



# INDIAN JOURNAL OF PRACTICAL PEDIATRICS



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Editor-in-Chief

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Executive Editor

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## FROM THE EDITOR'S DESK

Topic of interest for the fourth issue of IJPP for the year 2008 is "Procedures in pediatric practice".

Procedures can be diagnostic or therapeutic in nature. Knowing how exactly the procedure is to be carried out is more important. An improper technique will lead on to error in the management, reduce the chance of recovery and increase the morbidity of the child. To gain experience and expertise in a particular procedure one should search and read literature extensively. This is not always possible for everybody to go through this tedious exercise. In these situations, it will be easy if we get the first hand information from a person who has the knowledge and expertise in the field. Bringing out an issue dedicated to pediatric procedures is one such attempt to fulfill the needs of clinicians.

Before carrying out the procedure certain initial requirements are to be satisfied. The first and foremost is counseling about the procedure to the parents and the patient if they are old enough to understand. This is one step which is most often overlooked. The counseling should include the need for the procedure, whether diagnostic or therapeutic, sedation planned, complication if any expected and time and place of the procedure. This will make the responsibility of informed consent easy. Next step is to organize the needed instruments, monitoring equipments, container for the sample collection and the drugs for sedation and analgesia. Success of the procedure depends on ideal positioning, restraining the patient, adequate sedation and analgesia wherever indicated. Time taken for procedure should be shorter and specimen

collected in appropriate containers should be transported to the laboratory without any delay. Some post procedure requirements like lying down with head low position after lumbar puncture, etc to be adhered to. In some situations post procedure counseling also equally mandatory eg. post test counseling for positive and negative HIV screening. Being methodical in all stages starting from deciding about the indication to completion, ensures the success of the procedure.

The procedures covered here are selected in such a way that they are of practical importance for a practicing pediatrician in his day to day practice. Most of the procedures discussed in the issue are of therapeutic importance and few may be diagnostic as well as therapeutic eg. abdominal paracentesis. Articles are written in a simple, lucid manner which are contributed by experts in their respective fields. I am sure that this issue will enable the readers to be confident enough to carry out the procedures by themselves without seeking help of experts. Apart from articles on pediatric procedures, there are two more articles of general interest. First one is on "Human papillomavirus burden and vaccine" which is a vaccine targeting prevention of cervical cancer. Second general article deals with approach to "Gynecomastia", a problem mostly of adolescents. Under "Radiologist talks to you" column "Neural tube defects" is covered and "Common skin infestations in children" is covered under dermatology series. This issue includes two interesting Case studies too.

**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

#### 1<sup>st</sup> 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

#### 2<sup>nd</sup> Page –

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

#### 3<sup>rd</sup> 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) G l o s s y 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.

### 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.

### 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.

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## PROCEDURES

### INTUBATION, SUCTIONING AND TRACHEOSTOMY

**\* Meera Ramakrishnan**

**Abstract:** *Evaluation and management of any critical patient starts with assessing and stabilizing the airway. Pediatric airway differs from that of the adult airway and needs the operator to be familiar with these differences. In most situations orotracheal intubation is the safest and the easiest method of securing the airway. Pre-oxygenation and suctioning are important aspects of airway management. In children with altered sensorium the tongue often falls back and occludes the airway. This can be relieved by placing the patient in a sniffing position and by gentle jaw thrust. Secretions have to be suctioned to allow free passage of air. It is important to use a large blunt suction catheter capable of removing particulate matter from the oropharynx. Intubation can be facilitated by appropriately sedating and paralyzing the patient. Prior to this, however the difficulty of the airway has to be assessed so as to avoid unnecessary failures. Pediatric tracheostomy is extremely difficult and when performed in an emergency situation is associated with high mortality.*

**Key words:** *Intubation, oropharynx, tracheostomy, suction, laryngoscope blade, endotracheal tubes, cricoid cartilage, mandible.*

### INTUBATION

Airway management is one of the most important and integral skills that the emergency room (ER) physician needs to have. Airway stabilization takes precedence over all else in any emergency. Ororotracheal intubation is the preferred method for securing the airway in most critical situations. It requires the presence of skilled personnel and equipment. Airway management starts with careful assessment. Methodical management avoids unnecessary surprises and reduces mortality. This article goes over common techniques that can be used to facilitate appropriate management of the pediatric airway.

#### **Equipment and technique used in intubation <sup>1</sup>**

**Large suction catheter :** It is advisable to have two suction devices and catheters at the bedside of a patient needing intubation. One can be a portable device and another one wall mounted. The suction unit should be able to generate a vacuum of about 300mmHg when the tube is clamped. In addition to the tonsil suction tip that can be used for oropharyngeal suction, appropriate sized flexible suction catheters for the endotracheal tubes should also be present. Often just repositioning the head to prevent the tongue from falling back and suctioning the oropharynx is all that is needed to convert a partially occluded airway to a stable airway.

**Ambu bag and mask :** The mask should be chosen such that it covers the mouth and nose but not go over the eyes or extend beyond the ramus of the mandible. The bag used can be either

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an anesthesia bag or the self inflating bag. Disconnection of the oxygen source is easily recognizable with anesthesia bag while the latter is easier to use. The bag has to be connected to an oxygen source such that at least 10-12 liters of oxygen is provided. This ensures the delivery of more than 95% oxygen. While ventilating the child with bag and mask, care should be taken that the fingers that encircle the mask do not press into the sub mental area. The head should be maintained in the sniffing position, the thumb and index finger should press down on the mask and remainder of fingers should be on the mandible. The bags are available in neonatal, pediatric and adult sizes and the bag that is appropriate for the child's age should be used.

**Laryngoscopes and blade:** Either curved or straight blades can be used. In general straight blades are used for children younger than 1 year of age. Curved blades are used for older children. The size of the blade used should at least cover the length from the angle of the mouth to the ear

lobe. While using a straight blade the epiglottis is lifted up. With a curved blade the blade is advanced up to the vallecula and then the scope is lifted up such that the epiglottis with the cords drops down and is visualized by the operator.

**Endotracheal tubes:** The approximate size of the tube is calculated using the formula, (age in years/4) + 4 for uncuffed tubes and (age in years/4) + 3 for cuffed tubes. Tubes which are one size smaller and one size larger should also be available. The depth of insertion of the orotracheal tube in centimeter is calculated by the formula (age in years/2) + 12 or internal diameter of the endotracheal tube x 3. In general, uncuffed tubes are used in children up to the age of 8 years as the cricoid cartilage acts as the natural cuff in these children. The anatomic differences in pediatric airway and their implications in intubation are described in Table 1.

**Nasogastric tubes:** Appropriate size should be kept ready to decompress the stomach.

**Table 1. Anatomic differences in pediatric airway-implications in intubation <sup>2</sup>**

Differences	Implications
Relatively larger tongue, which can obstruct the airway	Most common cause of airway obstruction  May necessitate better head positioning or use of airway adjunct (oropharyngeal [OP] or nasopharyngeal [NP] airway)  Nasopharyngeal airway is contraindicated in the presence of basilar skull fracture.
Epiglottis is floppy and more omega shaped	Necessitates use of a straight blade in a young child. This however is operator dependent.
Larynx more cephalad and anterior	More difficult to visualize the cords; may need to get lower than the patient and look up at 45-degree angle or greater while intubating. A shoulder roll rather than a head roll will help.
Cricoid ring is the narrowest portion of the airway	uncuffed tubes are used in children up to 8 years of age. Numerous studies have however shown that it is safe to use cuffed tubes in younger children if needed.



Tapes to secure the airway, airway adjuncts such as oral and nasal airway should be kept ready. Laryngeal mask airway (LMA) is especially useful in case of a difficult airway. End tidal carbon dioxide (ETCO<sub>2</sub>) detector is very useful to confirm successful intubation especially if the airway is difficult. An extra set of batteries should be available.

### **Rapid sequence intubation**

In an emergency a patient is assumed to have a full stomach. Hence the risk of aspiration of stomach contents during bag and mask ventilation is high. In these situations rapid sequence intubation is performed. For this the patient is pre-oxygenated using high flow oxygen with the face mask. This enables the denitrogenation of functional residual capacity (FRC). Nitrogen is replaced by oxygen. Following this, medications are given to facilitate intubation.

There is a choice of several sedatives and neuromuscular blocking agents and hence the physician has to be familiar with their use and the side effects of the same. A list of drugs with certain caveats to their use is given below (Table 2).

Atropine is used as a premedication to avoid bradycardia especially in children younger than

8 years of age and it also helps to reduce secretions. If the patient is hypertensive as can happen in a patient with traumatic brain injury propofol or pentobarb is used for intubation. In patients where increased ICP is anticipated, lidocaine is used in a dose of 1mg/kg. It takes one minute for lidocaine to work and hence it would be the first drug to be administered in situations of increased ICP. Most of the patients have respiratory problems as well and hence are able to tolerate only modified rapid sequence intubation. The most commonly used combination in our emergency room is atropine + Fentanyl + midazolam + vecuronium. Vecuronium is used in a dose of 0.3mg/kg because it is faster acting in this dose and works similar to rapid sequence intubation. Once sedation is started it is important to provide cricoid pressure until the ET tube position is confirmed.

### **Monitoring during intubation**

Continuous ECG recording

Continuous oxygen saturation

Blood pressure every 5 minutes

Document carbon-di-oxide presence by way of ETCO<sub>2</sub> monitor whenever feasible

**Table 2. Sedatives and neuromuscular blocking agents**

MEDICATIONS	DOSE	IMPLICATIONS
Fentanyl	1-3mcg/kg	Bradycardia, hypotension in patients with shock
Midazolam	0.1-0.2mg/kg	Hypotension in patients with shock Can be used in situations of increased ICP (intracranial pressure) and in seizures.
Pentobarbitone	5mg/kg	Severe hypotension in patients with shock Can be used in situation of increased ICP and in seizures
Propofol	1-3mg/kg	Severe hypotension in patients with shock. Can be used in situations of increased ICP and in seizures
Vecuronium	0.1-0.3mg/kg	Does not cause hypotension or change in heart rate.



## Difficult airway assessment<sup>1</sup>

One has to anticipate difficult intubation by appropriate examination. It is prudent to believe that it may be difficult to even bag mask ventilate a patient with a difficult airway and hence avoid paralysis and even long acting sedatives in such patients. The extent of difficulty can be predicted by performing the following examinations.

## Oropharyngeal examination

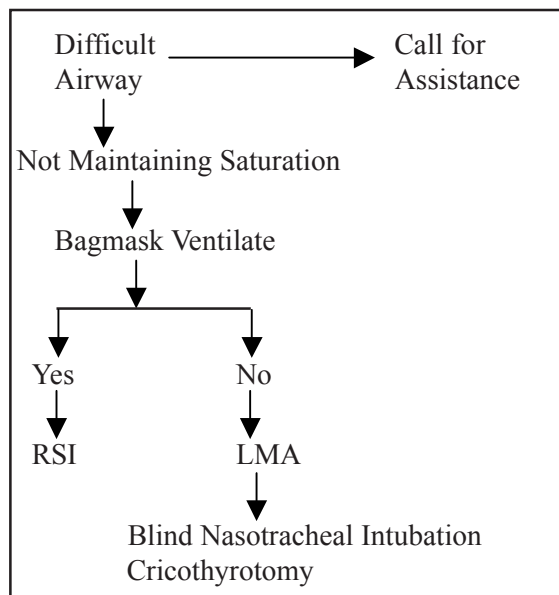
This examination consists of asking the patient to open the mouth wide. The difficulty is predicted by determining the difficulty in visualizing the faucial pillars, soft palate and the uvula. The degree is classified from I –IV with I being the easiest and IV being the most difficult. This however requires that the patient is conscious and cooperative and hence is not very practical in pediatric emergencies. A child with high arched palate, micrognathia, macroglossia, glossoptosis, etc are all to be considered to have difficult airway as it may be difficult to get the tongue out of the way to visualize the glottis.

**Atlanto- Axial mobility:** It is usual to be able to obtain a 35 degree range of motion at the neck. Patients with neck injuries, Down's syndrome, ankylosing spondylitis, etc are patients with potentially difficult airway as it is difficult to obtain this mobility.

**Thyro mental distance:** The distance between the anterior ramus of the mandible and the hyoid, with atlanto- axial extension represents the potential space that is available into which the tongue and the soft tissues can be compressed into to enable visualization of the glottis. It should be at least two finger breadth in children. In bigger children and adults it should be about 6cm for laryngoscopy to be easy.

When a potentially difficult airway is identified it is essential not to paralyze until

ability to bag mask ventilate can be documented. This means rapid sequence intubation cannot be used. Alternative options should be kept ready should the intubation be unsuccessful. The American Association of Anesthesiologists uses the following algorithm for a difficult airway (Fig.1).



**Fig.1. Algorithm for difficult airway intubation**

(Adapted from Marx: Rosen's Emergency Medicine: Concepts and Clinical Practice, 6<sup>th</sup> Edn.)

## SUCTIONING

Secretions can block the airway and may increase the work of breathing. Suctioning consists of removing these secretions by applying vacuum pressure through tubing to the affected part of the body.

Secretions can cause hypoxia, hypercarbia and can increase work of breathing by increasing the resistance of the airway. Suctioning can be done to both upper airway and to the lower airway.

## Pharyngeal suctioning

Suctioning the upper airway (oropharynx) is done to remove secretions which can be large particulate matter such as blood clots and vomitus. It is hence better to use large non collapsible tube such as rigid tonsillar or Yankauer suction catheter. Care should be taken to avoid stimulating the back of the throat to prevent the gag reflex.

Suctioning of the nasopharynx has to be gentle to prevent trauma to the mucosa. In a patient with upper airway problems a nasopharyngeal tube may be placed. This prevents the tongue from falling back and also serves as a conduit for repeated suctioning without traumatizing the mucosa.

Suctioning of the lower airway up to the level of the carina needs the presence of either the endotracheal tube or a tracheostomy tube. Below the level of the carina one has to suction with a flexible bronchoscope and requires skilled personnel.

## Endotracheal suctioning<sup>3</sup>

This is the most common suctioning that is done and the focus will be limited to the same. The endotracheal tube suctioning (ET tube) can be done either by disconnecting from the ventilator and bagging between suction attempts or by the in line suction method. The latter is recommended when the ventilator settings are high, such as PEEP >10, FiO<sub>2</sub> >60%, mean airway pressure (MAP)>20. It is also recommended when there is significant hemodynamic instability especially during ventilator disconnections. Studies have failed to show any difference in the incidence of ventilator associated pneumonia between either group.

## Technique

Prior to suctioning it is important to set the maximum pressure to be used. This differs for

different age groups. For infants the pressure to be used should be set at -60 to -80. For older children it can be set at -80 to -120. The rule of thumb is to use a catheter that is smaller than twice the inner diameter of the tube- i.e. one multiplies the inner diameter of the tube by 2 and then use the next smaller catheter. This is done to prevent the development of atelectasis and hypoxia that can occur while suctioning large lung volumes.

Pass the suction catheter into the ET tube till it goes no further, and then gently pull it out by a centimeter before applying the suction pressure. Withdraw the catheter in a rotatory fashion to remove the secretions along the wall of the ET tube. It is a sterile procedure and to limit the chances of ventilator associated pneumonia (VAP) it is important to suction the oropharynx prior to the suctioning of the endotracheal tube. A different sterile catheter is then used to enter the ET tube. Each suction attempt should not exceed 10 seconds. To limit VAP it is better to avoid routine irrigation of the ET tube prior to suctioning. If the secretions are tenacious then it is reasonable to irrigate with saline or 2% sodium bicarbonate. It is important to never suction on a predetermined protocol

## Indications for suctioning

a) Presence of visible secretions, b) Coarse breath sounds with features suggestive of secretions, c) Increase in peak airway pressure in a child on volume control mode of ventilation or decreased tidal volume in a child on pressure control mode of ventilation and d) Ventilator graphics suggesting the presence of secretions.

## Monitoring while suctioning

The following parameters have to be monitored during and after suctioning: Pulse rate, oxygen saturation, color, breath sounds, quantity and color of the sputum, effectiveness of the cough and change in the ventilator parameters

## Complications of suctioning

Hypoxemia, trauma, bronchospasm especially in an asthmatic, increase in intracranial pressure, infection, hemodynamic instability, arrhythmias and cardiac arrest are the complications related to endotracheal suctioning.

## TRACHEOSTOMY

In children tracheostomy is very difficult to perform in an emergency. It is easier and safer to perform needle cricothyrotomy. The cricothyroid membrane extends between the inferior edge of the thyroid cartilage to the cricoid cartilage. If it is not possible to bag mask ventilate or intubate the child then the next attempt should be to maintain oxygenation and ventilation by ventilating with a laryngeal mask airway. Should this also fail then the needle cricothyrotomy is done using a 14 gauge needle which is directed caudad at the cricothyroid membrane. The patient's neck is kept extended using a neck roll. The position is confirmed by aspirating air. The adaptor of the 3mm endotracheal tube is connected to the 14 gauge catheter and the adaptor is connected to the resuscitation bag. If a cricothyrotomy set is available then Seldinger technique is used. A guide wire is passed through the catheter. The pathway is dilated and then a cricotracheostomy tube is placed through which oxygenation and ventilation can be performed.

