinesh Chirla
Mobile : 09849790003,   E-Mail: dchirla@gmail.com

DERMATOLOGY

ICHTHYOSIS - AN APPROACH

* Anandan V

Abstract: *Ichthyosis is an age old genetically mediated problem known as "Ekakushtha" which means fish like scales, appears in an Indian text in 250BC. Ichthyosis is basically a disorder of keratinisation where the cell turn over time is altered by which there is retention of cells leading to dry scaly skin which could be primary or secondary leading to cosmetic disfigurement and prolonged morbidity. Advance researches in this field has focused that various keratins, proteins and enzymes are at fault and various treatment options are being suggested which boosts the physician's confidence in treating these disorders.*

Key words : *Ichthyosis, Fish like scales, Syndromes.*

Ichthyosis is an age old genetically mediated problem known as "Ekakushtha" which means fish like scales, appears in an Indian text in 250BC.[1]

The clinical diversity and rarity of some of the ichthyosis has led to a confusing array of classifications by various workers, but the one given by Esterly identified four categories which is widely followed globally[2] and which is as follows.

* Assistant Professor,
  Dept. of Dermatology,
  Govt. General Hospital and
  Pediatric Dermatologist, ICH & HC, Chennai

1) Major primary forms. 2) Ichthyosiform syndromes. 3) Related disorders of cornification and 4) Acquired ichthyosis.

Each of these in turn has got many types of ichthyosis, of which some common types will be discussed in this article.

1. Major primary forms

This group includes ichthyosis vulgaris, X-linked recessive ichthyosis, non bullous ichthyosiform erythroderma, lamellar ichthyosis, harlequin ichthyosis, bullous ichthyosiform erythroderma, ichthyosis bullosa of Siemens and ichthyosis hystrix.

a) Ichthyosis vulgaris

This is the commonest type of ichthyosis reported which is inherited as autosomal dominant condition with a reported incidence of 1 in 250 and common in temperate climates with equal sex incidence sometimes found to be associated with atopic dermatitis.[3] The aetiopathogeneis in short is said to be absence of profilaggrin and reduced expression of filaggrin mRNA.

Clinically the skin appears dry and scaly which becomes more obvious from two months onwards, the scales are small, white, flaky and semi adherent with turned up edges more pronounced on the extensor surfaces of the extremities characteristically sparing the flexures. It is found that atopic eczema and keratosis pilaris (Follicular hyperkeratosis) are commonly associated with ichthysis vulgaris.[3] Symptomatically these children may have pruritis and lichenification and an apparent increased risk of testicular cancer in men is very difficult to explain.[4]

b) X-linked recessive ichthyosis (XLRI)

XLRI has an incidence of 1 in 6190 which affects the male offspring's of asymptomatic female carriers often associated with extracutaneous manifestations with obstetric and perinatal complications which was found to have steroid sulphatase deficiency and the gene locus has been identified at the distal end of the short arm of the chromosome.[5] Clinically 75% of the affected newborns present with scaling within the first week of life[6] which progresses till teens spreading from legs to trunk with remissions in summer.[6] The scales are typically medium to large, polygonal, adhernt, dull, light brown to muddy in colour commonly involving posterolateral neck, superolateral abdominal wall and the preauricular facial skin. In contrast to ichthyosis vulgaris the flexures will be involved and pruritis may be absent with palms and soles being spared. XLRI is associated with extracutaneous manifestations like testicular maldescent, cryptorchidism, infertility, testicular cancer,[7] inguinal herniae and unilateral renal agenesis. It is interesting to note that nearly 50-100% may present with comma shaped corneal opacities.[8]

The syndromes worth metioning with XLRI are

1) Kallmans syndrome : Hypogonodotrophic hypogonodism, anosmia, nystagmus, mirror movements of hands and feet (synkinesis) and

2) Ruds syndrome : Obesity, hypogonodism, mental retardation, epilepsy and endocrinopathies.

c) Non-bullous ichthyosiform erythroderma (NBIE)

NBIE is a autosomal recessive inflammatory ichthyosis with an incidence of 1 in 300000.[9] It occurs in all races, but especially in those where consanguinous marriage is common. Clinically 90% of NBIE presents at birth with colodion membrane with scales appearing white to grey, light, superficial, semi adherent and feathery scales above the groin and plate like below the groin which could be cyclical over periods of 2-4 weeks. Palmoplantar hyperkeratosis can occur in 90% of the cases and cicatricial alopecia has been reported. Ectropion, exposure keratitis, blindness, loss of eye brows and lashes with hypoplasia of the nasal and aural cartilage with or without nail dystrophies may be present. Pruritis could be very severe.

d) Collodion baby

The incidence of collodion baby is on the rise recently, clinically presenting at birth as a glistening, taut, yellowish film stretched over the skin with obliteration of normal skin markings. It can present with ectropion, eclabion, crumpled ears, sausage shaped digits and constricting bands. Shortly after birth the membrance dries, cracks around the flexures and is usually shed within first few weeks of life leaving back erythrodermic ichthyosis. As a pediatrician one has to watch for hypernatremic dehydration[10] and bacterial sepsis. Usually the collodion baby slips into NBIE and lamellar ichthyosis commonly but 10% of the collodion babies become normal and they are referred as self healing collodion babies.

2. Ichthyosiform syndromes

Even though increasing number of syndromes with ichthyosis are being reported in the literature, only a few clinically important syndromes like (a) Netherton, (b) Sjogren-Larson and (c) Refsum disease will be discussed in this article.

a. Netherton syndrome (NSI)

This is the commnest of the multisystem ichthyosiform syndromes which comprises of ichthyosis with variable erythroderma, hair shaft

defects and atopic features with autosomal recessive inheritance occurring globally with an incidence of 1 in 100000. Clinically NS presents soon after birth with varying erythrodema, temperture instability and infections. During childhood 50% of NS patients develop the characteristic lesion which is called as ichthyosis linearis circumflexa (ILC) presenting as erythematous, scaly, polycyclic, migrating flat patches with incomplete advancing double edge of peeling skin evolving cephalo caudally with flexural lichenification and with increased tendency to develop bacterial and viral infections. The major diagnostic clue to the diagnos of NS is the hair shaft defect known as trichorrhexis invaginata. In addition the hairs are sparse, spiky, lusterless, brittle, unruly with broken hair shaft at follicular orifice producing "peppered" appearance.[11]

b) Sjogren - Larsson syndrome (SLS)

SLS is an autosomal recessive condition with an incidence of 1 in 100000 clinically comprising of congenital ichthyosis, spastic diplegia, mental retardation and retinopathy. Metabolically SLS was found to have a deficiency of delta 6 desaturase with elevated plasma levels of hexadecanol and octadecanol. SLS clinically presents with collodion membrane later to have erythroderma with the development of scaling by three months of age predominantly affecting the limbs and the face. A velvety orange brown flexural lichenification may help in the diagnosis. Delayed mile stones and uper motor neuron signs are noted in early infancy resulting in non progressive spastic paraperesis. 50-80% of these patients were found to have a characteristic retinopathy consisting of glistening dots in the fovea and Para fovea.[12]

c) Refsum disease (RD)

RD is a rare autosomal recessive neuro-cutaneous disorder caused by defective fatty acid metabolism described by Refsum in 1946 as Heredopathia atactica polyneuritiformis.[13] These patients were found to have deficiency of phytanic acid oxidase. RD is as such a disease of adolescence which is characaterized by mild form of ichthyosis, retinitis pigmentosa, sensory neural deafness, mixed peripheral neural polyneuropathies, cardiomegaly and conduction defects.Infantile RD could present as a neurodegenerative disease similar to adult form devoid of ichthyosis.

3. Isolated genetic syndromes with ichthyosis

There have been various reports about the extracutaneous associations with congenital ichthyosis which could be interesting to an academician. To mention a few are,

A) Ichthyosis with CNS defects :

  a) CHIME : Coloboma, heart disease, ichthyosis, mental retardation and eye defects.

  b) KID syndrome : Keratitis, ichthyosis and deafness.

  c) Sjogren - Larson syndrome

  d) Refsum disease

B) Ichthyosis with renal defects

  a) Fanconi syndrome with ichthyosis has been reported.

C) Ichthyosis with skeletal defects

  a) ICE syndrome : ichthyosis, fullness of cheeks, thinning of eyebrows.

  b) CHILD syndrome : congenital hemi dysplasia, ichthyosis, limb defects.

D) Ichthyosis with immune defects

  a) Nezelof syndrome : Ichthysosis, severe congenital immunodeficiency with thymic hypoplasia.

E) Ichthyosis with malignancy

   a) XLRI : Testicular malignancy.

   b) KID syndrome : Squamous cell carcinoma.

   c) NS : Squamous cell carcinoma.

4. Acquired ichthyosis

Acquired or late onset ichthyosis is associated with or could be a manifestation of underlying disease the knowledge of which is important for the early detection and efficient treatment of the primary cause. To mention a few underlying causes are : Drugs like nicotinic acid, hypocholestroloemic agents, maprotiline and clofazimine and diseases like chronic hepatitis, renal failure, thyroid and parathyroid disease, malabsorption states, sarcoidosis, leprosy, AIDS[14] and lymphoma.

Treatment

Topical : The main stay of treatment is going to be emollients like liquid paraffin and white soft paraffin which keeps the ichthyotic area moist and soft by reducing the trans epidermal water loss and it is also recommended to use it immediately after the bath . Keratolytics like 1 to 5% Salicylic acid, Alpha hydroxyl acids, 5 to 10% urea cream is also being used to remove the scales and to make the skin soft and smooth. Topical retinoids, calcipotriol and topical evening primrose oil are also being used with varying success .

Systemic: Systemic drugs are very rarely used unless and otherwise the ichthyosis is very much resistant and which could endanger life in the form of non bullous ichthyosiform erythroderma where oral retinoids like acitretin 0.5 to 0.75mg/kg body weight could be life saving . Usage of oral antibiotics to combat secondary infection is also justified. Oral primrose oil is also being used as an adjuvant.

Future trends: Gene therapy in future is the only ray of hope in these patients .

Points to Remember

- *Ichthyosis could be genetic and acquired.*

- *Holistic approach will highlight the underlying syndromes.*

- *Sympathetic approach is always rewarding.*

References

1. Menon IA, Haberman HF. Dermatological writings of ancient India. Med His 1969;13:387-392.

2. Esterly NB. The ichthyosiform dermatosis. Pediatrics 1968;42:990-1004.

3. Wells RS, Kerr CB. Clinical features of autosomal dominant and sex-linked ichthyosis in an English population. Br Med J 1966;1:947-950.