### Emergency tracheostomy<sup>4</sup>

It is best to have a person with surgical skills perform tracheostomy. Pediatric tracheostomy is difficult to perform and is associated with high mortality. The neck is hyperextended by placement of a shoulder roll. It is best a second person holds the child's chin to stabilize the tissues and to keep the neck hyperextended. The neck is prepared and draped in the usual fashion

but the face should be left uncovered. The thyroid and cricoid cartilages are then identified by palpation. Important landmarks such as the thyroid and cricoid cartilages, suprasternal notch are identified. Local lidocaine is used at the proposed skin incision. The skin incision is made one fingerbreadth above the suprasternal notch. A vertical skin incision is made and is carried through the subcutaneous tissues. The fascia of the strap muscles is grasped on each side of the midline with hemostats. The fascia is lifted, divided with scissors in the midline. The trachea is again palpated to ensure its location. Retractors can be used to gently retract the strap muscles laterally. The thyroid gland can be retracted if necessary. Rarely does the thyroid isthmus need to be divided in a child. If this is necessary, the isthmus should be clamped, divided and suture ligated. A vertical tracheal incision is made in the midline of the second, third, and the fourth tracheal rings. No cartilage should be removed. The tracheostomy tube is inserted after applying anterolateral traction on the stay sutures that are placed on either sides of the incision. The tube is held in place while the shoulder roll is removed. The chest is auscultated for bilateral equal breath sounds. The neck is then slightly flexed and the tracheostomy ties are secured around the neck allowing for one finger to pass underneath the ties. The stay sutures are then secured to the neck. A chest x-ray should be obtained post-operatively to ensure proper placement of the tracheostomy tube.

### Points to Remember

- *Rapid sequence intubation (RSI) requires denitrogenation of the FRC with oxygen. Patient is not bag mask ventilated during RSI. Prior to RSI it is important to assess the difficulty of the airway and obtain history using the mnemonic AMPLE (Allergies, Medications, Past history, Last*

*meal, Events leading to the current episode).*

- *It is essential to be able to bag mask ventilate effectively. This skill is more important than even intubation.*

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## NEWS AND NOTES

### DR. JC PATEL BIRTH CENTENARY CELEBRATIONS

**International Conference of Iron Deficiency,**

**Mount Abu, Rajasthan**

**December 4-8, 2008**

#### **Contact**

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### **Fellowships in Pediatric Nephrology – 2009**

Applications are invited for the three fellowships in pediatric Nephrology for year 2009; Shalini Rakesh fellowship, Dr. Pravin V. Mehta fellowship and Indian Society of Pediatric Nephrology fellowship. The applicant should be a postgraduate in Pediatrics and below 45 years old. Those working on a permanent position in a hospital will be preferred. The trainee would spend 3 to 4 months at a center recognized for training in pediatric nephrology in the country. A training grant will be provided.

Application forms may be obtained from Dr. Pankaj Hari, Honorary Secretary, Indian Society of Pediatric Nephrology, Department of Pediatrics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029. Email: pankajhari@hotmail.com. The last date of sending the completed application is 31 November 2008

## PROCEDURES

### HEMATO-ONCOLOGIC PROCEDURES

*\* Poonam Patil*

**Abstract:** *Pediatric hemato oncologic procedures are specialized procedures which should be performed by trained personnel. Children are very sensitive to pain and unlikely to cooperate for procedures. Anesthesia techniques in children undergoing short painful procedures will allow greater cooperation and rapid recovery without side effects. Handling of chemotherapy agents, their mode of administration, side effects and management techniques should be well known to the treating physician.*

**Key words:** *Children, Procedures, Hematology and Oncology.*

Pediatric hemato-oncologic procedures are specialized procedures which should be performed by trained personnel. The most commonly performed procedures in hematology, oncology include bone marrow aspiration and biopsy, fine needle aspiration cytology, intrathecal chemotherapy. This article describes these procedures.

#### BONE MARROW ASPIRATION

Bone marrow aspiration is drawing of the liquid content of bone marrow which is similar to blood in appearance. Biopsy is sampling the solid portion of bone marrow. Often both the procedures are done together in succession.

---

\* Consultant Medical Oncologist,  
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#### Indications

The indications are diagnosis, staging and monitoring therapy in primary diseases of bone marrow like anemias, leukemias, lymphomas, myeloma, myelofibrosis or secondary involvement of bone marrow like neuroblastoma, myeloproliferative disorders, storage disorders and metastatic nonhemato-poietic malignancies.

#### Contraindications

Infection at biopsy site, Thrombocytopenia, however is not an absolute contraindication.

#### Studies performed

Bone marrow smear examination, cytogenetics, flow cytometry, molecular genetics and bacterial and fungal culture are carried out depending on the clinical diagnosis.

#### Check list before procedure

- a) Confirm need of bone marrow testing.
- b) Obtain informed written consent for procedure from the parent or guardian.
- c) See if aspiration or biopsy or both are required. In lymphomas, a bone marrow biopsy may be required from different sites for staging purposes.

#### Site selection

The sites from where the bone marrow sampling can be done are as follows: a) Posterior superior iliac spine is the safest site. Both aspiration and biopsy can be performed. b) Anterior iliac crest - both aspiration and biopsy can be performed. c) sternum is generally not recommended in children, may be used in

adolescents. Needle can be advanced only upto 5 mm (core biopsy should not be performed from the sterum), and d) Tibial tuberosity is the preferred site in infants.

### **Procedure of aspiration**

As it is a painful procedure, it is recommended to perform the procedure under a short sedation. The child is placed in lateral decubitus with upper leg flexed and lower leg straight. Left lateral decubitus is a preferred position. Wear sterile gloves. Clean the site identified with povidone iodine scrub. Drape the site with a sterile towel with a central hole. Give IV sedation and local anesthesia at the local site. Infiltrate the skin and the soft tissue up to the periosteum with approximately 5 ml of a local anesthetic agent such as 1% Xylocaine.

Take a bone marrow needle with stylet (Jamshidi needle is most commonly used). Adjust the position of the guard to the required depth. This is especially critical in sternal aspiration to avoid mediastinal injury. Insert the needle through the skin into the bone with clockwise - counterclockwise movements till the needle is fixed in the bone. Withdraw the stylet and attach a 2 cc syringe to it and aspirate the contents. The amount of aspirate depends on the studies to be done. Adequacy of aspirate is checked on site by presence of marrow particles in the aspirate. If it is a dry tap, the procedure can be repeated.

**Dry tap :** True dry tap is seen in myelofibrosis, carcinomatous infiltration of marrow, aplastic anemia and sometimes in leukemias.

### **BONE MARROW BIOPSY**

For bone marrow trephine biopsy, use the same skin puncture site. Introduce the bone marrow set assembly as for aspiration. Once the needle is fixed in bone, take the stylet out and introduce the outer needle into the bone marrow,

advancing with clockwise and counterclockwise movements further inside to a depth of approximately 1.5 to 2 cm. Rotate the needle inside both ways to have a good core of marrow material in the hollow of the needle. Withdraw the needle and take the marrow core out of the needle with the help of probe provided with the set. Apply firm pressure to the biopsy site till hemostasis is achieved and then apply a dressing on the site.

A hematopathology technician who is trained in the technique should process the bone marrow sample immediately by making smear preparations on glass slides and avoiding dilution with blood. Imprint or touch smears are also made on glass slides. These are especially helpful if the aspirate is a dry tap.

### **Complications**

Excessive bleeding or a hematoma may occur, particularly in those with low platelet count or those taking aspirin or anticoagulants, such as warfarin. Breaking of needles within the bone, which may cause infection or bleeding is an uncommon complication. A rare complication of sternal puncture is injury to a great vessel or the heart leading to fatal hemorrhage. Rarely, if tibial tuberosity is the chosen site for marrow biopsy, damage to the growing epiphyseal plate can occur resulting in limb shortening. Complications related to IV sedation, such as an allergic reaction, nausea or arrhythmias should be watched for and the child should be accordingly monitored.

### **FINE NEEDLE ASPIRATION CYTOLOGY**

It is the procedure of aspirating cellular material from a lump or mass by a syringe. It allows evaluation of the cellular detail morphologically. The procedure is safe, accurate, rapid and cost effective. Patient acceptance is high and complications are minimal.



## Indications

The procedure is indicated in the diagnosis of malignancy, infections and benign tumors.

## Studies performed

Cytology, cell block, cytogenetics, molecular diagnostics done with flow cytometry or immunohistochemistry and culture and sensitivity are the various tests that can be performed depending on the clinical situation.

## Procedure

The aspirate can be done in palpable external masses and nodes or under ultrasound or CT guidance for deep seated masses. Patient is positioned to allow best digital palpation of the mass. The skin over the mass is cleaned with povidone iodine. Under aseptic precautions, the mass is fixed by the left hand and local anesthesia is given at the external site. A 10 cc syringe with a 23 gauge needle is preferred to thicker gauge needles, as this reduces the chances of contamination of the specimen with blood. The mass is entered with the needle and multiple passes are made within the mass with negative pressure applied with the syringe, without bringing the needle-syringe assembly out of the skin. The to and from motion of the needle tip should be at least 1 cm. This dislodges the cells and allows a better quality of aspirate. In case of internal, non palpable masses, an ultrasound guided or CT guided aspiration can be performed.

Use of commercially available syringe holder device, makes the procedure easy to carry out. Using such devices allows a high degree of suction and control of movement of the needle-syringe assembly with one hand and the second hand can be used to stabilize the tumor. Watch carefully for some material coming into the hub of needle. Stop at that time and gently release the negative pressure. Only then pull the needle out of the skin. The negative pressure in the

syringe must be completely released before withdrawing the needle out of the skin to avoid aspirating the cellular material from the needle into the syringe, which then cannot be easily expelled onto the slide.

Expel the aspirate on to glass slides and make smears. Fix them immediately in 95% ethyl alcohol. In cases of cystic lesions, the aspirated fluid will come into the syringe. This aspirated material can be centrifuged and the cellular cytospin material can be used in paraffin blocks as with any other biopsy specimen. The microscopic evaluation, however may not be complete as these are individual cells without their background stroma.

## Precautions

Aspirate can be diluted with blood, or normal tissue, making sample inconclusive. Visceral bleed can occur, hence watch out for signs of internal bleed such as tachycardia, hypotension and pallor. Aspiration from lung lesion can cause a pneumothorax, which needs to be managed accordingly.

## INTRATHECAL CHEMOTHERAPY

Intrathecal chemotherapy is given for treatment of CNS invasion or to protect the CNS against infiltration by malignant cells. It is most often used in leukemias to protect the CNS against leukemic cell infiltration (CNS prophylaxis). It is also used in cases of documented CNS infiltration. Intrathecal chemotherapy must only be administered by a doctor adequately trained in the performance of this procedure. Obtain informed consent.

## Indications

For treatment of meningeal infiltration by malignant cells or for CNS prophylaxis. Most common indication in children is in treatment of leukemias.



## Drugs given

Methotrexate, cytosine arabinoside or hydrocortisone, given singly or in combination.

## Procedure

The procedure can be performed under local anesthesia or a short sedation. Place the child in lateral decubitus as for lumbar puncture. Check the diagnosis and the dose of prescribed drugs. Under aseptic precautions, load the desired amount of drugs into syringes. Always use a separate syringe for each drug and use the smallest possible syringe for the required volume. Generally, only small volumes are given intrathecally. Perform a lumbar puncture under sterile conditions and check for free flow of CSF. Let some CSF out and collect the sample for laboratory analysis as indicated. Under strict aseptic precautions, inject the chemotherapy medications one by one into the intrathecal space. Ensure that the needle does not move during the changing of syringes. It is especially important that the child should be adequately sedated to avoid needle dislodgement during the injection. Once the injection is complete, withdraw the needle. Place a small dressing on the puncture site. Turn the child supine after the procedure and the child should remain supine for approximately an hour as for routine lumbar puncture.

## Precautions

Check the drugs to be given. Some drugs when accidentally given intrathecally can prove

to be fatal. Check the platelet count and coagulation profile. Do not perform a lumbar puncture if platelet counts are low or if coagulation profile is abnormal. The needle must be in the intrathecal space and free flow of CSF should be obtained to ensure the same. Extradural injection of chemotherapeutic drugs must be avoided.

## Points to Remember

- *Pediatric hemato oncology procedures should be done by trained personnel.*
- *Children should be sedated adequately during the procedure and be given appropriate care after the procedure.*
- *Interpretation of results should be correlated with clinical condition of the child.*

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## NEWS AND NOTES

### JHARKHAND PEDICON 2008, Dhanbad

November 22-23, 2008

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## PROCEDURES

### THORACIC PROCEDURES

\* **Vidya S**  
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***Abstract:** Most of the respiratory diseases can be diagnosed clinically with a reasonable amount of accuracy. There is yet another set of cases which require investigations to confirm our clinical diagnosis. Among the invasive modalities three commonly practiced thoracic procedures are the pleural tap, intercostal drainage and lung tap, some of which are of therapeutic benefit as well.*

**Key words:** *Pleural tap, Intercostal drainage, Lung tap.*

Three thoracic procedures which are commonly done are pleural tap (thoracocentesis), intercostal drainage and lung tap. These investigations help in the diagnosis and management of common respiratory problems in children like pneumonia, empyema, pleural effusion, pneumothorax and tuberculosis. Informed written consent should be taken after briefing the parents regarding the procedure and pain-relief measures.

#### PLEURAL TAP (THORACOCENTESIS)

It refers to the procedure of insertion of a needle into the pleural space for removal of fluid or air from the pleural cavity.

**Instruments :** Antiseptic solution, gauze pieces, cotton swabs, towels, disposable syringes 5ml, 10ml, 20ml, disposable needle size 24G, 21G, 18G, 16G, lignocaine 1%, disposable three way stopcock, extension tubing, bowls.

#### Indications

1. **Diagnostic:** To know the type of pleural fluid whether serous, purulent, blood or chyle, transudate or exudate, tuberculous or non-tuberculous.
2. **Therapeutic:** To drain a large pleural effusion causing respiratory embarrassment, as a temporary measure in tension pneumothorax and for instillation of drugs especially in pleural malignancy.

**Contraindications:** Local skin infection, coagulopathy.

#### Procedure

**Site:** Ideally using USG guidance, the needle is introduced at the point of maximum dullness on percussion in pleural effusion or using chest x-ray.

**Position:** Ideally, sitting position or lateral decubitus position.

**Technique:** Proper sterilisation should be done with spirit and povidone iodine over an area from anterior axillary line to spine and from axilla to the lower ribs. 1% lignocaine is infiltrated at the upper border of the lower rib in the space chosen. A wide bore needle is connected to one-way of the three-way stopcock and opposite to it a syringe is attached and arranged in such a

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way that there is a single track between the needle, stopcock and syringe. The needle is then inserted into the chest by finding the intercostal space and stepping over the lower rib with care (Fig.1). Slight negative pressure is applied to the syringe so that fluid is aspirated immediately as the needle enters the pleural space. Fluid is to be aspirated slowly and steadily. As fluid is removed, lung expands and this causes cough. This indicates that volume of fluid remaining in the chest is very small and aspiration should be stopped to prevent lung injury. Needle is then withdrawn and the puncture site is covered with a tincture benzoin seal. A sterile gauze is put over it and micropore tape is applied over it pinching the skin edges together.

### Post – procedure management

Child is then kept nil per oral for 2 hours with temperature, pulse, respiratory monitoring and watched for hemoptysis, dyspnoea, cyanosis, tachycardia, bradycardia and hypotension even though such eventualities are rare. Post tap chest x-ray is taken if the child has any set back.

### Complications

Pneumothorax, hemothorax, infection, hemoperitoneum, unilateral pulmonary oedema, hypoproteinemia, air embolism.

### INTERCOSTAL DRAINAGE

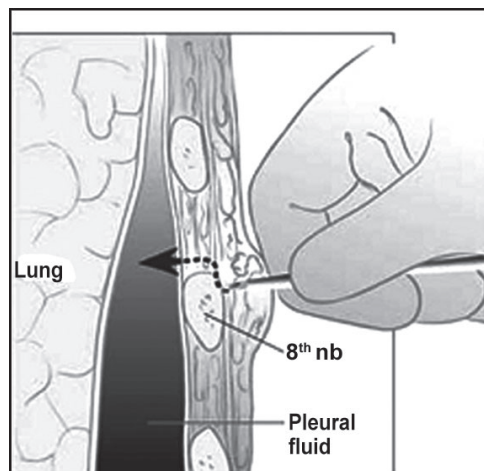
It is a procedure for drainage of the pleural space by means of an intercostal catheter allowing negative intrathoracic pressure to be re-established leading to lung re-expansion.

### Indications

Empyema, pyopneumothorax, hemothorax, pneumothorax.

### Equipments

Mallecot's catheter, chest tubes, Argyll type thoracic catheters with radio-opaque marker line, intercostal catheters (Newborn 8-12 FG, infant



**Fig.1. Pleural tap**

12-16 FG, child 16-24 FG, adolescent 20-32 FG), scalpel blade, needle holder, straight artery forceps, curved and straight scissors, clamps, under water seal drain system, 1% lignocaine and 1 in 10,000 adrenaline, gauze, cotton balls, suture materials, black silk or nylon with appropriate needle size.

### Position

**For basal insertion:** Sitting position at 45° with arm of the same side placed above the head or lateral decubitus position with affected side upwards and arms above the head.

**For apical insertion:** Patient is placed in supine position with head end of the bed elevated through 45-60° and both arms placed by the side of the body. Apical insertion of ICD is for pneumothorax (2<sup>nd</sup> space mid clavicular) and basal insertion for empyema and pyopneumothorax (5<sup>th</sup>-7<sup>th</sup> space in mid axillary line).

### Anaesthesia

Local anaesthesia.