4. Lykkesfeldt G, Bennett P, Lykkesfeldt AE, et al. Testis cancer; ichthyosis constitutes a significant risk factor. Cancer 1991;67: 730-734.

5. Jobsis AC, Van de sen chr Y, Van de uries GP, et al. Trophoblast sulphatase deficiency associated with X-chromosomal ichthyosis. Med Tijidschr Geneesk 1976 ; 120:130-136.

6. Paige DG, Emilion GG, Boutoux PMG, Harper IL. A clinical and genetic study of X-linked recessive ichthyosis and contiguous gene defects . Br J Dermatol 1994; 131: 622-629.

7. Lykkesfeldt G, Lykkesfeldt AE, Hayer H, Shakke baek NE. Steroid sulphatase deficiency associated with testis cancer. Lancet 1983;2:1456.

8. Costagliola C, Fabbrocini G, Illiano GM et al. Ocular findings in X-linked ichthyosis; a survey of 38 cases. Opthalmogica 1991;202:152-155.

9. Wells RS, Kerr CB. Clinical features of autosomal dominant and X-linked ichthyosis.in an English population. Br Med J 1966;1:947-950.

10. Buyse L, Graves C, Marks et al.Collodion baby dehydration; the danger of high trans epidermal water loss. Br J Dermatol 1993;129:86-88.

11. Greene SE, Muller SA.Netherton syndrome; a report of a case and review of the literature. J Am Acad Dermatol 1985;13:329-337.

12. Nilsson SEG, Jagell S. Lipofuscin and melanin content of the retinal pigment epithelium in a case of Sjogren-Laesson syndrome. Br J Opthalmol 1987; 71:224-226.

13. Refsum S. Heredopathica actactica polyneuritiformis. Acta Psychiatric scand (suppl) 1946;38:1-3.

14. Young L, Stenman HK. Acquired ichthyosis in a patient with AIDS and kaposis sarcoma. J Am Acad Dermatol 1987;16:395-396.

NEWS AND NOTES

IAP-IJPP CME 2009

NATIONAL CME ORGANIZED BY

INDIAN ACADEMY OF PEDIATRICS (IAP)

and

INDIAN JOURNAL OF PRACTICAL PEDIATRICS (IJPP)

AT KAMARAJAR ARANGAM,

492, ANNA SALAI, CHENNAI - 600 006.

ON SUNDAY, 7TH JUNE 2009

Delegate fee:

Up to 31st May, 2009 Rs.300/- for Post Graduates, Rs.500/- for others. From 1st June, 2009 Rs.750/- (as Cash / Cheque/DD drawn in favour of "IAP-IJPP CME 2009", payable at Chennai)

For further details contact:

Dr.K.Nedunchelian and Dr.S.Thangavelu
Organizing Secretaries, IAP-IJPP CME 2009
1A, Block II, Krsna Apartments,
50, Halls Road, Egmore,
Chennai – 600 008.India.
Phone: 044-28190032,42052900
E-mail: ijpp_iap@rediffmail.com

PICTURE QUIZ

Can you spot the diagnosis?

Compiled by
*Dr.Baldev S Prajapati
*Dr.Rajal B Prajapati
**Dr.Panna S. Patel

*Associate Professors, Smt. N.H.L.Municipal Medical College, Ahmedabad.
**Counsultant Pediatrician, Aakanksha Children Hospital and Neonatal Nursery, Ahmedabad.

Answer on page: 96

RADIOLOGIST TALKS TO YOU

DISORDERS OF VENTRAL INDUCTION AND SIMILAR CONDITIONS - 1

* **Vijayalakshmi G**
** **Elavarasu E**
*** **Vijayalakshmi M**
*** **Venkatesan MD**

Ultrasound of the neonatal brain is excellent for studying the ventricular system. One reason is the central location of the ventricles that makes it easily accessible to the ultrasound beam while laterally placed structures are shadowed by the bony edges of the fontanelle. The other reason is the black colour of fluid that is easy to appreciate. Sometimes, almost the entire cranium is filled with fluid. Hydranencephaly is one such condition. It is a rare abnormality where the cerebral cortex is completely destroyed. It occurs after the brain and ventricles have formed, usually in the second trimester. Intrauterine infections and vascular insult are implicated in the pathogenesis. The brain destruction is in a bilateral internal carotid distribution and both cerebral hemispheres are seen as bags of fluid covered by the meninges. Since the prosencephalon has already cleaved into two, the falx is present. This is one important feature that differentiates it from holoprosencephaly. Fig.1 is an ultrasound image

* Associate Professor
** Asst. Professor
*** Professor
Department of Radiology,
Chenglepet Medical College Hospital,
Chenglepet, Tamilnadu.
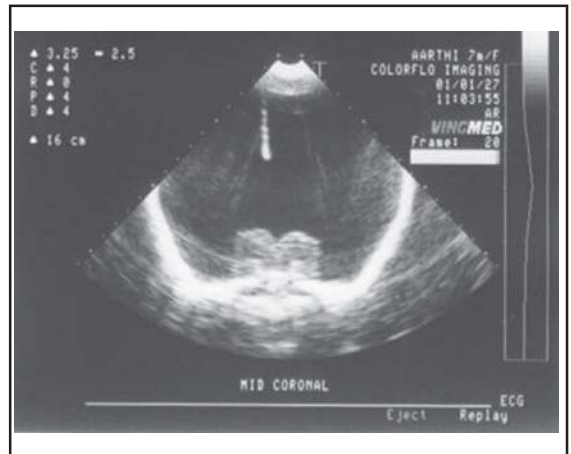
Fig. 1. Hydranencephaly. Note the falx

of hydranencephaly.The falx is seen as a vertical white line within a large bag of black fluid.

Holoprosencephaly is a very early event (4-8 weeks) unlike hydranencephaly which occurs later. It is a developmental abnormality that results from absent or incomplete diverticulation of the forebrain into two hemispheres.. Therefore the falx is not formed. There is a large single ventricle. The cavum septum pellucidum is also absent.

There are three types of holoprosencephaly depending on the degree of cleavage or separation of the telencephalon into the two cerebral hemispheres. Fig.2 is the alobar type. There is no falx, no cerebral tissue, and the thalami are fused. MRI will also demonstrate the large monoventricle. The falx is absent. It therefore follows the three sinuses in the edges of the falx - superior sagital sinus, inferior sagital sinus and the straight sinus -are also absent. There is a single

Fig.2. Holoprosencephaly-alobar type. Falx is absent
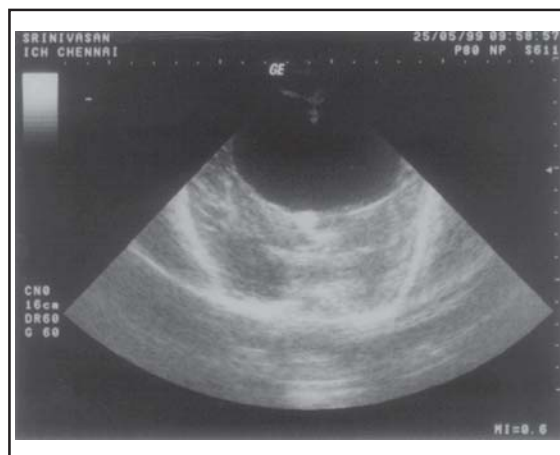
Fig.3. Holoprosencephaly-semilobar type. Monoventricle with cerebral lobe formation
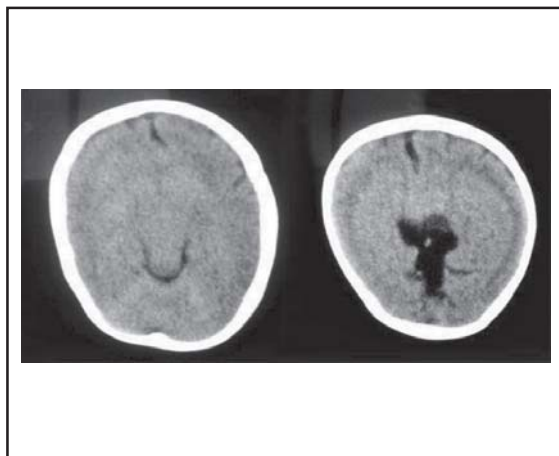

Fig.4. Lobar holoprosencephaly

Fig.5. Syntelencephaly

midline artery instead of two pericallosal arteries. In the semilobar type (Fig.3) there is partial separation into hemispheres posteriorly while the frontal lobes are fused anteriorly. The corpus callosum is present only posteriorly. There is still a single ventricle but there is an attempt to form temporal and occipital horns. The lobar type is shown in Fig.4. There is complete ventricular division. The ventricles are almost normal but the frontal horns will be placed closely as the cavum is absent. The frontal horns also have a squared-off appearance. Cortical separation is however, incomplete. MRI will show grey and white matter fused across the midline usually on the inferior aspect of the frontal lobe. The squared-off appearance of the frontal horns is also seen in septo-optic dyspalsia where there is optic nerve hypoplasia and pituitary hypoplasia. Syntelencephaly (Fig.5) is sometimes described as a variant of the lobar type. In this, there is a
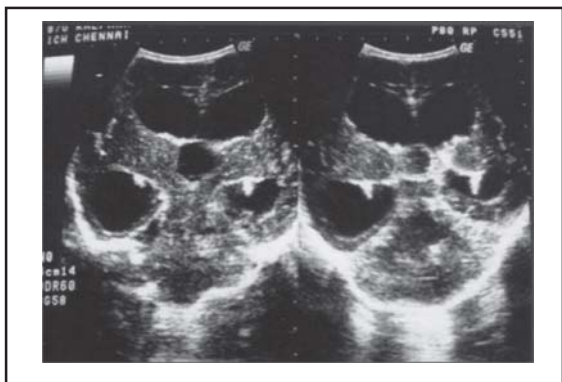
Fig.6. Hydrocephalus.

normal or hypoplastic falx and fusion of grey matter in the midfrontal region. There is heterotopic grey matter in the region of the corpus callosum and the septum pellucidum is absent.

It is important to differentiate the above two conditions from gross hydrocephalus as these children require shunting of CSF. Gross hydrocephalus, however severe it may be, usually has a thin cerebral mantle while hydranencephaly is devoid of cerebral parenchyma. The third ventricle is present (Fig.6) and both thalami are separate in hydrocephalus unlike holoprosencephaly where they are fused. Confusion may arise between hydrocephalus of the lateral ventricles alone and semilobar holoprosencephaly. In the former the frontal horns are well formed , while in the latter the frontal horns are not well developed.

In holoprosencephaly the head is considerably smaller than expected and there maybe other midline abnormalities which will aid in diagnosis. But in hydranencephaly the head may be large as in hydrocephalus. Careful interpretation is then necessary to differentiate the two, so that a shunting procedure may be advised appropriately.