### Procedure

The child must be on continuous cardiac and pulse oximetry monitoring. Pre-procedure chest Xray should be taken unless it is an emergency.

The area is then prepared surgically and anaesthetised. The skin parallel to the upper border of the lower rib in the chosen intercostal space is incised down to fascia and blunt dissection continued until the pleura is reached. A trocar and cannula, held perpendicular to the skin is inserted through the parietal pleura. A loss of resistance is felt when pleura is pierced. A gush of fluid or hiss of air on removal of trocar indicates correct position. The outer open end of the cannula is covered immediately to prevent air from entering the pleural space. The largest possible catheter is passed through the cannula into pleural space. One has to ensure that all the fenestrae in the catheter are well in pleural space. The catheter is then attached to under water seal drain below the patient's chest level. The drain is then anchored and the wound sutured. Instead of using trocar and cannula and catheter, a Mallecot's catheter can be used for ICD. A Mallecot's catheter is stretched over a straight artery forceps and inserted through the parietal pleura. The outer end of Mallecot's catheter is connected to under water seal drain system and anchored in the same way as above.

### **Post-procedure care**

Airway, breathing and circulation have to be reassessed and intercostal catheter functioning is ensured. Chest x-ray has to be taken to confirm proper placement of the tube.

### **Dos and don'ts of chest drainage**

Avoid clamping the drain other than at the time of changing the ICD bag as it can result in a tension pneumothorax. Always keep drain below the level of the patient or else the drain contents can siphon back into the chest. If disconnection occurs re-connect and ask patient to cough. When there is a block in the tube, remove it and reinsert a new tube at the same site. Observe for post expansion pulmonary edema.

### **Removal**

The drain can be removed as soon as it has served its purpose i.e. when there is a) no bubbling of air for 24 hours, b) no bubbling on coughing and c) when rate of fluid accumulation is less than 30ml/day. Drain has to be slowly removed by one person while other ties the suture. A gauze swab with collodion suspension is placed on the wound immediately after purse string suture has been tied. Post procedure chest x-ray to exclude pneumothorax is needed.

### **Complications**

Local incision site infection, pneumonia, osteomyelitis; bleeding from laceration of intercostal vessels, local wound hematoma, organ injury (lung, spleen, liver, stomach, diaphragm), inappropriate placement of the tube causing air leak, blocked drainage, subcutaneous emphysema.

### **LUNG TAP**

**Synonyms:** Lung aspiration, puncture, suction.

Percutaneous transthoracic lung aspiration is the most acceptable and uncontaminated means of describing microbiology of pneumonic lung.

### **Equipments**

Oxygen supply, chest drain insertion kit.

### **Indications**

Persistent pneumonia, chest x-ray infiltrates of undetermined cause, especially those unresponsive to therapy in immunocompromised patients who are susceptible to unusual organisms.

### **Procedure**

The identified area is sterilized and anaesthetised. A 20-25 gauge needle is attached

to a 10 ml syringe containing sterile saline and inserted through the inferior aspect of an intercostal space in the area of interest. The area of interest is determined by chest x-ray in two planes to localize the consolidation which is refined by clinical examination by selecting the area of most pronounced bronchial breathing or with the help of chest computed tomography films if available. A safe location is the 7<sup>th</sup> intercostal space in midscapular line for lower lobe puncture. While patient withholds respiration, needle is pushed rapidly 2-3 cm into the consolidated lung and 2 ml saline is injected and reaspirated quickly and the needle is withdrawn. The aspirate (lung juice, fluid or pulmonary exudate) is expelled by in and out movements of syringe plunger after needle tip is immersed in broth. The lung aspirate is sent for Gram stain, culture and sensitivity, AFB staining and culture for mycobacteria.

### Post procedure care

Vitals are monitored for 24-48 hrs. Chest x-ray is repeated 1 hour after the procedure.

### Advantages

Enhances sensitivity in etiological studies of pneumonia, obtains live organisms for susceptibility testing, evaluation of unresponsive or complex pneumonia, detection of disease specific end points in vaccine efficacy trials and is useful in nosocomial superinfection in immunocompromised and suspected tuberculosis.

### Complications

Pneumothorax, empyema, minimal hemothysis, air embolism, pulmonary hemorrhage, pleural pain (rare).

### Points to Remember

- *The three common thoracic procedures are pleural tap, intercostal drainage and lung tap.*
- *These procedures are quite safe and useful when done under adequate precautions.*
- *They yield tissue diagnosis and some of them are of therapeutic benefit also.*

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## PROCEDURES

### NEUROLOGICAL PROCEDURES

**\* Anandam R**  
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**Abstract :** *Three important neurological procedures which are routinely done by a clinician are lumbar puncture, subdural and ventricular taps. The preparation of patients, technique, indications and contraindications of these procedures are discussed.*

**Keywords :** *Lumbar puncture, Subdural tap, Ventricular tap, Children.*

#### LUMBAR PUNCTURE

Examination of cerebrospinal fluid (CSF) is essential in pediatric practice to confirm the diagnosis of certain diseases of brain like meningitis, subarachnoid hemorrhage, and encephalitis and is often helpful in evaluation of demyelinating, degenerative and collagen vascular diseases involving brain and spinal cord. As the procedure is very simple it should be practiced by all internists and pediatricians.

Before doing lumbar puncture (LP), the procedure should be explained to the parents and consent must be obtained. A general physical examination with recording of vital signs is done prior to the procedure. A baseline neurological assesment including features of increased intra

cranial pressure should be carried out. LP kit containing sterile towels for draping, gloves. LP needle with stylet and 3 bottles for collection of CSF should be kept ready by the staff nurse. 22 gauge needle is used for older children. For small children pediatric LP needles of size, 24 gauge with stylets may be used.

Physician should scrub his hands with soap and water and should use an antiseptic and wear gown, gloves, cap and mask.

#### Preparation of the patient

This is extremely important. Skin is thoroughly cleaned with povidone and 70% alcohol. The site should be covered by a sterile towel exposing only the area of lumbar puncture. Local anesthetic lignocaine 1% in a dose of 0.4 ml per kg may be used. In very small babies and in new born, local anaesthetic can be avoided.

The ideal site for LP would be the inter vertebral space between L3-L4 or L4-L5 as normally the spinal cord ends at L2 level. This L<sub>3</sub> which is identified by drawing a horizontal line between the two anterior superior iliac spines and by choosing this site we will not be injuring the cord.

The child is made to lie in lateral recumbent position with the back at the edge and perpendicular to examination cot. The neck and legs of the patients are flexed by an assistant to widen the intervertebral spaces. Local anesthetic is infiltrated into skin and subcutaneous plane using a 25 G needle. Keep the left thumb on the spinous process above the interspace. Introduce

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the needle with stylet midway between the two spinous processes almost perpendicular to the surface directed slightly in the cephalad direction. A "Pop" is felt as the needle penetrates the dura and enters the subarachnoid space. The stylet is removed a few times to see whether CSF is coming out. If CSF is under pressure, flow can be controlled with stylet. Never aspirate CSF with a syringe.

CSF is collected in 3 or more bottles for biochemical investigations (sugar and protein), cell count, grams stain, AFB stain and culture. CSF is also collected for viral studies for detection of some specific antigens, and in investigation of metabolic diseases.

After collection of CSF, the stylet is replaced. Then the needle withdrawn along with stylet and local dressing is applied. After LP, child should lie down in a slightly head low position for four hours. This helps in reducing the post procedural headache.

### **Contraindications**

Contraindications for performing LP include (1) Raised intracranial pressure due to suspected mass lesion of the brain and spinal cord which may lead to transtentorial herniation and some times sudden death due to respiratory arrest. So all children being subjected for lumbar puncture should be examined for papilloedema, before LP. CT scan head may be done to rule out mass lesions if indicated, (2) In critically ill and moribund patients, (3) Severe skin infection at the site of LP and (4) Thrombocytopenia with bleeding tendency it may be deferred.

### **Normal CSF**

Normal CSF has the color of water. Cloudy CSF results from an elevated white blood cells (WBC) or red blood cells (RBC) count. Normal CSF contains cells up to 5 lymphocytes and newborn may have as many as 15 cells per cubic mm.

Polymorpho nuclear (PMN) cells are almost always abnormal in children, 1-2 PMN/cubic mm may be within normal limits in a neonate. An elevated PMN count suggests pyogenic meningitis. CSF lymphocytosis indicates viral, tuberculous or fungal meningitis, it may also occur in demyelinating diseases and collagen vascular disease.

Gram stain of the CSF is essential to diagnose bacterial meningitis. An acid fast stain or India ink preparation is used if tuberculous or fungal meningitis is suspected.

CSF is kept in appropriate culture media depending upon the clinical findings. CSF may also be examined for specific bacterial antigens by latex agglutination tests.

There are no RBCs in normal CSF. Presence of RBCs indicate a traumatic tap or a subarachnoid hemorrhage. Bloody CSF should be centrifuged. If it is traumatic, the supernatant part will be clear but it will be xanthochromic in subarachnoid haemorrhage. Xanthochromia can also occur in hyperbilirubinemia.

Normal CSF protein ranges from 10-40 mg/dl in the child but upto 120 mg/dL can occur in the neonate. The CSF protein falls to the normal childhood range by 3 months of age. Protein may be elevated in many conditions including infections, immunologic, vascular and degenerative diseases and in brain and spinal cord tumors. CSF Immunoglobulin G (IgG) represents approximately 10% of the total protein and is elevated in SSPE, in Acute Disseminated Encephalomyelitis (ADEM), and in multiple sclerosis. In Guillain Barre Syndrome the classic picture of albumino cytologic dissociation is seen. CSF glucose content is about 60% of the blood glucose in normal child. Low sugar levels are seen in meningitis, especially in bacterial and tuberculous meningitis. Blood glucose estimation should be done just prior to the LP.



CSF may also be examined for lactate, pyruvate and amino acids in metabolic diseases

## **VENTRICULAR PUNCTURE AND SUBDURAL TAPPING**

These procedures may be done for diagnostic or therapeutic purposes. The former is done not only to sample CSF but also to reduce the intracranial pressure if it is elevated, paediatricians may be called upon to do a ventricular puncture in the emergency room if a child with a VP shunt malfunction comes in a state of altered consciousness. The latter may have to be done to sample the post meningitic collections in the subdural space this is often diagnostic and in some instances therapeutic too.

### **Technique**

**Anesthesia:** General anesthesia is not required for these procedures. Nor will sedation be needed. However, the child should be gently but firmly restrained. The best way to achieve this is to wrap the child in a sheet, blanket or towel – this will be needed only if the child is uncooperative or restless. The nurse or the assistant holds the child and the head is kept immobilised by placing the palms on either side of the face/ malar eminence. It is important to keep the head in the midline and the sagittal plane vertical so the landmarks are not missed.

**Preparation:** Shaving the hair has been advocated but the author feels it is really not necessary. But there can be no compromise in the preparation. The entry point and a wide area surrounding it has to be prepared. After handwashing and wearing sterile gloves, the area is painted 4 - 5 times with povidine iodine.

The area is then draped. Since the root of the nose is an important landmark the nurse or assistant keeps his/ her finger at that site under the drape. One can look at the finger through the drape or even feel it if need be.

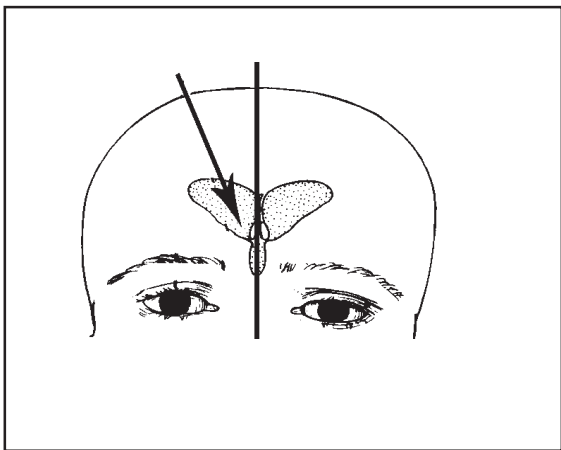
It has to be underscored here that a strict aseptic technique has to be used.

### **Ventricular puncture**

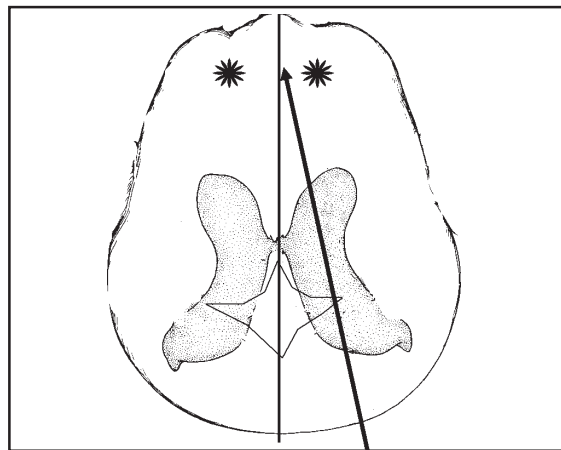
This can be done easily with a lumbar puncture needle. It is recommended a fine needle be used (22/ 23 g) unless the CSF is expected to be bloody or thick and purulent. The approach is usually on the right side. The needle is placed at the lateral angle of the anterior fontanelle perpendicular to the skin. The hub of the needle is angled laterally till the tip points to the root of the nose (Figs.1 & 2). The needle is gently inserted through the skin. This is done gently without using undue pressure. The skin and dura are penetrated and then the cortex. The “pop” feeling one gets when doing a lumbar puncture will not be felt here. This has to be borne in mind all the time. The only way to ascertain if the ventricle has been entered is to remove the stylette and check for CSF flow. In children very often the ventricle will be entered at a distance of less than 5 -6 cm from the skin. If the attempt is unsuccessful two further attempts may be made one directed towards the ipsilateral inner canthus and if still unsuccessful another towards the contralateral inner canthus. If all three attempts are unsuccessful the procedure has to be stopped or the help of a more experienced person has to be sought. CSF should not be vigorously aspirated with a syringe but be allowed to flow out into the receptacle. Aspiration may set up a bleeding or choroid plexus may be injured. Very gentle aspiration may be tried once if the CSF is thick and does not flow out.

After the samples are obtained the area is cleaned and a small dressing is applied.

If the fontanelle is closed and a ventricular tap is mandatory then the child is referred to a neurosurgeon who will place a burrhole and obtain CSF through that.



**Fig. 1. Shows the trajectory in the coronal view. The vertical line represents the midline and passes through the root of the nose. The trajectory when the needle is directed towards the inner canthus can be easily determined.**



**Fig. 2. Shows as the trajectory as the child is lying. The vertical line representing the midline passes through the root of the nose. The stars represent the inner canthus on the right and left sides.**

### **Subdural tapping**

Preparation is the same as for LP. It is indicated in suspected cases of subdural effusion in meningitis. The technique is basically the same as described above with few important differences. Site for subdural tap is the junction of the lateral aspect of anterior fontanelle and coronal suture. Ensure that it is 2-3 cm lateral to the midline to avoid injury to the sagittal sinus. Shave the scalp, clean the area and drape. Bring the head to the end of the table and firmly restrain by holding on to the sides of the head. Since the collections on either side are often in communication, tapping on one side will suffice. The hub of the needle (20 gauge with stylet) is angled well lateral and advanced about 0.5cm. The needle need not be directed towards the root of the nose or the inner canthus. After insertion of the needle through the skin, pulling the scalp posteriorly may prevent fluid leakage after the procedure. The technique of sampling are as described before. Again it has to be emphasised

that aspiration is best avoided. Fluid collected is sent for relevant investigations. Head is kept slightly elevated with a pillow after the procedure.

### **Points to Remember**

- *Lumbar puncture is a simple but important procedure.*
- *Every clinician has to be familiar and skillful in performing the procedure.*
- *Fundus examinations to rule out papilledema is essential prior to doing lumbar puncture.*
- *Ventricular puncture is a life saving procedure in a child with VP shunt malfunctions.*

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## PROCEDURES

### RENAL PROCEDURES

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**Abstract:** *Renal procedures are important for a correct diagnosis and for adequate management of childhood renal ailments. Certain procedures require radiological and surgical assistance. The physician limits his responsibility to suprapubic aspiration of urine, bladder catheterization, renal biopsy, gaining vascular access and initiating dialysis. Suprapubic aspiration of urine is used for urine sampling in difficult situations and used as an emergency procedure in acute urethral obstruction. In the new born it forms a part of new born sepsis screening. Renal biopsy has become an important extension of clinical practice of nephrology. Changes in the technique of doing biopsy with improved needles under ultrasonographic guidance in an operation theatre under short anesthesia have made it easy with very few complications. Renal histopathology is utilized for the diagnosis of glomerular, tubulointerstitial and small blood vessel diseases. Adequate pre-biopsy evaluation and careful immediate post-biopsy monitoring will reduce the complications. Hematuria is the main complication seen following renal biopsy. Arterial and venous catheterisation are needed in acute situations and arteriovenous fistula*

*creation is done for hemodialysis in chronic renal failure. Peritoneal dialysis and hemodialysis (different types) are used in children with renal ailments.*

**Keywords:** *Renal procedure, Suprapubic aspiration, Urethral catheterisation, Vascular access, Renal biopsy, Peritoneal dialysis.*

Management of children with any illness involves careful and complete history taking, physical examination, investigations, arriving at a diagnosis, management and follow-up. The physician will be called upon to do certain procedures in the process of investigations and management. Certain procedures may need more expertise and surgeons or urologist may be needed. In renal medicine, procedures can be classified into medical, surgical and radiological. The surgical procedures can be summarized as endoscopic surgeries for urinary tract obstruction, renal stone diseases, flexible and rigid ureterorenoscopies, percutaneous nephrolithotomy, laparoscopic ureterolithotomy, cystostomy and open renal biopsies via classical, sub-costal approach or lumbar approach. The radiologist is responsible for ultrasonography, intravenous pyelography, micturating cystourethrography, radionuclide studies, computed tomography, magnetic resonance imaging, arteriography, venography and renal arterial angioplasty. This article will discuss the procedures that are within the ambit of the physician. The physician limits his responsibility to 1) suprapubic aspiration of urine, 2) bladder catheterization, 3) renal biopsy, 4) vascular access and 5) dialysis.