CLIPPINGS

Admission avoidance hospital at home

Admission avoidance hospital at home is a service that provides active treatment by health care professionals in the patient's home for a condition that otherwise would require acute hospital in-patient care, and always for a limited time period. We conducted a systematic review and meta analysis, using individual patient data when available, to determine the effectiveness and cost of managing patients with admission avoidance hospital at home compared with in-patient hospital care. We performed meta-analyses where there was sufficient similarity among the trials and where common outcomes had been measured. There is no evidence from these analyses to suggest that admission avoidance hospital at home leads to outcomes that differ from inpatient hospital care.

Shepperd S, Doll H, Angus RM, Clarke MJ, Iliffe S, Kalra L, Ricauda NA, Wilson AD. Admission avoidance hospital at home. *Cochrane Database of Systematic Reviews* **2008, Issue 4. Art. No.: CD007491. DOI: 10.1002/14651858.CD007491. This version first published online: October 08. 2008**

UNUSUAL COMPLICATION OF NASOGASTRIC TUBE INSERTION IN A CHILD

* *Poovazhagi V*
* *Shanthi S*
* *Vijayaraghavan A*
** *Kulandai Kasturi R*

Naso gastric tube placement is a common intervention in any pediatric intensive care unit (PICU) while managing a critically ill child. We report a rare complication of knotting of nasogastric tube (NGT) in a child, who was admitted with suspected poisoning of an unknown drug. The difficulty encountered during NGT removal was later found to be due to knotting of the distal end of the NG tube. Care has to be taken during routine procedures like insertion of naso gastric tube or else complications may occur with varied consequences.

Case Report

A 6 year old child presented to our emergency room (ER) in a state of unresponsiveness and was suspected to have poisoning due to some medication. As part of initial stabilization a 12 French nasogastric tube was inserted and child received a stomach wash at the ER. Child was shifted to the PICU and needed mechanical ventilation. Child's clinical parameters improved and he regained consciousness after 48 hours. Surprisingly an

* Assistant Professor,

** Professor of Pediatrics,
PICU, Institute of Child Health and Hospital for Children, Chennai.

attempt to remove the nasogastric tube on the second day by the nursing staff was difficult and there appeared to be some resistance while withdrawing, at the level of the nasopharynx. Further effort to remove the tube by a senior member of the team proved successful, only to reveal a tight knot at the tip of the nasogastric tube (Fig.1). In this case, a loose knot had most probably formed in the nasogastric tube at insertion or later and during retrieval the knot might have got tightened up. Knots form in the stomach when excess tubing is advanced inadvertently, allowing it to loop back on itself and form a knot in the stomach cavity.

Fig.1. Knot at the end of the nasogastric tube

Discussion

Nasogastric tubes are commonly used in daily practice both for stomach decompression and for feeding purposes. Though their use is very frequent and simple, they are at times associated with complications. Reported complication rates vary widely from 0.3% to 8%. Pneumothoraces

accounted for approximately 60% of complications. Fifty percent of these required a chest drain. In 15%, the misdirected NG tube in the bronchus did not cause any complications.[1] In the case of knot posing difficulty in removal at the level of nasopharynx it can be removed retrograde via the oral cavity. Difficulty in removal of the knotted NGT can be managed by endoscopic removal. The complication of knotting of nasogastric (NG) tubes on removal occurs infrequently with small diameter feeding tubes. Knotting of large caliber NG tubes is even more uncommon.[2]

Too much of insertion of NGT has been recognized as a risk factor for knotting . A small gastric remnant has also been reported to be a risk factor to knot formation.[3] The severity of complications in NGT placement can be from asymptomatic coiling to life threatening inadvertent misplacement. Complications of nasoenteric tubes frequently include inadvertent malposition, epistaxis, sinusitis, inadvertent tube removal, tube clogging and aspiration pneumonia.[4] Rarely reported are misplacement of the tube in the bronchus leading to complications, intravascular penetration and intra cranial entry.[1] Most of this morbidity is avoidable with careful attention to details when placing the tube and careful management of the tube on a day to day basis. Tube designs influence its safety. Current polyurethane fine bore tubes have evolved from the earlier use of latex, silicon and polyvinylchloride tubes. Polyurethane does not stiffen, embrittle or biodegrade in vivo. This reduces the risk of enteric perforation and tube cracks. Polyurethane is very flexible and has a larger lumen to wall thickness ratio.

Most of the important complications of NGT placement are related to penetrating the esophagus or passing the tube in trachea and bronchi. These misplacements will not be seen in the abdominal x-ray. The traditional physical examination-based methods of assessing proper NGT placement are inadequate when applied to the small-bore tubes. Only a chest x-ray can assure placement in the stomach. Hence appropriate care has to be taken during the simple procedure of NGT insertion to prevent the rare complications.

References

1. Pillai JB, Vegas A, Brister S. Thoracic complications of nasogastric tube: Review of safe practice. Interact CardioVasc Thorac Surg 2005;4:429-433.

2. Dinsmore RC, Benson JF. Endoscopic removal of a knotted nasogastric tube lodged in the posterior nasopharynx. South Med J 1999; 92:1005-1007.

3. Cappel MS, Scarpa PJ, Nadler S, Miller SH . Complications of nasoenteral tubes. Intragastric tube knotting and intragastric tube breakage. J Clin Gastroenterol 1992; 14:144-147.