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## **SUPRAPUBIC ASPIRATION OF URINE**

It is a simple procedure that can be done by the physician. The indication is collection of urine for culture from very small infant, unconscious children, uncooperative male or female child where clean catch method for collection of urine for culture is difficult and usually contaminated or in children with urinary tract outlet anomalies. It can be used as an emergency procedure for letting out urine in acute urethral obstruction. The procedure involves sterilizing an area of 3 cms in diameter, 1.5-2.0 cms above the pubic symphysis. After assurance to the parents and consent, appropriate restraint of the child, a 5 cc syringe with a 20 gauge needle can be plunged perpendicularly for about 2-4 cms depending upon the subcutaneous fat in the child. During the procedure, constant negative pressure is applied so that the urine is aspirated into the syringe as soon as the bladder is entered. Before commencement of the procedure one should ensure that bladder is full as confirmed by percussion. Ultrasound guided aspiration would be ideal. But with experience and practice this can be done without ultrasound guidance. If one or two attempts have failed it is better to have an ultrasound guided aspiration. No complications are generally observed. Occasionally, a few drops of blood may be passed along with the urine after the procedure.

## **URETHRAL CATHETERIZATION**

For the important question "What size of catheter can you safely use in children?" the ideal answer can be that there is no definite size to recommend in general. The rule followed is that the catheter that will negotiate the urethral meatus will be the ideal size for that age. Prior to catheterization the glans is pinched between the index finger and thumb and when the meatus opens out, the size of catheter can be assessed.

There are however some guidelines that are helpful for a safe catheterization.

1. Foley catheters have a bulb at the end which is sometimes difficult to negotiate through the urethral meatus. If this difficulty is encountered, a smaller size catheter should be chosen. If one persists with a larger size catheter, it can result in injury to the meatus. Meatal stenosis and scarring are potential complications.
2. Foley catheters are available in French sizes 6, 8, 10, 12, 14 and beyond. Catheters up to size 10 have a stylet to make the catheter stiff and easy to push. Unfortunately the stylet also makes the catheter tip very stiff and this stiff tip can easily cause a false passage if pushed hard into the urethra of an infant. To avoid this, following introduction, the stylet is withdrawn slightly. This makes the tip flexible and the catheter can now be negotiated with ease.
3. In a situation where the catheter does not pass, it may be helpful for another person to put a finger in the rectum and guide the catheter. Often the catheter will glide into the bladder with this maneuver.
4. Once urine is dripping, the catheter should not be pushed in any further as it may coil and make a knot. This is very common with feeding tubes used for catheterisation. Occasionally in this situation, the bladder has to be opened to retrieve the knotted catheter.
5. Foley catheters normally have only a silastic coating on them. In the urethra this tends to wear off and the rubber in the Foley can cause stricture, if the catheter is left in-situ for a long time. If it is necessary to keep a Foley catheter for longer than 5 days, a silastic catheter is preferred. These fully

siliconised catheters are available in all sizes and can be kept safely for as long as 3-6 months.

6. In newborns, there is no need to open out the prepuce orifice prior to catheterization. This is because the act of opening out the prepuce orifice will cause tears and subsequent scarring necessitating circumcision later. Secondly, there is practically no space between the prepuce orifice and the urethral meatus. A catheter passed into the prepuce will directly go into the urethra.
7. In a newborn less than 3 kg in weight, a 6 Fr feeding tube or Foley catheter is a good first choice. If larger than 3.5 kg an 8 Fr feeding tube or Foley will be accepted with ease.
8. When inflating the Foley bulb, only 3 ml of water must be used. Larger quantities tend to, a) elevate the tip of the Foley thus making it inefficient to drain small quantities of urine at the bladder base and b) cause bladder spasms which is shown by perianal itching and a sensation of incomplete defecation which can be very distressing.
9. There are plenty of Foley catheters available in the market today and quality is a real concern. Before inserting a catheter the ability of the balloon to inflate and deflate must be checked.
10. In preterm and small neonates appropriate feeding tubes can be used. This can be lubricated with an antibiotic cream or a sterile local anesthetic cream. If cultures are to be done, this lubrication should be avoided.

If all the above concerns are carefully considered at the time of urinary catheterization, the procedure will be successful in most of the instances.

## **RENAL BIOPSY**

Over the course of many years, the methodology of renal biopsy has changed remarkably towards its safer usage with almost negligible complications. Iversen and Brun introduced percutaneous renal biopsy technique in 1951 and in 1954 several modifications were made by Kark and Muerche<sup>1,2</sup>. This procedure now has become an important extension of clinical practice of nephrology. From the initial days of Vim Silverman needle usage to its present form of automated devices of biopsy gun, the procedure has become simple with minimal side effects. Tru-cut needle method has replaced Vim Silverman needle in between only to be changed over to automated biopsy gun method which is now popularly used. Histopathology of the kidney biopsy sample is utilized for the diagnosis of glomerular, tubulointerstitial and small blood vessel diseases. It is useful in the evaluation of children with proteinuria, glomerular hematuria, small vessel disease and renal manifestations of systemic diseases and in acute renal failure where natural course is not followed and hence renal biopsy becomes very important.

### **Indications for renal biopsy**

It differs among different renal diseases and it is better that we classify them as per the group of renal diseases (Table 1).<sup>1,3,4</sup>

### **Contraindications for percutaneous renal biopsy**

Conditions like uncontrolled bleeding diathesis, severe refractory hypertension and congenital anomalies like solitary native kidney and horse shoe kidney are considered as absolute contraindications. If a child has severe renal failure it is better to dialyse the child to stabilize the renal function before biopsy. Skin infections at the biopsy site or the presence of arterial

**Table 1. Common indications for renal biopsy**

<p><b>Acute nephritic syndrome</b></p> <p>Macroscopic hematuria beyond 4-6 weeks</p> <p>Persistent hypertension beyond 6 weeks</p> <p>Persistent nephrotic proteinuria (if present) for more than 2 weeks especially with renal failure</p> <p>Presenting with or progressing to severe renal failure</p> <p>Persistent mild-to-moderate renal failure</p> <p>Persistent hypocomplementemia beyond 8 weeks or absence of it at the onset</p> <p>Associated systemic features like arthralgia, arthritis, skin rashes and recurrent abdominal pain</p>	<p>Nephrotic children with acute renal failure (as mentioned above)</p> <p>Presenting with evidence of vasculitis</p> <p>Rapidly progressive glomerulonephritis</p> <p>Occurring with evidence of systemic diseases</p> <p>When the cause is not clear and with persistence of renal failure</p>
<p><b>Nephrotic syndrome</b></p> <p>At the onset of nephrotic syndrome (NS)</p> <ul style="list-style-type: none"> <li>• Age &lt; 1 year and &gt; 12 years</li> <li>• Persistent microscopic/gross hematuria, low C3</li> <li>• Sustained hypertension</li> <li>• Renal failure not attributable to hypovolemia</li> <li>• Suspected secondary causes of NS</li> </ul> <p>After initial treatment of the disease</p> <ul style="list-style-type: none"> <li>• Steroid resistant NS</li> <li>• Steroid dependent NS / frequently relapsing NS as per need</li> <li>• Before cytotoxic therapy</li> </ul>	<p><b>Isolated persistent hematuria</b></p> <p>When glomerular hematuria is suspected</p> <ul style="list-style-type: none"> <li>• After ruling out hypercalciurea</li> <li>• After ruling out familial or urological disease</li> </ul>
<p><b>Acute renal failure</b></p> <p>Associated with acute nephritic syndrome (as mentioned above)</p>	<p><b>Chronic renal failure</b></p> <p>To determine the risk of recurrence on eventual renal transplant if etiology of CRF is uncertain</p> <p><b>Systemic diseases</b></p> <p>To assess activity and chronicity of the renal involvement in diseases like HUS, HSP and SLE</p> <p><b>Follow-up diseases</b></p> <p>To document renal toxicity of cytotoxic therapy</p> <ul style="list-style-type: none"> <li>• In glomerulonephritis</li> <li>• In transplantation follow-up</li> </ul> <p><b>Transplantation</b></p> <p>Suspected acute rejection</p> <p>Drug toxicity</p> <p>Detecting the development of de novo or recurrent disease</p> <p>Chronic rejection with important therapeutic implications</p>



aneurysms over the biopsy site are considered as relative contraindications. It is always difficult to do a biopsy in a kidney with hydronephrosis or a large cyst. A child on drugs like anti-platelet adhesive agents or anticoagulants, is a relative contraindication. If needed, they can be discontinued for a sufficient time of 3-4 days before biopsy and restarted after adequate time. Open renal biopsy procedure is a safe alternative to percutaneous renal biopsy in high-risk patients to reduce the complications<sup>1,4</sup>.

### **Evaluation before biopsy**

A detailed history including personal and family history of bleeding diathesis should be taken and a good physical examination is mandatory. Laboratory evaluation should include complete blood count with platelet count, coagulation profile, urinalysis, blood grouping and Rh- typing in addition to blood urea and serum creatinine estimation. Pre-biopsy ultrasound evaluation of kidney to assess anatomic abnormalities and to confirm the presence of both the kidneys will reduce the risk of failures and complications. This will also help us to pinpoint the renal biopsy as the cause for post biopsy sonographic changes if any. Coagulation dysfunction if present must be managed before doing biopsy.

### **Biopsy procedure**

Now-a-days biopsy gun with automated system is used with needles (16 G or 18 G) for doing the renal biopsy without much complications. A written informed consent is obtained and a detailed discussion with the parents regarding the procedure, the need for it and the complications will reduce the post biopsy confusions and allay the apprehensions in their mind. Solids can be given 4-6 hours before the procedure. Intravenous fluid during the period of starvation is given as per the need of the child. Kidney biopsy is done under aseptic precautions

in a sterile operation theater with ultrasound guidance. The anesthetist uses IV ketamine (1-2mg/kg) or propofol (1-2 mg.kg) for short anesthesia<sup>1</sup>. Biopsy is done after putting the child in a prone position with sandbag or rolled sheet under the abdomen. The usual biopsy site is the angle made by the lower edge of 12<sup>th</sup> rib and the lateral border of sacrospinalis. Alternatively the site can be the junction of medial 2/3<sup>rd</sup> and lateral 1/3<sup>rd</sup> of the horizontal line joining the tip of the 12<sup>th</sup> rib with the vertebral column<sup>1</sup>. The lower pole, often left kidney, is confirmed with ultrasound guidance and marked on the skin. Biopsy site is prepared, draped and locally anesthetised. A 20-gauge spinal needle is used to localize the depth from the surface of the skin as it moves with respiration upon penetrating the capsule of the lower pole. The distance can also be confirmed by ultrasound. The biopsy needle is then passed under real time ultrasound guidance and biopsy specimen is taken<sup>1</sup>. Usually two cores of tissue are necessary for optimum evaluation. One bit is sent in a bottle containing the transport alcoholic Bouin solution for light microscopic studies and the other one is kept in a small plastic cover and kept inside a flask with ice for immunofluorescent studies and sent to the histopathology department. For electron microscopic evaluation, gluteraldehyde solution is used as the transport medium.

Once the procedure is over a firm dressing is applied over the biopsy site and the child is kept in full bed rest in supine position for 24 hours. Monitoring of vital signs like pulse, temperature, respiration and blood pressure is done periodically, every 15 minutes for 4 hrs, then every hour for next 20 hrs<sup>1</sup>. Parents should be instructed to collect the urine samples serially for monitoring hematuria. If child develops pallor, hemoglobin concentration is tested and steps are taken if there is a sudden fall in hematocrit. Child may be discharged the next day if no complications are documented.



## Complications

Over the years incidence of complications have come down. Hematuria is one of the complications commonly seen in most of the children and it resolves spontaneously in 48 hours<sup>1</sup>. This is usually very mild, warranting no blood transfusion. But in 5%-10% of children, the hematuria may be gross and may take longer time to resolve. Perinephric hematoma can occur in < 2% and it can be identified by gross hematuria, flank pain and drop in hematocrit. Usually it can be identified by a good ultrasound but few may need even plain CT scanning. Arterio-venous fistula formation can occur in a small number of patients and is usually identified by angiography or by Doppler studies. Most of them are asymptomatic and surgical intervention is indicated only if it is large and the child is symptomatic. Majority respond to adequate conservative therapy. A repeat ultrasound after 24-48 hours of biopsy may be needed if child is not comfortable or if the parents are apprehensive.

## VASCULAR ACCESS

Provision of dialysis requires reliable, repeated access to the patient's circulation that is capable of providing adequate blood flow. The vascular access may be needed for an acute clinical indication as in acute renal failure, acute poisoning and rarely in chronic kidney disease for maintenance hemodialysis.

### Acute vascular access

Procedures like arterial and venous catheterization are done in an intensive care set up as per need. Subclavian and internal jugular venous catheters have become the preferred temporary vascular accesses. Modern catheters are placed for emergency dialysis and are useful until a more permanent access is ready. The flexible, silicon-based catheters, which are

tunnelled subcutaneously and sutured in place, may be left for extended periods. Less commonly, femoral vein catheterization is used as a temporary access for up to 48 hours. It is not suitable for ambulatory patients and carries a significant risk of infection. Possible complications include bleeding, infections, thrombosis or stenosis of the vessel, pneumothorax and air embolism. Temporary dialysis catheters should not be used as routine intravenous lines, since breaks in sterile technique greatly increase the risk of infection and catheter thrombosis. Catheters obstructed by clot can be successfully cleared using thrombolytic agents (streptokinase, urokinase).

### Chronic vascular access

**Arteriovenous fistula:** The arteriovenous fistula (AVF) is the preferred vascular access for chronic hemodialysis and may last for years. When progression to end stage renal disease (ESRD) is imminent, an effort should be made to spare the non-dominant arm from venipuncture and arterial puncture. Fistulae are created by the surgical anastomosis of artery and vein, most commonly the radial artery to the cephalic vein. After approximately one month, the vein enlarges, matures (arterializes) and is then used for the two needle sites (to and from the dialyzer). Examination of the functioning AVF reveals a palpable pulsation and a bruit by auscultation.

**Arteriovenous grafts:** When the patient's own vessels are inadequate to create an AVF, native, bovine or preferably polytetrafluoroethylene grafts (PTFE, ie Gore-Tex) can be used to form a conduit from artery to vein. These procedures are generally done by the vascular surgeon. However, many nephrologists have developed expertise to do the above two procedures. Antibiotic prophylaxis for synthetic grafts should precede procedures for which bacteremia is anticipated.

## DIALYSIS

### Extracorporeal dialysis

Dialysis or renal replacement therapy (RRT) have great utility in the ICU setting. Indications for RRT can be simplified to the mnemonic 'AEIOU': Acidosis, electrolyte disorders, drug intoxication, volume overload and uremia. Modalities can be classified as a) continuous renal replacement therapies namely slow continuous ultrafiltration, continuous venovenous hemofiltration, continuous venovenous hemodialysis and continuous venovenous hemodiafiltration, b) intermittent renal replacement therapies namely conventional hemodialysis and slow, low efficiency daily dialysis<sup>5</sup>. These procedures are within the purview of the nephrologist.

### Intracorporeal dialysis

This involves two procedures a) Continuous ambulatory peritoneal dialysis (CAPD) useful in chronic kidney diseases as maintenance RRT and b) Acute intermittent peritoneal dialysis.

#### a) Continuous ambulatory peritoneal dialysis (CAPD)

With CAPD, a catheter is surgically implanted into the abdominal wall. Inside the body the tube hangs down into the abdominal cavity. This will drain a cleaning solution called dialysate through the tube 3 or 4 times a day, which carries the toxic waste matters away from the body as the kidneys do. CAPD takes place inside the body using the natural lining of the abdomen, the peritoneum. The peritoneum acts as the dialysis membrane. CAPD is done at home usually 4 times every day. It takes less than 30 minutes each time and is a very simple, painless procedure. Because dialysis is carried out at home, patients must be able and willing to take major responsibility for their own care. Surgeons or nephrologists do this procedure of catheter insertion.

#### b) Acute intermittent peritoneal dialysis

This can be done in the ICU or at the bedside of the patient. This can be done by a pediatrician with training.

**Usefulness :** Peritoneal dialysis (PD) is essentially a substitution therapy and it replaces partially the excretory function and contributes to the maintenance of fluid, electrolyte and acid-base balance of the child. It is a short-term management until the kidney recovers its function in acute renal failure or replaced by a transplanted kidney in chronic renal failure<sup>6</sup>. Peritoneal dialysis is useful to remove whatever is more in the body like urea, creatinine, water, uremic toxins and phosphorous. It replaces whatever is less in the body like sodium, bicarbonate, calcium and glucose.