4. Baskin WN. Acute complications associated with bedside placement of feeding tubes. Nutr Clin Pract 2006; 21:40-55.

Answer to picture quiz : Cornelia de Lange Syndrome

This 6 months old male have typical facies with bushy eyebrows meeting in midline (synophrys), long curly eyelashes, hirsuitism, long philtrum, antiverted nostrils and down turned angles of mouth (Fig.1). Also has bifid scrotum and undescended testis on the left side (Fig.2).

<div style="text-align:center">

CASE STUDY

</div>

CONGENITAL MILIARY TUBERCULOSIS

*** Vijaya Kumari**
**** Suresh V**

Congenital tuberculosis (TB) is a rare entity and only few authentic cases have been reported so far in India.[1,2] Tuberculous bacillemia during pregnancy may result in infection of the maternal genital tract.[3,4] Such infection may then be transmitted to the fetus by hematogenous spread through placenta, in-utero aspiration and ingestion of infected amniotic fluid or secretions during delivery.[5] The hematogenous route and in-utero aspiration accounts for approximately half of the cases. In addition postnatal infection may occur from contact with a contagious mother or carer or ingestion of infected breast milk from a mother with TB breast abscess.[6] Congenital TB is rare if the mother received adequate treatment during pregnancy.[4] We report an infant with congenital TB who presented to us with respiratory distress and abdominal distension.

Case Report

An 88 days old male baby weighing 4.5 kg delivered via naturalis presented with fever, recurrent cough and respiratory distress since 20 days of birth. Baby was treated for acute exacerbations with antibiotics, nebulization and steroids. As respiratory distress increased and baby did not feed for 2 days he was admitted for

* Post Graduate,

** Consultant Pediatrician and Neonatal Intensivist, SKS Hospital, Salem, Tamilnadu.

evaluation. Birth weight was 2.5kg and there was no history of birth asphyxia. Baby was kept in NICU for respiratory distress, treated as transient tachypnea of newborn initially and later for hyperbilirubinemia for 7 days. Baby was given BCG vaccination at birth and triple antigen with OPV at the age of 1½ month. Antenatally mother was registered and she gave history of recurrent cough with fever during her 8th month of pregnancy which was treated symptomatically.

On examination the baby was irritable, febrile [102°F], had severe respiratory distress and subcostal retraction. His respiratory rate was 80/min and heart rate was 166/min with oxygen saturation at 78% in room air. Baby had mild abdominal distension with hepatomegaly 7cm below right costal margin and splenomegaly 3cm below left costal margin. Neurologically, anterior fontenelle was normal and there was no focal deficit.

As chest x-ray revealed extensive miliary mottling in both lungs (Fig.1), baby was investigated for possible causes of mottling in an infant. Blood tests revealed mild anemia (8.5g/dL), total leukocyte count of 14,600 cells/cubic mm, differential count of 72% neutrophils and ESR of 16mm in 1 hour. HIV 1 and 2 were non reactive and his liver functions were normal with SGOT of 34 IU/L and SGPT 37 IU/L. Mantoux test was 13mm positive. Smear from gastric aspirate for AFB was positive (1+) on day 1. IgM and IgG Elisa tests for CMV were positive. CSF analysis was normal. Ultrasound abdomen revealed hepatosplenomegaly. Blood culture and CSF culture were sterile. CT brain was normal.
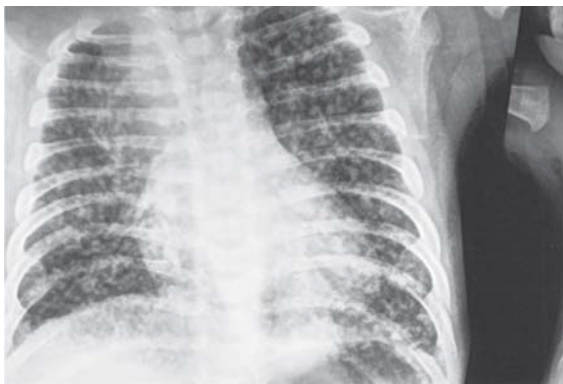
Fig 1. Chest X- ray showing extensive miliary mottling both lungs

Fig 2. CT Scan of Chest showing multiple centri-acinar nodules symmetrically in both lungs

Fundus examination was negative for choroiditis or choroidal tubercles and was confirmed by ophthalmologist. CT thorax revealed segmental consolidation in the left lower lobe, multiple small discrete and confluent centriacinar nodules in a symmetrical basal distribution in both lungs (Fig.2). There were multiple enlarged, confluent, necrotic mediastinal and right hilar lymph nodes present (Fig.3).

ESR was raised, Mantoux test was positive and smear for AFB was positive, tuberculous etiology for military mottling in this infant was confirmed. Family members were screened for the probable source of infection. Father and grandmother's chest X-rays were normal and Mantoux test was negative in grandmother though weakly positive in father [9mm]. Mother's chest X-ray was not significant but her ESR was high [57mm in 1 hour] and Mantoux test was highly positive [60mm x 30mm] with ulceration. She was advised endometrial biopsy to look for genital tuberculous lesion for which she did not return. During his week long hospital stay baby was managed with O_2, nebulization, IV steroids and antituberculous treatment with four drugs. Baby was supported with antibiotics, anti-emetics and H_2 blockers. At discharge, baby's respiratory distress and hepatospleno-megaly decreased;

repeat chest x-ray revealed miliary mottling with decrease in size of hilar lymphadenopatahy. Baby was advised prednisolone 2.5mg twice daily and antituberculous drugs, four drugs regimen [Streptomycin, Rifampicin, Pyrazinamide and Isoniazid] for 2 months and two drugs for 9 months at discharge. He came for follow-up after one week with mild distress which decreased with nebulisation and later he didnot turn up.

Discussion

The diagnosis of congenital TB is often difficult. According to Cantwell, et al[7], the infant must have proved tuberculous lesions and at least one of the following: (1) lesion in the first week of life, (2) a primary hepatic complex or caseating hepatic granulomas, (3) tuberculous infection of the placenta or the maternal genital tract or (4) exclusion of the possibility of post natal transmission by a thorough investigation of contacts. The median age at presentation is 24 days, range 1 to 84. The onset of symptoms varies from the first few days of life to a few months of age with an average 2-4 weeks. The clinical manifestations are often nonspecific and include fever, respiratory distress, abdominal distension, lethargy, irritability, hepato-splenomegaly, lymphadenopathy, jaundice, ear
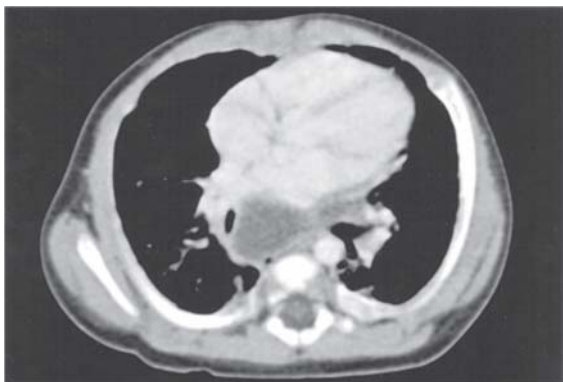
Fig 3. CT Thorax showing necrotic enlarged multiple mediastinal and right hilar Lymph nodes

discharge and skin papules.[3] CNS involvement occurs in fewer than 50% cases.[8] In most infants with congenital TB chest radiographs are abnormal at presentation and include non specific parenchymal infiltrates, adenopathy and miliary mottling (50%).

Although gastric aspirate cultures are said to be a poor diagnostic tool, it has been associated with a high yield of positive cultures of M. tuberculosis in most of the reported cases of congenital TB.[8] Gastric aspirate and PCR for AFB are the most expedient and reliable ways of establishing the diagnosis. The yield in CSF is usually low. Demonstration of a primary hepatic complex which requires an open surgical procedure or autopsy is not essential for diagnosis.[6] A percutaneous liver biopsy specimen demonstrating caseating granulomas is sufficient for diagnosis. Our patient presented with respiratory distress and hepato splenomegaly. Chest Xray revealed miliary mottling which prompted us to evaluate the probable source of infection which is baby's mother in this case. As the baby didn't have features of intrauterine

CMV infection like IUGR, microcephaly, congenital chorioretinitis, periventricular calcifications, thrombocytopenia, sensorineural deafness[9,10] CMV in this baby could have been acquired after birth.

References

1. Sosa LM, Calla LL, Mantilla JC. Congenital tuberculosis associated with maternal disseminated miliary tuberculosis. Biomedica 2007; 27:475-482.

2. Kumar R, Gupta N, Sabharwal AS. Congenital Tuberculosis. Indian J Pediatr 2005;72: 631- 633.

3. Skevaki CL, Kafetzis D. Tuberculosis in neonates and infants: Epidemiology, pathogenesis, clinical manifestations, diagnosis and management issues. Pediatr Drugs 2005; 7: 219-234.

4. Vallejo JG, Starke JR. Tuberculosis and pregnancy. Clin Chest Med 1992; 13:693-707.

5. Chotpitayasunondh T, Sangtawesin V. Congenital tuberculosis. J Med Assoc Thai 2003;86:689-695.

6. Pablo JS, Amina A. Tuberculosis. In: Taeusch HW, Ballard RA and Gleason CA. Eds, Avery's Diseases of the Newborn. 8th Edn, Philadelphia, W. B. Saunders, 2005; pp 542-547.

7. Cantwell MF, shehab ZM, Costello AM, et al. Brief report: Congenital tuberculosis. N Engl J Med 1994; 330: 1051 - 1054.

8. Chanta C, Jariyapongpaibul Y, Triratanapa K. Congenital Tuberculosis presenting as Sepsis Syndrome. J Med Assoc Thai 2004;87:573-577.

9. Fowler KB, Pass RF. Risk factors for congenital cytomegalovirus infection in the offspring of young women. Pediatrics 2006; 118:286-292.

10. Schleiss MR, Mc Voy MA. Overview of congenitally and perinatally acquired cytomegalovirus infections. Expert rev Anti Infect Ther 2004; 2:389-403.