**Physiology :** The basic principles involved in PD are diffusion, osmosis and solvent drag<sup>6</sup>. Unlike adults, in children with the presence of more peritoneal surface area in relation to the body surface area, it is natural that PD should be twice as efficient in infants as in adults. The mechanism of dialysis includes a) diffusion and b) osmosis between two compartments namely the peritoneal cavity with dialysis fluid and the vascular compartment with plasma separated by the peritoneal membrane. Diffusion takes place from a higher concentration to lower concentration. Substances which are more in the blood like urea, creatinine, potassium or toxins diffuse from the body through peritoneal membrane to the peritoneal cavity. Whereas, substances which are less like bicarbonate or sodium, diffuse from the peritoneal cavity to the blood compartment. This is called solute flux. In osmosis, the hypertonic PD fluid in the peritoneal cavity will draw out plasma water from the vascular compartment of the peritoneum. In this process, various solutes dissolved in the plasma water like urea, creatinine or potassium are also dragged out along with the plasma water.

This is called solvent drag. By increasing the hypertonicity of the PD fluid, we can achieve two things. More fluid can be removed rapidly from the vascular compartment and this is useful in children with congestive cardiac failure, pulmonary oedema and anasarca. Secondly, it rapidly removes urea, creatinine, potassium and uremic toxins, which is important in severe renal failure and in conditions of dyselectrolytemia<sup>6</sup>.

**Types of PD catheters :** Polyurethane catheter is used for acute dialysis. Various sizes are available like infant, pediatric and adult sizes. In intermittent peritoneal dialysis, a catheter is inserted for every dialysis, which may extend for a few days but generally not more than a week. It is preferable not to keep the catheter beyond 24 to 48 hours, as increase in duration increases the possibility of infection. For this reason and to examine whether the renal function is recovering, the catheter is removed and PD is discontinued. If the renal functions do not show recovery, the PD is restarted at a different site using a new catheter or other modalities of renal replacement therapy are started<sup>6</sup>.

**Dialysis fluid :** Usual PD fluid contains dextrose 1.5-1.7g/100 mL and is isotonic. When more fluid has to be removed from the body, hypertonic PD fluid containing 4.5 g/100 mL can be used. Other constituents of PD fluid include sodium 130-140 mEq/L, chloride 100-110 mEq/L, acetate or lactate 35-45mEq/L, magnesium 0.5-1.5mEq/L, calcium 3.0-3.5 mEq/L, contributing to an osmolality of 340-360 mOsm/kg with a pH of 5.0-5.8. Isotonic fluid can be converted into hypertonic fluid by adding 100 mL of 25% dextrose solution to one liter of isotonic PD fluid. Acetate is preferable to lactate because the final pH is in the range of 5.8-6.2, whereas the pH of lactate solution is below 5.4. Secondly, acetate is more effective source of  $\text{HCO}_3^-$  and is metabolized even in lactic acidosis. Thirdly, it is more bacteriostatic.

**Indications for peritoneal dialysis :** Indications differ with conditions. Biochemical indications when the child has renal failure include a serum creatinine of more than 4.0 mg/dL, intractable metabolic acidosis, refractory hyperkalemia and hyponatremia with serum sodium of less than 120 mEq/L. Clinical indications on this background include refractory fluid overload, pulmonary oedema and uncontrollable hypertension. Persistent vomiting, drowsiness and convulsions with no definable cause are considered as indications for PD in renal failure<sup>6</sup>.

**Uses of peritoneal dialysis :** The commonest use of PD is in renal failure, both acute and chronic for the above indications. It is also useful in salicylates, phenobarbitone and phenytoin sodium poisoning. In inborn errors of metabolism with hyperammonia syndrome and in urea cycle defect PD is indicated in the initial stages though continuous renal replacement therapy is the choice in the present day. Other uses of PD are noted in copper sulphate poisoning along with d-penicillamine, hypercalcemia, prophylactic PD in open heart surgeries, Reye syndrome, hyperkalemia in neonates with congenital adrenal hyperplasia and neem oil poisoning in children.

**Procedure :** Written informed consent for PD is obtained from the parents and ideally is started in a sterile room with utmost precautions to prevent sepsis. Explanation about the procedure and the need for it to the parents is very important. Palpate the abdomen for renal mass or other abnormalities. Make sure that the bladder is empty and the colon is not loaded. If the bladder is full and child is not able to void urine, catheterization has to be done. This will avoid injury to the bladder if it is full. Clean the entire anterior abdominal wall with povidine iodine and then with spirit. Cover the abdominal wall with a sterile towel with a centre hole making the patient in a supine position. Infiltrate 3-5 mL of

1% xylocaine to produce 1-2 cm wheal adjacent to the umbilicus, preferably lateral to it. Some prefer a site just below the umbilicus in the midline to avoid injuries to the blood vessels. Fill the peritoneal cavity with peritoneal dialysis fluid with 16G intravenous needle (20-40 mL/kg), so that the intestines move away from the midline. If there is ascites, we can skip this step. Using an 11-size blade, make a stab puncture in the different layers of the abdominal wall until the peritoneal cavity is reached and this has to be done very carefully to avoid accidental slippage of the blade into the abdominal cavity. Through this puncture, pass the PD catheter with stylet. Once the catheter enters the peritoneal cavity, pass the catheter towards the paravertebral gutter caudally until resistance is felt. As the catheter goes down from the abdominal wall inside, remove the stylet there by preventing injury to the viscera. Then connect it to the outer end of the bend connecting tube in the PD set. Next connect the end of the bend connecting tube to PD drip set (commercially available) or to ordinary IV drip set via a three-way adapter. One line is drawn from the PD fluid bottle kept at about one meter above the cot level. This acts as an inlet. One more line is drawn from the three-way adapter to another empty bottle placed below the cot. At the turn of the handle of the adapter, PD fluid can be run in or out. After an appropriate and predetermined exchange time, the PD fluid in the peritoneal cavity is drained. This procedure is very much like that done in exchange transfusions. This ensures closed circuit and less chance of infection. Secure the catheter by suturing the catheter entry site in the skin with silk, close the wound with antiseptic cream, gauze and adhesive plaster. In newborns and infants keep a nasogastric tube in situ. This prevents aspiration of gastric contents into the lungs during the filling phase of the abdomen. Use isotonic fluid, 20-40 mL/kg per exchange. Hypertonic fluid is

used in special situations as already mentioned. Even if hypertonic PD fluid has to be used, many prefer alternate hypertonic and isotonic fluid exchanges and not continuous hypertonic fluid exchanges alone. Add heparin 125 IU/L of PD fluid to avoid clogging of the lines. Usually potassium is added after 10 exchanges unless child has hypokalemia where 4 mEq of potassium is added to a litre of PD fluid from the beginning. If serum potassium is between 3.5-4.9 mEq/L, then add potassium 3 mEq/L of PD fluid after 10 exchanges. If there is hyperkalemia continue potassium free dialysis until serum potassium level is normalized. Allow the fluid to be in the abdomen for 45-60 minutes and this is known as "dwell time" during which "the exchange" takes place. The PD fluid input will take about 5 minutes. The drain of this fluid (dialysate) after the dwell time will take about 15 minutes. The entire cycle will last for about one hour. By reducing the dwell time by rapid dialysis, more fluid can be removed as in cardiac failure. By increasing the dwell time, more time is given for exchanges to occur thereby facilitating solute clearance like creatinine, uric acid, potassium, etc in conditions like severe renal failure and dyselectrolytemia<sup>6</sup>.

**Complications and management :** Pain shock can be seen in children if the child is not informed of the procedure in advance. It can be minimised by minimal sedation and with the use of local anesthetic agents as mentioned in the procedure. Next problem is the leakage from catheter entry site in the abdominal wall and usually re-suturing will stop it. Rarely, perforation of viscera can occur and hence one should not forcibly push the catheter into the abdominal cavity on entering through the abdominal wall. Failure to remove the stylet simultaneously can also cause it and we have to be careful at this point. Respiratory distress can occur either due to the basic disease causing fluid overload or due to the instilled PD

fluid. We can reduce the quantity of PD fluid to 20 mL/kg/exchange which will definitely reduce the distress. Once the child is relatively better the fluid can be increased to 30 mL and then exchanges with 40 mL/kg can be done for better dialysis. Subcutaneous extravasation can occur if the distal end of the PD catheter is placed with all the openings not fully inside the peritoneal cavity. Ideally the PD catheter should be inserted still deeper and secured properly<sup>6</sup>.

Peritonitis is one of the commonest complications seen with PD. The common organisms encountered include E.coli and species of klebsiella, proteus and pseudomonas. Child can present with abdominal pain, fever, increasing vomiting, tenderness of the abdomen and the draining PD fluid will be cloudy with 50-100 neutrophils/mm<sup>3</sup> on microscopic examination. Micro-organisms can be demonstrated by Grams stain or culture. Parenteral broad-spectrum antibiotics like combination of ampicillin and cloxacilin or amoxicillin and cefotaxime to cover common organisms are given after sending the PD fluid for culture. On getting the antibiogram report, antibiotics can be changed accordingly. In addition intra-peritoneal instillation of ampicillin (250 mg/L of PD fluid) or gentamycin (8 mg/L of PD fluid) is also found useful in some centers. Aseptic precautions with minimal handling and restriction on the entry of visitors to the PD room will definitely reduce this problem. Though PD is a very useful procedure, 0.6 g/kg/day of protein is lost during PD and adequate extra amount of protein intake is needed to maintain protein balance. Failure to modulate protein intake can push the child into malnutrition and the resultant complications.

Hypothermia, hyperglycemia, hypo or hypernatremia, metabolic alkalosis, hypokalemia and hypocalcaemia can occur in children with PD. PD fluid if not warmed can lead to

hypothermia in newborns and small infants. Focusing a lamp on the PD fluid is popular for this purpose. Periodic monitoring of blood glucose is a must especially with a background of diabetes mellitus in the family or in the child. Serum sodium disturbances can also be rarely noted. Metabolic alkalosis can be documented if dialysis is maintained for a very long time for correction of metabolic acidosis. Hypokalemia is mostly iatrogenic when potassium is not added to the PD fluid especially when the child is already hypokalemic and in newborns this can precipitate respiratory paralysis<sup>6</sup>.

Causes of convulsions during PD include hypertension, primary disease like HUS, hypocalcemia, hyponatremia, uremic encephalopathy and dialysis dysequilibrium syndrome (DDS). Following rapid dialysis, extracellular acidosis is corrected but intracellular acidosis persists in the brain cells leading to the formation of idiogenic osmoles causing cerebral edema and convulsions and is known as DDS. Continuation of dialysis and administration of mannitol is the treatment modality. Fortunately DDS is more common in hemodialysis than in peritoneal dialysis.

**Advantages :** Peritoneal dialysis is a safe and simple procedure and it could be started at short notice. There is no need for vascular access, machine, water supply, electricity or technician. Uremic toxins, which are responsible for renal osteodystrophy and peripheral neuritis in CRF, are better removed by PD. The clearance of various materials is better in children since surface area per kg body weight is more as compared to adult. In acute renal failure the mortality with peritoneal dialysis is much less in patients than in patients treated with hemodialysis

**Limitations :** Although extremely effective for volume control and better tolerated in the hemodynamically unstable patient than



hemodialysis, clearance of small molecules may be inadequate in hypercatabolic patients or in patients on total parenteral nutrition receiving large protein loads. In addition, in the hospital setting, there is considerable risk of peritonitis. For these reasons, intermittent peritoneal dialysis is being largely replaced by continuous renal replacement therapy (CRRT) in the management of acute renal failure in ICU setting as well as in children with renal failure and hypercatabolic states<sup>6</sup>.

### Points to Remember

- *Suprapubic aspiration for urine sampling is useful in very young children where midstream urine sampling is difficult*
- *Urethral catheterization becomes simple and easy on following essential guidelines.*
- *Vascular access have become more common in pediatric intensive care and AV fistula creation is needed for longterm hemodialysis.*
- *Renal biopsy with biopty gun under ultrasound guidance using short anesthesia is a relatively safe and useful diagnostic procedure in children.*
- *Peritoneal dialysis is useful in situations of acute renal failure and chronic ambulatory peritoneal dialysis is also gaining importance in chronic renal diseases.*

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### NEWS AND NOTES

The Indian Academy of Pediatrics Committee on Immunization has recently launched its website [www.iapcoi.com](http://www.iapcoi.com) This website provides detailed information on all vaccines, contains an electronic copy of the IAPCOI guidebook on immunization and provides links to recent IAPCOI policy updates and internet resources on immunization. Importantly, it has a question and answer facility where in immunization related queries will be answered by an expert in immunization. Up gradation of the website is in process.

## PROCEDURES

### ABDOMINAL PROCEDURES

\* **Anshu Srivastava**

**Abstract:** *Ascites is a common clinical problem in children and a diagnostic paracentesis should be done at diagnosis and at each hospital admission with ascites. Ascitic fluid should be routinely evaluated for cell count with differential, albumin level, total protein and culture. Serum-ascites albumin gradient (SAAG) is the best single test for classifying ascites into portal hypertensive and non-portal hypertensive causes.*

*Liver biopsy is a very useful diagnostic tool and can be done percutaneously in majority of subjects. Menghini and trucut needle are commonly used in children and choice is largely operator dependent. Ultrasound guided procedure may help reduce complications and should be done in subjects with segmental liver transplant and focal lesions of liver. Knowledge of indications, correct procedural technique and post biopsy monitoring is essential.*

**Keywords:** *Ascites, Paracentesis, Serum ascites albumin gradient, Spontaneous bacterial peritonitis, Percutaneous liver biopsy, Children, Complications.*

### PARACENTESIS

Paracentesis means removal of ascitic fluid from abdomen and is a very useful diagnostic tool for patients with ascites. The indications for

paracentesis include :

#### A. Diagnostic

1. Any child with recent onset ascites to determine the etiology.
2. Pre-existing ascites with suspected spontaneous bacterial peritonitis (SBP). This is suspected clinically when a patient with cirrhosis presents with fever, abdominal pain, worsening hepatic encephalopathy, sepsis or diarrhoea.<sup>1</sup>
3. All subjects with cirrhosis and ascites requiring hospitalisation for ruling out occult spontaneous bacterial peritonitis (SBP).

#### B. Therapeutic

Large volume paracentesis.

#### Contraindications

There are no absolute contraindications for a diagnostic paracentesis. The following points need to be considered before doing a tap.

1. Presence of coagulopathy or decreased platelet count is not a contraindication and routine use of FFP or platelet concentrate is not recommended.<sup>2</sup>
2. One has to be careful in the presence of bowel obstruction or massive organomegaly and in these cases paracentesis is best done with ultrasound guidance to reduce risk of injury.
3. It should not be done through cutaneous infection site, engorged vessel, abdominal wall hematoma or surgical scar.
4. It is relatively contraindicated in the presence of disseminated intravascular coagulation (DIC).

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## Preparation and technique

The following steps need to be followed while doing paracentesis.

- Obtain written consent after explaining procedure and complications to patient and parents.
- Presence of ascites is confirmed by clinical examination and it is ensured that the urinary bladder is empty.
- The patient is asked to lie in supine position with head slightly elevated.
- Skin cleaning and draping is done in standard manner. The person performing the procedure should wash hands and wear gloves.
- There are two sites from which paracentesis is usually done.<sup>3</sup> These are:
  1. Midline, about 2 cm below umbilicus and
  2. Right/left iliac fossa (2-4 cm medial and above anterior superior iliac spine and lateral to rectus sheath). The left side is preferred more than right as the depth of ascitic fluid is deeper than in midline, abdominal wall is thinner here in obese patients and there is no risk of injury to a distended cecum as in the right iliac fossa.
- A 25 gauge, 1.5 inches long needle is used to infiltrate 2% lignocaine in epidermis and deeper tissues along the track, slowly checking by intermittent aspiration to make sure that needle has not penetrated a vascular structure, till parietal peritoneum is reached. Then a metallic 18-22 gauge, 1.5 inches needle is taken with a 10-20 cc syringe attached. Two methods may be used for paracentesis (Fig. 1a and b). In the Z-track method, the cutaneous tissue is pulled down

by 2 cm before making a vertical puncture and after needle withdrawal the cutaneous puncture site goes to its original position. Whereas in the angular insertion method, needle is held at 45 degrees angle when it pierces epidermis, subcutaneous tissue and peritoneal cavity. The aim of both methods is that the skin and peritoneal puncture sites do not overlap preventing leakage of ascitic fluid. A sudden loss of resistance is felt as the needle enters the peritoneal cavity. The syringe is used to aspirate the ascitic fluid. After removal of needle, a sterile occlusive dressing is applied and child is asked to lie on opposite side (in lateral tap) or supine (in midline tap) if tense ascites is present.