National Assembly on Pediatric Emergency Medicine

"India-International Conference on Pediatric Emergency and Acute care"

27th Feb to 1st March 2009

Organized by : Society for Trauma and Emergency Pediatrics, India

IAP, Delhi Branch and Centre for Child Health, Sir Ganga Ram Hospital, New Delhi

Venue: India International Centre, 40 Max Mueller Marg, New Delhi

*The **National Assembly on Pediatric Emergency Medicine** is not just another pediatric conference. It is going to be an amazing learning experience, designed specifically for those who are involved in pediatric emergency care whether in a hospital setting or out of hospital setting. It will provide insight for most critical areas of your practice and empower the delegates with the knowledge necessary to translate science into practice and enhance the ability to treat not only common but most bizarre pediatric emergencies as well. This will provide current, evidence-based practice information and promises to reach further and deliver more by featuring:*

- *Outstanding National and International faculty*
- *Contentious and Contemporary topics based on leading-edge research*
- *An extraordinary amalgamation of wisdom and knowledge*

If you practice Pediatric Emergency Medicine, Pediatric Intensive Care, General Pediatrics, or Family practice and treat emergent patients, this conference is designed for you! Don't delay, register now.

- Pediatric Emergency Medicine and Acute Care in India: Past, Present and Future
- Pediatric Pre-hospital Care in India: Need of innovation and instigation
- ***Trauma Emergencies:*** **T**rauma fluid resuscitation, **H**ead injury, **S**port concussion, **T**rauma panel
- ***Neuro-Emergencies:*** **P**ediatric Meningitis in 2009, Status Epilepticus: Beyond benzodiazepines, Pediatric Stroke- Investigation and Management,
- ***Cardiovascular Emergencies:*** **S**epsis Guidelines 2008 : The Indian Adaptation and Implementation , **W**hen the pump fails: Contemporary management strategies for pediatricians
- ***Respiratory Emergencies:*** **E**vidence Based Management of Bronchiolitis, **C**roup and **A**sthma
- ***Infections:*** **C**ommunity Acquired Infections including MRSA, **M**anaging a febrile infant < 3 months in era of Hib and Pneumoccoccal Vaccination, **D**efiant Malaria- How the management has changed
- ***Surgical Emergencies:*** **I**dentification and Medical Management of Surgical Emergencies, **S**urgeon's View on Medical Management
- ***Emergency Services:*** **S**etting up Pediatric Emergency Services, **M**edical Transport, **D**isaster Triage, **P**rehospital Care
- ***Meet the Emergency Experts:*** **L**isten to his clinical case or bring your own
- ***Pediatric Office Emergencies***: **P**earls from the pediatric eye, ENT, dental and emergency experts, **C**hest pain- when to worry and what to do, **F**ainting fallacies- investigating a pediatric syncope- when, what and how much, **D**o you know what are you seeing- perplexing visual diagnosis, **O**ne pill can kill

Pre-conference Workshops

For Doctors: Workshop on Pediatric Emergency Procedures, **For Nurses, Paramedics and General Public:** Pediatric Advanced Life Support Course for Nurses, Emergency Preparedness Workshop for School Healthcare Providers, PEARS (Pediatric Emergency Assessment, Recognition and Stabilization) Course, Basil Life Support

Registration Details

Registration Fee: Upto 31st Jan 2009: Rs 2000/- After 31st Jan 2009: Rs 2500/- by Cash/Cheque/Draft in favor of "**STEP, India"** payable at Delhi (Spot Registration may not be available due to heavy booking)

Conference Secretariat: Pediatric Ground Floor (Ward No. 6), Centre for Child Health, Sir Ganga Ram Hospital, Rajender Nagar New Delhi 110060, Phone: 42251094/42251156, pedemergency@gmail.com

Organizing Chairman
Prof. Sunit Singhi (PGI, Chandigarh)
Phone: 09417089782, sunit.singhi@gmail.com

Organizing Secretary
Dr Suresh Gupta (Sir Ganga Ram Hospital)
Phone: 9811426628, sureshgupta62@gmail.com

INDIAN JOURNAL OF PRACTICAL PEDIATRICS
SUBSCRIPTION TARIFF

IJPP

JOURNAL OFFICE
1A, Block II, Krsna Apartments,
50, Halls Road, Egmore,
Chennai 600 008, Tamilnadu, India.
Phone: +91-44-28190032, 42052900.
Email: ijpp_iap@rediffmail.com

Official Journal of the Indian Academy of Pediatrics
A quarterly medical journal committed to practical
pediatric problems and management update

For office use
Ref. No.
Cash / DD for Rs.
DD No.
Receipt No. & Date

Enter
Subscription
for

ONE year

TEN years

Name ....

Address ....

....

City ....State........ ....

Pin .... Phone (R) .... (O)...

Mobile .... Email ....

Designation .... Qualification...

I am enclosing a DD No. …………….. dated ……………… drawn on ………..……..............

favoring **Indian Journal of Practical Pediatrics** for Rs……………

Signature

Subscription rate

Individual	Annual	Rs.400/-	Send your subscription, only by crossed demand draft, drawn in favour of **INDIAN JOURNAL OF PRACTICAL PEDIATRICS**, payable at **Chennai** and mail to **Dr. K. NENDUNCHELIAN,** Editor-in-Chief, 1A, Block II, Krsna Apartments, 50, Halls Road, Egmore, Chennai 600 008, Tamilnadu, India.
	Ten Years	Rs.4000/-	
Institution	Annual	Rs.500/-	
	Ten Years	Rs.5000/-	
Foreign	Annual	US $ 60/-	

TOXICOLOGY

TOXICOLOGY

Indian Academy of Pediatrics

Kailash Darshan, Kennedy Bridge, Mumbai - 400 007.

1A, Block II, Krsna Apartments,
50, Halls Road, Egmore, Chennai 600 008,

1A, Block II, Krsna Apartments,
50, Halls Road, Egmore, Chennai 600 008,