## Special precautions

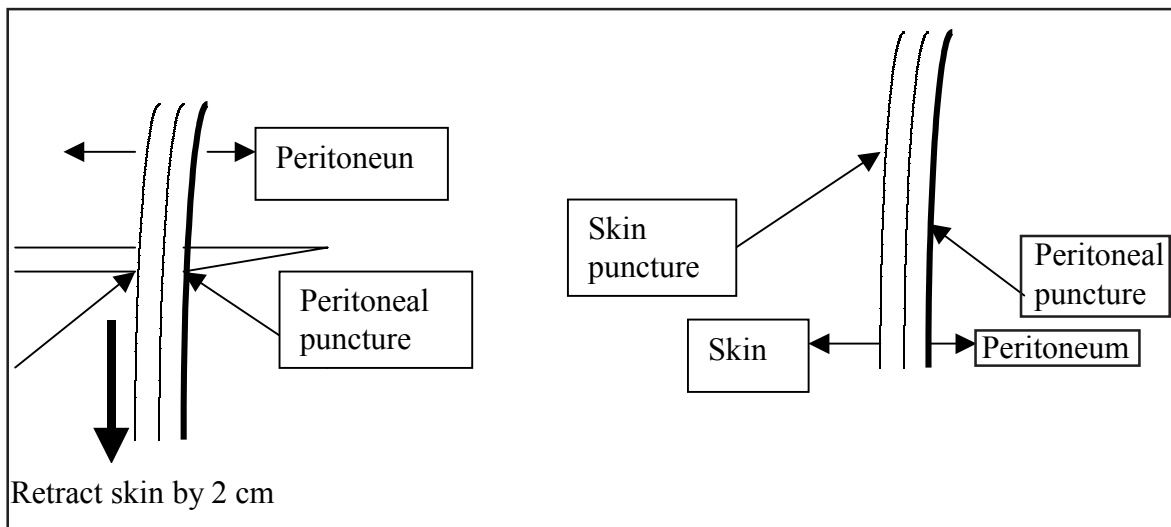
1. The percutaneous site should be marked by ultrasonography if there is presence of less fluid, multiple surgical scars or dilated bowel loops.
2. Sterility has to be maintained throughout the procedure.
3. The tubes for ascitic fluid examination including culture bottles should be available bedside.

## Ascitic fluid analysis

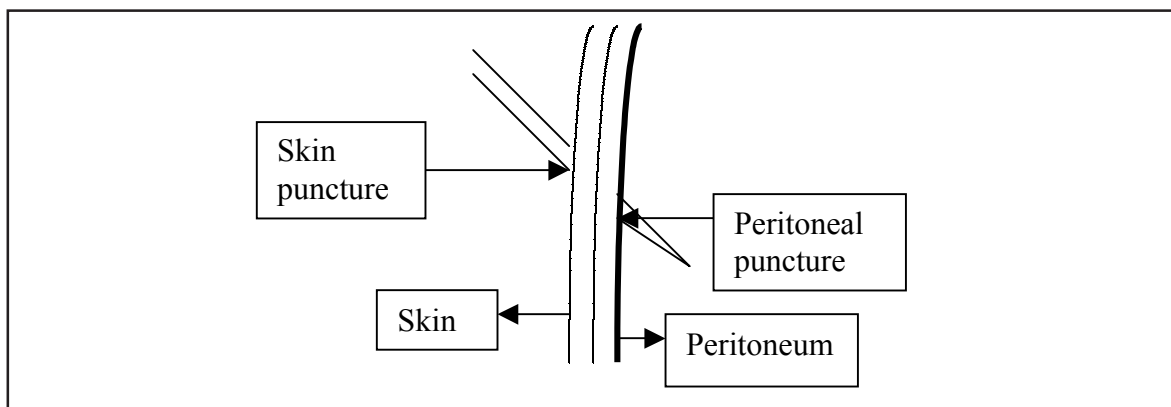
The ascitic fluid is observed for its appearance which may be, clear/straw coloured/turbid/ chylous or bloody as it gives important clues to the diagnosis.

A sample is taken in EDTA tube for total and differential cell count and in a plain vial for total protein/albumin.

Immediate inoculation of ascitic fluid for culture increases the positivity rate of identification of organism in SBP. Anaerobic and aerobic culture bottle should be inoculated with 10 cc of ascitic fluid and incubated for 5-7 days.



**Fig.1a. The Z track technique**



**Fig.1b. The angular insertion technique**

Other tests are done according to the clinical situation and are as follows.<sup>2</sup>

**Amylase:** It is raised in pancreatic ascites (>5 times serum level or >2000 U/L) and in gut perforation.

**Triglyceride:** more than 200 mg/dL is seen in chylous ascites.

**Bilirubin:** The presence of dark brown fluid on ascitic tap is suggestive of bile leak. If the ascitic fluid bilirubin is greater than serum

bilirubin or it is more than 6 mg/dL, it suggests biliary or upper gut perforation.

**Adenosine deaminase (ADA)** is raised in tubercular peritonitis.

**LDH, glucose and gram stain** should be done if secondary peritonitis is suspected and it helps to differentiate it from SBP as discussed later.

**Cytology:** It is mainly indicated when there is suspicion of malignant ascites and multiple samples increase the sensitivity.

Mycobacterial culture (BACTEC) is useful in tubercular ascites.

**Serum ascites albumin gradient (SAAG):** It is obtained by subtracting ascitic fluid albumin from serum albumin. A value of  $>1.1$  g/dL suggests portal hypertension as the cause of ascites and it has a very high diagnostic accuracy.<sup>4</sup> Simultaneous blood and ascitic fluid samples should be taken for measuring albumin levels. High albumin gradient and low albumin gradient should replace the “transudative” and “exudative” classification of ascites.

Currently the ascites is broadly divided into high and low serum-ascites albumin gradient for narrowing the etiological diagnosis as shown in Table 1.

Common causes of failure of paracentesis include:

1. Continuous aspiration during insertion of needle, 2. Rapid insertion and withdrawal of needle before piercing the peritoneum.

### Complications

Although the following complications are described, they are uncommon.

1. Persistent leakage of ascitic fluid, 2. Infection, 3. Abdominal wall hematoma,

4. Hemorrhage due to puncture of inferior epigastric artery, 5. Injury to intra-abdominal organs, 6. Circulatory dysfunction and renal failure after large volume paracentesis.

**Spontaneous bacterial peritonitis (SBP):** It is most commonly seen in children with cirrhosis or nephrotic syndrome with ascites. It is diagnosed if polymorphonuclear (PMN) cells count is more than 250 cells/cu.mm and the ascitic fluid culture is positive in absence of an alternate source of infection. In case of a traumatic tap, 1 PMN should be subtracted for every 250 red cells and 1 WBC for 750 RBCs. The analysis of ascitic fluid helps to differentiate spontaneous and secondary bacterial peritonitis (Table 2).

### Therapeutic paracentesis

Therapeutic paracentesis is also known as large volume paracentesis (LVP) and is done to alleviate respiratory distress or abdominal discomfort in a patient with ascites. It is also done in subjects with refractory ascites not responding to diuretics.

As discussed above, the procedure is done in the same way and the needle is connected to a vacuum bottle with non-collapsible tubing so as to facilitate drainage of large volumes of ascitic fluid. Aspiration of more than 50ml/kg of ascitic

**Table 1. Etiology of ascites according to SAAG**

SAAG $>1.1$ g/dl (s/o portal hypertension)	SAAG $<1.1$ g/dl
Cirrhosis	Tubercular peritonitis
Cardiac ascites	Pancreatic ascites
Budd-Chiari syndrome	Biliary ascites
Portal vein thrombosis	Nephrotic syndrome
Fulminant hepatic failure	Serositis
Myxedema	Peritoneal carcinomatosis
Veno-occlusive disease	Chylous ascites

**Table 2. Differentiation between SBP and secondary peritonitis**

Ascitic fluid	SBP	Secondary peritonitis
Gram stain/culture	Single organism	Multiple organisms
Glucose	>50 mg/dl	<50 mg/dl
LDH	< serum LDH	> serum LDH
Protein	<1 g/dl	> 1 g/dl

fluid at one time in a child is considered as large volume paracentesis.<sup>5</sup> Careful monitoring of vitals and urine output is important after LVP.

### LIVER BIOPSY

Liver biopsy is a very useful diagnostic tool for children with liver disease.

Liver tissue can be obtained by three ways-percutaneous, trans-jugular or laparoscopic. Trans-jugular biopsy is done in special situations where percutaneous biopsy is not feasible e.g. significant ascites and coagulopathy and it requires special skills and is more expensive.

Percutaneous biopsy is the one which is practiced most and will be discussed in this article. It can be done either as a blind procedure or under radiologic guidance (ultrasound or CT). Due to ease of availability, no radiation exposure and less cost ultrasound is preferred over CT guided biopsy. In blind biopsy, the site of biopsy is selected only by clinical examination. US guided procedure can be done in 2 ways, one uses ultrasound for only marking the site of liver biopsy after ensuring that no major vessel or duct will come in the track of the biopsy needle and in other, the entire biopsy procedure is done under continuous ultrasound guidance with the probe in situ.

Both US marked and continuously guided procedures are equally safe. Literature is still not very clear about the need for US guided biopsy

in all cases routinely<sup>6,7</sup>. In one study in 58 children, 25% subjects needed a change in biopsy site determined clinically after ultrasound largely due to risk of other organ or vessel injury<sup>8</sup>. An initial ultrasound is a must in all cases before the procedure to look for any silent focal lesions, significant biliary radical dilatation, size of liver and position of gall bladder so as to minimize the risk of complications. Then the site of biopsy may either be marked by ultrasound just before the procedure or determined clinically. But in patients with focal lesions (targeted biopsy is needed), segmental liver transplant recipients or shrunken liver an ultrasound guided biopsy is always preferred. The choice depends on expertise, personal preference, ease of availability of ultrasound facilities and the clinical scenario. Adequate training of the physician performing the procedure is a must and the physician should always mentally go through the steps of the procedure before performing the biopsy.

Two types of biopsy needles are used for liver biopsy:

a) Aspiration or suction method : Menghini or Jamshidi needle and b) Cutting method : Trucut, Vim Silverman or automatic disposable gun.

The Menghini, trucut or automatic disposable guns are most commonly used in pediatric practice. The risk of fragmentation of biopsy in a cirrhotic patient is higher with the

Menghini needle than the Trucut. But the risk of bleeding is slightly higher with the cutting needles in comparison to the suction type.

Apart from routine histopathological analysis the liver tissue obtained by biopsy can be used for bacterial and viral culture, enzymatic analysis in metabolic diseases, chemical content of tissue as in Wilson' disease and hemochromatosis, immunohistochemistry and electron microscopy depending on the diagnostic possibilities.

## Indications

1. Diagnosis of etiology of neonatal cholestasis.
2. Diagnosis of metabolic/ storage diseases presenting with hepatomegaly.
3. Evaluation, grading and staging of chronic hepatitis and in follow up to assess response to therapy.
4. Evaluation of obscure abnormality of liver function tests and PUO (pyrexia of unknown origin).
5. Evaluation of recurrent conjugated hyperbilirubinemia.
6. Diagnosis of infiltrative/ granulomatous disorders.
7. Diagnosis of intrahepatic neoplasm.
8. Evaluation of liver status (infection, rejection etc) after liver transplantation.
9. Evaluation of type/ extent of drug induced liver injury.

## Contraindications

Can be broadly divided into two groups:

1. **Absolute** : a) Prothrombin time more than 3 seconds prolonged over control b) Platelet count less than 50,000/mm<sup>3</sup> c) Angiomatous

malformation of liver d) Hydatid disease of right lobe of liver e) Non-availability of blood and blood products after liver biopsy.

**2. Relative** : If there is higher risk of complications, one has to weigh the benefit versus risk of procedure carefully.

a) Mild Ascites, b) Intrahepatic biliary radical dilatation, c) Infection of right pleura or lung, d) Sub diaphragmatic abscess.

The following steps need to be followed before proceeding for the biopsy.

## Preparation before liver biopsy

1. History, physical examination and clear indication with list of likely clinical possibilities. This is very useful as the pathologist needs to do special diagnostic tests in specific diseases.
2. The procedure should be explained to parents and consent should be taken.
3. Check for presence of any contra-indications mainly the hemogram, coagulation profile and USG abdomen.
4. Adequate fasting (minimum 4-6 hours to prevent aspiration) should be ensured and an intravenous line (preferably in left arm) is placed for sedation and resuscitation if required.
5. Check for any medications e.g. beta blockers as these children may not develop tachycardia in case of complications like bleed. Patient should not be on anticoagulants or antiplatelet agents preferably for a week before the procedure.

6. Always check the needle before the procedure and load saline in the syringe if using a Menghini needle.

## Biopsy technique

The procedure should always be done under sedation, both to reduce anxiety and

post procedure pain. Either midazolam (0.1-0.2 mg/kg) with meperidine (1 mg/kg/dose) or midazolam with fentanyl (0.5-1 µg/kg) or ketamine (1-2 mg/kg) is used for sedation and choice varies from centre to centre.

The patient is placed in supine position with the right side exposed and right arm drawn up beside the head.

The site of biopsy is selected either by USG and marked or it is determined by percussion between the anterior and mid axillary line. One intercostal space below the maximum liver dullness which is usually in the 7-9<sup>th</sup> intercostal space is selected and marked.

Local site is cleaned and prepared according to standard method.

1% lidocaine is infiltrated first in the skin over the upper border of the rib in the intercostal space to avoid intercostal vessels which run along the inferior border. Infiltration is done till the liver capsule, taking care to aspirate before injecting at each level<sup>9</sup>.

A nick is made in the skin with a small scalpel blade. The later steps are different depending on the type of needle used and are as follows:

**Menghini needle** : The needle is introduced keeping it at right angle to the liver surface and directed towards the left shoulder (acromian process). It is introduced through the subcutaneous tissue and peritoneum which can be felt as a pop or feeling of giving way. A few drops of saline are flushed through the needle to clear the tip of any debris. The needle is introduced into the liver for 2-5 cm with syringe barrel in full suction and then rapidly withdrawn. This is preferably done when the patient is in expiratory phase (if procedure is done under general anaesthesia) but it may not be possible in small children.

**Tru cut needle** : This has a sharp pointed needle with a 2cm notch and a cutting sleeve. The device is advanced just into the liver in the closed position. Then the needle alone is advanced into the liver followed by advancement of sleeve to close over the notch and thus cut a sleeve of liver tissue within the needle lumen. Then both the needle and sleeve are together withdrawn immediately.

Automatic needles are spring loaded devices, which automatically triggers a rapid firing side notch trucut type biopsy needle. Liver tissue should be promptly transferred into the desired medium without manipulation with needle or forceps and sent to the laboratory for fixation.

### Post procedure monitoring

1. Subject is advised to lie in lateral position with right side down so as to provide local pressure.

2. The vitals (pulse rate, respiratory rate, BP) need to be checked every 15 min for 1 hour, every 30 min for 2 hours, every hour for 3 hours and there after 4 hourly for next 18 hours. The exact minimum required duration of post biopsy monitoring is not known. Ideally the child should be in hospital for 24 hours but at least 6 hours of post biopsy observation is a must as recommended in adults<sup>10</sup>.

3. Most hospitals prefer to do repeat hemoglobin estimation at 6 hours to detect any bleed related complication, although it is not absolutely essential.

4. The person monitoring the child should be aware of the sign/symptoms of complications both related to liver biopsy and sedation so as to identify them early e.g. severe pain, respiratory depression and change in vitals.



## Adequacy of liver biopsy

Ideally the liver tissue should be non-fragmented and of an adequate size in order to get a proper diagnosis. A minimum of 6 complete portal tracts are recommended for diagnosis of paucity of intralobular bile ducts in infants with cholestasis and 11 portal tracts (about 2 cm length of liver tissue) are recommended for grading and staging of chronic hepatitis<sup>11</sup>.

Although the liver biopsy provides useful information in the majority of cases, in some cases, it can also lead to misdiagnosis. The main reasons for misinterpretation of biopsy finding include: a) small tissue with insufficient portal tracts, b) focal lesions which are not properly targeted, c) advanced cirrhosis due to metabolic causes like Wilson's disease when distribution of copper is irregular and diagnosis is based on determination of the copper content per gram of liver tissue, d) expertise of pathologist and over reading of minor changes.

## Complications

Nearly 60% of complications are encountered in 2 hours and 96% within 24 hours of the procedure. Over all, the major complications have been reported in 0-4.5% cases<sup>12,13</sup> of pediatric liver biopsies. Death due to liver biopsy is rare if the complication is recognized and managed in time. The complications include: 1. pain at biopsy site or right shoulder, 2. hemorrhage is the most severe of the complications and can be (a) intraperitoneal: It is due to laceration of liver or vascular injury and patient presents with abdominal pain, tachycardia and drop in BP. An ultrasound will show free intraperitoneal collection. Blood and FFP transfusion is usually sufficient but in patients with ongoing hemodynamic, instability angiography with embolization or surgical exploration are

required<sup>14</sup>. (b) intrahepatic/subcapsular: This may be asymptomatic or present with pain and delayed drop in haematocrit. Conservative treatment is usually all that is required. (c) hemobilia: If biliary colic, jaundice and GI bleed occur together then it suggests hemobilia. 3. bile peritonitis is usually due to puncture of gall bladder and presents with immediate pain and vasovagal hypotension. A HIDA scan confirms the biliary leak and USG shows presence of free fluid in peritoneal cavity, 4. bacteraemia, 5. sepsis and abscess formation, 6. pneumothorax, 7. hemothorax, 8. subcutaneous emphysema, 9. biopsy of other organs lung, gall bladder, kidney or colon, 10. sedation related problems.

Thus percutaneous liver biopsy is a very useful tool for management of liver disorders. The technique is easy and quite safe if learnt properly and performed carefully. Complete hemogram, coagulation profile and ultrasound of abdomen should always be done before the biopsy and adequate post-procedure monitoring is a must.

## Points to Remember

- *Diagnostic paracentesis and examination of ascitic fluid is recommended in all cases of ascites.*
- *The serum ascites albumin gradient should be used to classify subjects with ascites into high (>1.1g/dL, portal hypertensive) and low (<1.1g/dL, non-portal hypertensive) SAAG ascites.*
- *Spontaneous bacterial peritonitis should always be ruled out in a child with liver disease and ascites requiring hospitalization.*
- *Percutaneous liver biopsy in children is a safe procedure and provides useful information.*

- *Hemogram, coagulation profile and ultrasound of abdomen should always be done before liver biopsy.*
- *Proper technique of liver biopsy and post procedure monitoring is essential and helps in reduction and early detection of complications.*

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## NEWS AND NOTES

**3<sup>rd</sup> National Workshop for Medical Teachers on Research Methodology:  
Improving Quality of Postgraduate Thesis, New Delhi.  
November 27-30, 2008**

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## PROCEDURES

### UMBILICAL VESSEL CATHETERIZATION AND EXCHANGE TRANSFUSION

\* **Karthikeyan G**

**Abstract :** *As umbilical arteries and vein are easily accessible in the early neonatal period umbilical vessel catheterization forms an important procedure performed in neonatal intensive care unit. The description of these procedures, indications, contraindications and complications are covered. Umbilical catheterization is useful not only for performing procedures like total and partial exchange transfusions but is also in monitoring blood gases and hemodynamic status.*

**Keywords :** *Umbilical artery catheterization, Umbilical vessel catheterization, Exchange transfusion.*

Umbilical cord consists of Wharton's jelly, two umbilical arteries and one umbilical vein. Umbilical arteries and vein are easily accessible in the early neonatal period and hence umbilical venous and arterial catheterizations are important procedures performed in neonatal intensive care units. This article will review these procedures and also discuss about exchange transfusion.

#### UMBILICAL ARTERIAL CATHETERIZATION (UAC)

##### Indications

1) To obtain frequent blood gas in neonates with respiratory distress. (Usually with  $\text{FiO}_2$

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requirements above 0.4), 2) For continuous invasive BP monitoring in sick neonates, 3) To facilitate frequent blood sampling in sick VLBW neonates, 4) Rarely as a portal for administration of fluids and certain drugs.

##### Procedure

The aim is to place a catheter in the descending aorta avoiding its major tributaries like celiac axis, renal and superior mesenteric arteries. Since these tributaries arise between T12 – L2 vertebrae, the tip of UAC is placed either above T6 –T9 vertebrae level (high position) or below these reference points i.e L3, L4 (low position). A recent Cochrane review has concluded that high position has to be preferred because of the lower incidence of vascular complications, aortic thrombosis and longer catheter life<sup>1</sup> but concerns exist about the effect of rapid umbilical arterial blood sampling on cerebral oxygenation<sup>2</sup>.

1. Calculate the distance the catheter needs to be inserted by using the shoulder umbilical distance (the perpendicular distance from shoulder tip to umbilical line and not diagonal distance) reference charts or by using the formula (weight in kg x 3) + 9 cm + umbilical stump length.

2. Prepare the area thoroughly. Apply a cord tie around the base of umbilical stump tight enough to prevent blood oozing, but permitting vessel cannulation.

3. Cut the cord 1-1.5 cm from the base using a scalpel blade.

4. Identify the vessels: Umbilical vein is a thin walled vessel with a wider lumen and umbilical arteries are two sprouting thick walled vessels with a smaller lumen.

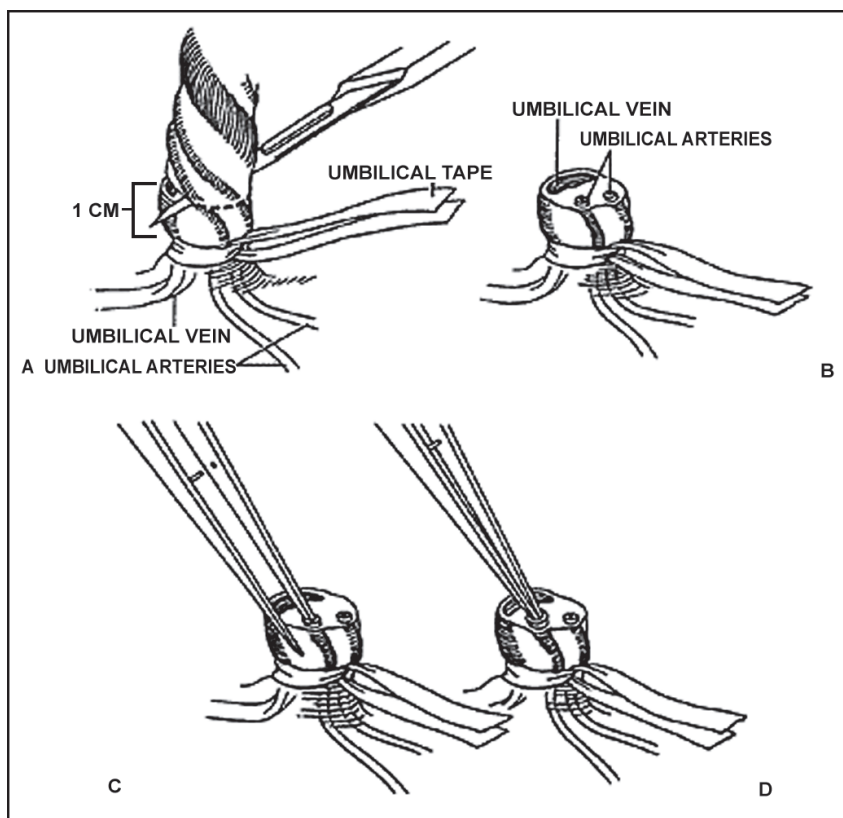
5. Dilate the lumen of the umbilical artery gently with iris forceps or using one limb of a curved artery forceps.

6. Insert the umbilical catheter attached to a three way stopcock and a 2ml syringe filled with saline (size 3.5 - 4F for less than 1500g neonates and size 5F for more than 1500g). If resistance is encountered, it is usually overcome with gentle pressure and twisting motion. But don't force a catheter through lest it create a false passage or rupture a major vessel like iliac artery. Insert up to the precalculated distance.

7. Confirm free blood flow by aspirating the syringe attached (pulsatile flow) and an arterial wave form display from a pressure transducer attached will confirm that it is UAC.

8. Always obtain an X-ray to confirm the tip position. A deeply inserted catheter can be pulled back but a low lying catheter cannot be advanced once sterile field has been broken and a new UAC needs to be inserted. The UAC takes a characteristic V shaped downturn before ascending upwards.

9. Apply purse string stitch in the Wharton's jelly at the base of umbilicus encircling the vessels and including a bite of umbilicus skin also and then stitch this string around the catheter at a distance of about 1 cm from the base. Alternatively a single anchoring stitch can be



**Fig.1. Technique of umbilical arterial catheterization**

applied to the cord and it can be tied to a flag of tape attached to the catheter 1 – 2 cm from the cord. The bridge tape method can be used to further secure the catheter (Fig.1).

10. A continuous infusion of heparinised normal saline (1 unit/ml) at 1ml/hr is necessary through an UAC to minimize the risk of thrombosis.

### **Monitoring**

1) Monitor both the lower limbs including the buttocks and toes for any sign of vascular insufficiency like blanching, cyanosis or poor pulses, 2) If a pressure transducer is attached check if a proper arterial wave form is displayed on the monitor, 3) Check the inserted catheter length frequently to prevent catheter migration.

### **Complications<sup>3</sup>**

1) Bleeding from accidental disconnection or from open connections, 2) Vasospasm of the femoral artery resulting in blanching of toes and foot. Warm the contralateral limb with a warm towel. If blanching persists, catheter should be removed, 3) Embolism of clot or air in the system, 4) Thrombosis which may involve: a) Renal artery resulting in hypertension, haematuria and renal failure, b) Femoral artery resulting in limb ischemia and gangrene, c) Mesenteric artery resulting in gut ischemia, necrotizing enterocolitis. Thrombosis is an indication for removal of catheter but before removing, fibrinolytic agents like tissue plasminogen activator may be infused through the catheter to achieve thrombolysis. 5) Catheter associated sepsis.

### **Catheter removal**

To prevent profuse bleeding, the catheter should be removed slowly in steps allowing the distal umbilical artery to go into vasospasm. Bleeding can be arrested by pinching the skin

below the umbilicus through which the umbilical arteries traverse.

## **UMBILICAL VENOUS CATHETERIZATION (UVC)**

### **Indications**

1) For emergency venous access especially during resuscitation, 2) As a central venous access portal in very low birth weight neonates or sick term neonates (those with meconium aspiration syndrome, persistent pulmonary hypertension etc), 3) For performing an exchange transfusion.

### **Procedure**

The umbilical vein joins the left portal vein and during the initial few hours to days of life, an UVC can be advanced across a patent ductus venosus into the Inferior Vena Cava (IVC) and the right atrium. The distance an UVC should be inserted to position its tip in the IVC is calculated either by measuring the xiphoid– umbilicus distance or two thirds of the shoulder –umbilicus distance and adding the umbilical stump length to it.

After the initial steps as for the UAC insertion mentioned above, the umbilical vein is identified as a single thin walled vessel with a larger lumen. After removing the small clots in its lumen, a 5F catheter with a 2 ml syringe attached to it and filled with normal saline is inserted cephalad upto the precalculated distance. For exchange transfusion it might suffice if it is inserted only as far until free flow of blood is obtained (tip in the umbilical vein)<sup>4</sup>. Secure the UVC in an identical manner as that of an UAC. A check X-ray will reveal the UVC proceeding cephalad right from the point of insertion. The UVC with tip in the IVC should never be exposed to the atmosphere to prevent air embolism.



## Complications

- 1) Thrombo embolic complications,
- 2) Catheter associated sepsis,
- 3) Air embolism,
- 4) Liver necrosis from injection of hypertonic solution into an UVC ending in portal vein,
- 5) Cardiac tamponade and pericardial effusion,
- 6) Necrotizing enterocolitis

## EXCHANGE TRANSFUSION

In this procedure, the infant's blood is replaced volume by volume with blood, plasma or normal saline. If less than the total volume of infant's blood is exchanged, the procedure is referred to as partial exchange transfusion. Single volume exchange transfusion is exchange of one unit volume of infant's blood (80ml/kg) which removes 63% of infant's blood and double volume exchange refers to exchange of twice the infant's total blood volume which removes 86% of infant's blood<sup>5</sup>.

## Indications

1) Neonatal hyperbilirubinemia when levels approach neurotoxic range or when the infant exhibits neurological signs of bilirubin toxicity. A double volume exchange transfusion rapidly lowers the bilirubin level by 50% at the end of the procedure, 2) For polycythemia and severe anemia (partial exchange), 3) Neonates with severe sepsis complicated by disseminated intravascular coagulation (DIC) or sclerema, 4) As a palliative measure in neonates with inborn errors of metabolism like urea cycle disorder to remove abnormally accumulated metabolites use  $\text{NH}_3$ , although hemodialysis is the preferred option.

## Procedure

Two techniques can be used to perform an exchange transfusion.

1. **Continuous (isovolumetric) exchange transfusion** is by simultaneous withdrawal of blood from an UAC or a peripheral arterial line and replacement of equal volume of blood, plasma or saline through an UVC or peripheral venous line. Peripheral arterial – venous exchange avoids the complications associated with umbilical vessel catheterization.

2. **The push – pull technique** involves use of a single major vessel usually the umbilical vein wherein an aliquot of blood is withdrawn and replaced through the same vessel. The aliquot used for exchange is usually 5 ml/kg and the operator calls out the in and out cycles for accurate recording (e.g, ten in – ten out) which is needed to prevent over transfusion or under transfusion. Care should be taken to prevent air entering the circuit when locking and unlocking the three way stop cock attached to the UVC. Continuous monitoring of the infant's temperature, pulse, saturation, blood pressure and ECG is essential and facilities for resuscitation should be available. The blood bag should be agitated every 10 minutes to prevent settling down of red cells. The whole procedure should take 45 – 60 minutes in a vigorous neonate and longer in a sick baby. There is no need for routine infusion of intravenous calcium or sodium bicarbonate as hypocalcemia, hyperkalemia and acidosis are uncommon with currently used preservatives. Monitor the bilirubin (in jaundiced neonates), Hb, electrolytes, calcium and blood sugar before and after the exchange transfusion.

## Complications

1) Hemodynamic complications like volume overload and congestive failure resulting from improper technique, 2) Hyperkalemia, hypocalcemia, acidosis and thrombocytopenia resulting from use of old blood, 3) Reactive hypoglycemia occurring 1-2 hours following the procedure.



## Points to Remember

- *Umbilical artery and vein catheterization remain important means for vascular access in neonatal intensive care units.*
- *They are useful in monitoring and serve as portal of administration of fluids / drugs and for exchange transfusion.*
- *Exchange transfusion, total or partial is still found to be a promising procedure in management of hyperbilirubinemia, polycythemia and removal of toxic metabolites.*

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## NEWS AND NOTES

### 2<sup>ND</sup> NATIONAL CONFERENCE OF COMMUNITY PEDIATRICS

Hotel Royal Residency, Bodh Gaya (World Heritage Town)

December 20<sup>th</sup> & 21<sup>st</sup>, 2008

#### Registration charges for the conference

Category	Upto 31 <sup>st</sup> Oct	After 31 <sup>st</sup> Oct
Delegate	Rs 2000/-	Rs 2500/-
Associate Delegate	Rs 1500/-	Rs 2200/-
PG Students	Rs 1000/-	Rs 1200/-

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## PROCEDURES

### INJECTION SAFETY

\* **Kamath SS**

\*\* **Sonowal BJ**

**Abstract:** *With approximately 300-500 crore injections being delivered to patients and only approximately 200-300 crore injections (syringe and needle) being sold in the market in India every year. It is estimated that over 60% injections are unsafe with a propensity to spread blood borne infections. This review discusses the magnitude of injections and the resulting blood borne infections, Post-exposure prophylaxis (PEP) and its protocols and immediate management following accidental needle-stick injuries. It also covers why guidelines and processes need to be kept abreast with newer and safer technology.*

**Key words:** *Safe Injections Global Network (SIGN), Post-exposure prophylaxis (PEP), Auto disable (AD) syringe.*

Injections are the most common health intervention (preventive, curative and diagnostic intervention), an average of 5.8 injections per person per year being administered according to INDIACLEN programme evaluation network (IPEN) study. Most of these injections are not rational and therefore not required. 51.1% of the injections are for fever, cough or diarrhea. Injection can be defined as “a skin-piercing event performed by a syringe and needle with the

purpose of introducing a curative substance or vaccine into a patient by the im/iv/sc/id route”

WHO defines safe injection as one, which “does no harm to the recipient, does not expose the health worker to any risk and does not result in waste that is dangerous for the community”.

To achieve this, first, the injection should be prepared in a clean workspace that is free from any blood contamination. Second, the provider should wash his hands in an appropriate and technically correct manner. Third, a sterile syringe and needle should be used. Fourth, medication and diluents should be drawn from a sterile vial. Fifth, the skin should be cleaned before injection. Sixth, the used syringe and needle should be collected in a puncture and liquid-proof container. Finally, sharps waste should be managed appropriately. Failure to respect any of these steps exposes the recipient, the provider or other people to unacceptable risks.

WHO estimates that approximately 16 billion injections are given in the developing and transitional countries. India, which accounts for a sizeable proportion of the world population gives about 300-500 crore injections annually. Records of manufacturing and imports show that about 200-300 crore syringes are sold in the market, which leaves a huge room for reuse. Most of the reuse happens in the private unorganized setups, but a sizeable proportion of reuse also happens in the organized sector.

Many of the injections that are administered annually world-wide are administered under unsafe conditions. In a review of published and

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unpublished studies, Adam Kane and his collaborators in the Bulletin of WHO estimated that in the developing world, the proportion of injections that are administered with a syringe and/or needle administered without sterilisation ranges from 15% in former socialist economies of Eastern Europe and in the Middle East crescent upto 50% in sub-Saharan Africa, China, India, and the rest of Asia.

Evidence points towards the spread of hepatitis B, C and HIV by means of unsafe injections. WHO estimates that 21 million cases of Hepatitis B, 2 million cases of Hepatitis C and 2,60,000 cases of HIV are spread by the route of unsafe injections every year. India has about 6.28 million cases of hepatitis B, 810,900 cases of hepatitis C and 8,600 cases of HIV spread every year by means of the unsafe injections.

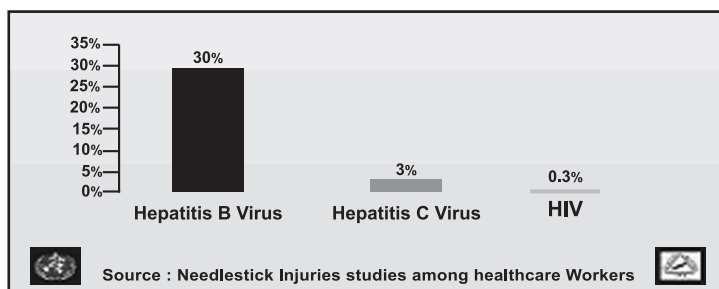
The transmission potential of HBV, HCV, and HIV is known from the studies for which healthcare workers have been followed for occurrence of infection with blood-borne pathogens after accidental needle-stick injuries. After an accidental needle-stick from an HBV infected source patient, the probability of infection for susceptible recipients averages 30%. After an accidental needle-stick from an HCV infected source patient, the probability of infection for susceptible recipients is 10 times

smaller and averages 3%. For HIV, the probability of infection for susceptible recipients after an accidental needle-stick is 100 times smaller than HBV and averages 0.3% (Fig.1). Thus, while the transmission of HIV through unsafe injections is of particular concern because of its severity, it is less common than HBV and HCV transmission. Hepatitis B is the most likely pathogen transmitted through unsafe injections.

With these statistics, we may well have a major epidemic of these latent diseases in the years to come. In addition to infections, injections may lead to traumatic lesions, including paralyses secondary to sciatic and other nerve lesions, and provocation paralysis associated with wild polio.

Several factors lead to reuse of syringes and needles, the major force for such is economics. Poor patients who cannot afford quality healthcare are often at the receiving end of the unsafe practices. Other factors like poor knowledge on the effects of safety, unavailability of equipments or poor distribution of syringes and needles in the health care setups also point towards reuse. Besides disposable technology, which entailed that each syringe be used only once is often recycled for reasons of profit.

6.7 billion injections (39.3%) are given each year via reused equipments because of financial



**Fig.1. Estimated risk of infection following a needlestick from an infected source - Patient**

constraints while for other medical reasons, over 50% are deemed unsafe.<sup>1</sup> Commonly, injected medications include drugs that could be taken orally, and are in case unnecessary.<sup>2</sup> Evidence points towards the spread of Hepatitis B, Hepatitis C and HIV by means of unsafe injections.<sup>2</sup> In response to this evidence WHO scaled up it's activities with the Safe Injections Global Network (SIGN).<sup>3</sup> Communicating the risk of HIV infection associated with unsafe health-care injections is now a core activity of any HIV programme. WHO's Department of Essential Drugs and Medicine Policy promotes rational use of drugs, including injections, through research, normative work, and capacity building, and works to increase access to safe injection equipment. The Department of Protection of the Human Environment has created a working group to ensure that contaminated sharps are not reused. The Department of Vaccines and Biologicals has given immunization safety a priority.

Wrong techniques and lack of knowledge on the injection sites also lead to unsafe injections being delivered across the country. Recent studies have highlighted the importance of administering vaccines correctly.<sup>4,7</sup> Choosing the right needle length and gauge of the needle is good clinical practice while administering vaccines and medications because it ensures that those vaccinated get the immunological benefits of the vaccine without the local side effects. Injecting a vaccine like hepatitis B,<sup>6</sup> rabies and influenza vaccine<sup>4</sup> into the poorly vascular subcutaneous tissue may result in slow mobilization and processing of the antigen and may therefore result in vaccine failure.<sup>5</sup> When injected into the subcutaneous tissue, Hepatitis B has significantly lower seroconversion rates and more rapid decay of antibody response.<sup>5</sup> Gluteal region which was a preferred site for most injections are not the recommended sites for most injections. In infants and children, sciatic nerve injury usually occur,

while in adults, the layers of fat do not contain the appropriate cells (phagocytic) that are necessary to initiate the immune response. The antigen take longer to reach the circulation after being deposited in the fat, leading to a delay in processing by macrophages and eventual presenting to T and B cells. The antigen may also be denatured by the enzymes if they remain in fat for hours or days. These facts are supported by data that thicker skinfolds are associated with a lowered antibody response to vaccines.<sup>5,6</sup>

Studies carried out to test for adverse reactions to intramuscular injection show that the reactions are limited or small in them (0.4%).<sup>8</sup> Subcutaneous injections could cause granulomas and abscesses.<sup>5,9</sup> Muscle is probably spared of these harmful effects due to the abundant vascularity. Vaccines where the antigen is adsorbed to aluminium salt adjuvant like hepatitis A, hepatitis B, DPT vaccines, the intramuscular route is strongly advocated because superficial administration leads to an increased incidence of local reactions such as irritation, inflammation, granuloma formation and necrosis.<sup>6,10</sup>

Unsterile administration of drugs also takes place on a large scale outside of formal medical practice. In many places in the less-developed world, injectable medications, syringes and needles are readily available in rural villages, where injecting by indigenous practitioners (injectionists) and self-injection are common practice.<sup>11,12</sup> Furthermore, syringes are now widely used for administration of illicit substances. Once restricted to North America and Europe, intravenous opioids are now taken in more than 120 countries,<sup>13</sup> where millions of drug addicts inject themselves daily using unsterile equipment. There are between 10 and 15 million people who inject illicit drugs worldwide.

Hepatitis C was not identified till 1989. Its epidemic spread seems to be closely associated

with 20th century medical developments, including (unsterile) injections, blood transfusions, and dialysis.<sup>14</sup> 170 million individuals worldwide are chronic carriers of hepatitis C, including 1–2% of the adult populations of developed countries and 5–10% in some less-developed countries.<sup>15</sup> The first documented large scale outbreak of the disease occurred in the early 1960s, at the time of a campaign for parenteral treatment of schistosomiasis in Egypt.<sup>16</sup> Between 1964 and 1969 more than 3 million injections were given per year to over 300 000 individuals. By the mid 1980s the campaign had infected 10% of the entire adult population of Egypt with hepatitis C, and it constituted the world's largest iatrogenic transmission of blood borne pathogens known to date.<sup>16</sup>

The large number of injections given to children in their first year of life may expose them repeatedly to the dangers of unsterile injections and consequently disease. The majority (70–90%) of the children infected with hepatitis B will become chronic carriers, compared with 6–10% of people infected as adults. Among chronic carriers 20–28% will die of causes related to their hepatitis infection.<sup>17</sup>

Ensuring safety, Safe Injection Global Network (SIGN) was established in October 1999 as a voluntary association of stakeholders who share a common interest in safe and appropriate use of injections. Associates of SIGN collaborate with other members for developing a common strategic framework and communication strategy on injection safety. SIGN recommends a three-part, multidisciplinary approach to achieve safe and appropriate use of injections. First, behavior of health care providers and patients must be changed to decrease injection overuse and achieve safety. Second, sufficient quantities of appropriate injection equipment and infection control supplies should be available. Third, a

sharps waste management system should be set up to ensure that disposable equipment is destroyed and not reused.<sup>18</sup>

Before SIGN, a number of successful efforts have reduced injection overuse and improved safety. In Indonesia rates of injections decreased from 73% to 14% after group discussions between health care providers and patients. In Tanzania, avoidable injections decreased from 16% to 6% after guidelines to improve injection practices were developed and communicated. In Hafizabad, Pakistan, the proportion of injections conducted with a new sterile syringe increased from 24% to 60% after a health education program was conducted in mosques. Indeed, wherever a plan to promote injection safety has been implemented, it has brought about at least some success.<sup>18</sup>

Technology has a role to play in supporting safe use of injections. First, newer injection devices are being developed, including auto-disable (AD) syringes, eg. that inactivate themselves after use, needle-less devices, and pre-filled monodose injection devices. In addition, newer waste management options are being studied to ensure destruction of sharps, including small scale incinerators for rural primary care centres, thermal processing to melt down syringes and needles into an innocuous plastic cake and waste volume reduction through development of better devices. However the Central Pollution Control Board (CPCB), needs to keep abreast of the new developments and put up appropriate waste management guidelines more frequently.

### **Post exposure prophylaxis**

Post exposure prophylaxis (PEP) is the use of therapeutic agents to prevent infection following possible exposure to a pathogen. Any type of exposure; percutaneous – needlestick injuries, splash, bite and sexual; needs PEP to be



instituted as early as possible, preferably within the critical period of 72 hours. The PEP commonly considered for health care workers and doctors following an accidental occupational exposure are for HIV and Hepatitis B.

Some of the other factors that also need to be considered while instituting PEP are:

- a. Viral load of the source patient
- b. Glove use – There is a 50% decrease in volume of blood transmitted with the use of gloves
- c. Large diameter needles are weakly associated with increased risk ( $p=0.08$ )<sup>19</sup>

PEP is to be considered in either of the three conditions:

- a. The source is known to be HIV positive
- b. There are reports of HIV risk behaviour in source or case
- c. The exposure occurred in settings where the local HIV seroprevalance is high / expected to be high

International guidelines say that PEP must be started as soon as possible following the exposure and it should be prescribed for 28 days. Animal studies have suggested that PEP is substantially less effective beyond 24-36 hours.<sup>20</sup>

**Table 1. Risk factors for seroconversion**<sup>19</sup>

Risk factor	Odds ratio*	95% CI
Deep injury	15	6.1 - 41
Visible bloody device	6.2	2.2 - 21
Device in artery/vein	4.3	1.7 - 12
Terminally ill	5.6	2.0 - 16
AZT PEP	0.19	0.06-0.52

\* $p<0.01$  for all

## PEP protocol and immediate management

It is important to cater immediate attention to any needlestick injury that happens either in the hospital / clinic or health care associated waste. The hospital should maintain a needlestick injury record register, preferably maintaining confidentiality, so as to ensure reporting. Several countries prescribe coding systems for this purpose. After assessing the risk of HIV transmission, a decision has to be taken on requirement of PEP. Start PEP as early as possible if risk is high (Table 1). A baseline blood sample for HIV, hepatitis B and C is mandatory and it is also important to have proper documentation of the case.

Immediate management should include washing the wound with soap and water. Mucous membranes should be flushed with water. The wound should not be squeezed / milked, as this would lead to more intermingling of individual's blood with the injured area. Applications of bleach, antiseptics or disinfectants into the wound are not recommended by CDC. The individual needs immediate tetanus and hepatitis B vaccination assessment and if required, provided. Counselling is required for the individual and anti retroviral therapy (ART) treatment institutionalized for those considered to be at risk. Follow up is required with repeat HIV test after 1, 3 and 6 months and for hep C at 1, 3, 6 and 12 months.

## Drugs for PEP

There would be two situations that should be considered:

- a. If it is unknown whether the source is HIV +ve, two Nucleotide reverse transcriptase inhibitors (NRTI) are prescribed.
- b. If it is known that the source is HIV +ve, the choice should be based upon the source's



current ARV's plus resistance test results and past ARV's used. Two NRTI's are usually prescribed, a third drug is added only under circumstances like if it is known that the source is HIV +ve and a high risk exposure has happened and all that is known about the source is that s/he has advanced HIV disease or if the source has recently had a very high HIV viral load or if the source has known drug resistance involving primary mutations to at least two drug classes.

It is important that the incidence of common side effects should be mentioned to the individual. Consideration of certain drugs that may cause deficiency of motor skills should be explained. Some of the common side effects include nausea, fatigue, headache, vomiting, diarrhoea and myalgia in decreasing order of magnitude. Some serious side effects have been experienced with Nevirapine that include hepatotoxicity and liver failure.

It is important that all healthcare workers should be immunized with hepatitis B. If exposure has occurred in individuals without hepatitis B vaccination, it should be provided immediately. Immunoglobulins need to be considered only if the source is known to be hepatitis B positive. This should be continued for one week following exposure.

The preferred dosing regimens are:

- a. AZT(Zidovudine) or TDF (Tenofovir) plus 3TC (Lamivudine) or FTC (Emtricitabine)
- b. Alternative basic regimens are d4T (Stavudine) or ddl (Didanosine) plus 3TC (Lamivudine) or FTC (Emtricitabine)

In conclusion, we can say that injection overuse and breaks in injection safety leads to large-scale blood borne pathogen transmission. Prevention should be achieved through multidisciplinary approaches to reduce overuse

and improve safety and improve quality of healthcare. However healthcare workers are in constant threat to receiving needlestick injuries as a part of their work. It is therefore important to have sharps disposal mechanisms in place that prevents a second contact with the sharps after disposal. Sharps collectors and hub cutters play a very important role in this process of safety. Sharps collectors (placed in every ward by the bedside) would ensure that immediately after use the entire needle and syringe is disposed off at the site of generation, thereby avoiding the chance of the healthcare worker from getting a needle stick injury. At places where the sharps collectors cannot be used (OPD / emergency / outreach), hub cutters ensure that the sharps are segregated and thereby help the healthcare worker for coming into contact with them and receiving a needlestick injury. It is also important to institutionalize PEP as early as possible after weighing the risks and ensure vaccination to all the health care workers.

### Points to Remember

- *Over 60% injections are unsafe resulting in blood borne infections.*
- *Hepatitis B,C and HIV are few common infections spread through unsafe injections.*
- *Vaccination to prevent hepatitis B and post exposure prophylaxis to prevent HIV infection are mandatory.*

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## NEWS AND NOTES

### GIAPCON 2008, Gujarat December 20-21, 2008

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<b>GENERAL ARTICLE</b>
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## **HUMAN PAPILLOMAVIRUS DISEASE AND VACCINE - THE INDIAN SCENARIO**

\* **Swati Y Bhave**

***Abstract** : India accounts for more than a quarter of the incidence of the world cases with approximately 1,32,000 cases of cervical cancer being diagnosed. It is the biggest killer of women in India accounting for one fourth of the world's cervical cancer mortality (74,000/ year). Cervical screening worldwide has had an impact on the incidence of cervical cancer, but is still in its nascent stage in India. More than 99% of cervical cancer cases show evidence of having human Papilloma virus (HPV) infection. Two vaccines; Bivalent vaccine covering types 16 and 18 and the quadrivalent vaccine covering types 16, 18 and 6, 11, have been launched worldwide. The bivalent vaccine protects against cervical pre cancers. The quadrivalent vaccine in addition to protecting against cervical precancers also protects against vaginal and vulvar precancers and anogenital warts. Once introduced in India both these vaccines are expected to have an impact on the high disease burden in India. There are many issues that have to be considered while introduction of this vaccine cost, age at which it will be acceptable and the moral, ethical, religious issues that will be related to a female only vaccine which will protect against cancer that arises from a sexually transmitted disease. The vaccine will not eliminate screening programs but will reduce the*

*number of cases that need follow up and invasive procedures . Both screening and vaccination will be needed to effectively reduce incidence of cervical cancer.*

**Keywords:** Human papilloma virus (HPV), Cervical cancer, Screening, Vaccines, Quadrivalent vaccine, Bivalent vaccine.

### **HUMAN PAPILLOMA VIRUS**

Human papilloma viruses (HPV) are a large family of small, double-stranded DNA viruses that cause benign epithelial proliferations or warts in the natural infection. HPV infection occurs throughout the world. Humans are the only natural reservoir of HPV. They are also tissue-specific and a complete infectious cycle occurs only in a fully differentiated keratinised squamous epithelium.<sup>1</sup> Most HPV infections are asymptomatic and do not result in clinical disease. The various clinical manifestations of HPV infection are: Anogenital warts, recurrent respiratory papillomatosis, cervical cancer precursors cervical intraepithelial neoplasia (CIN), and anogenital cancers, including cervical, anal, vaginal, vulvar, penile and some head and neck cancers.<sup>2</sup>

HPV are classified by genotype DNA sequence. More than 200 types have been identified. Approximately 40 HPV types infect the mucosal epithelial surfaces. There are two large groups: 1) Those infecting skin or cutaneous surfaces, and 2) Those infecting the internal wet-squamous mucosal surfaces.

Again these are classified as a) Low risk or non-oncogenic type e.g. type 6 and 11. They

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cause benign or low-grade cervical cell abnormalities, genital warts and laryngeal papillomas, and b) High-risk or oncogenic types, e.g. type 16 and 18 which act as carcinogens in the development of cervical cancer and other anogenital cancers (vulva, vagina, penis and anus). Few HPV types affecting anogenital area may also cause some oral and pharyngeal cancers.<sup>1</sup>

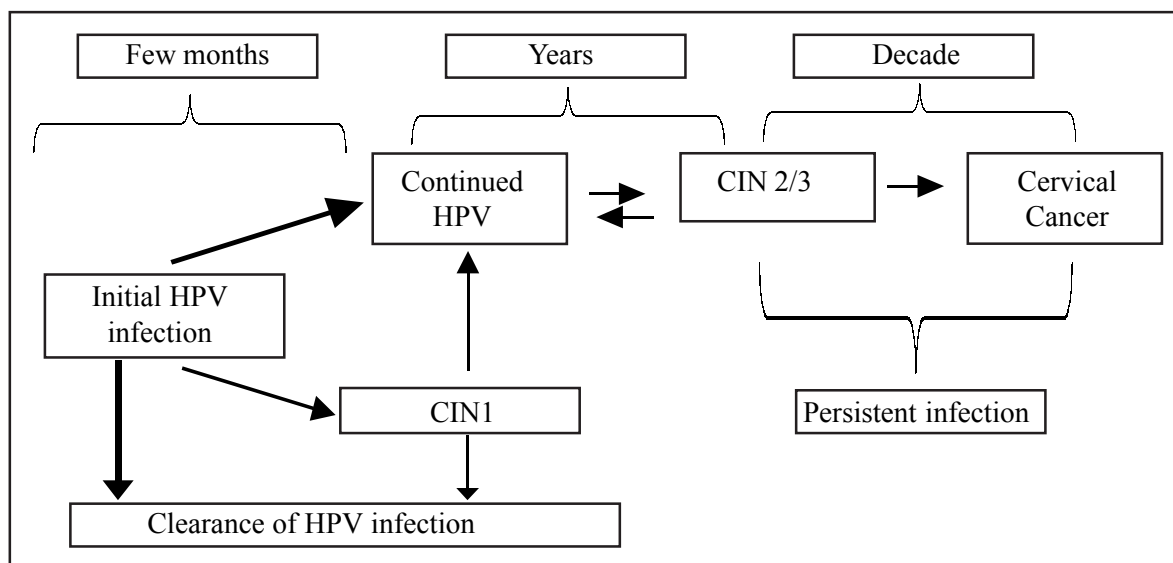
## Transmission

Infection occurs not only by sexual intercourse but also by non-penetrative sexual contact that is an important risk factor of adolescent sexual experimentation. Genital infections occur via genito-genital, oro-genital, hand-genital and ano-genital contact.<sup>2</sup>

Nonsexual routes: These are uncommon and include transmission from a woman to a newborn infant at the time of birth.<sup>2</sup> Lifetime risk among sexually active men and women is at least 50%. Studies of newly acquired HPV infection demonstrate that infection occurs soon after onset of sexual activity. In a prospective study of

college girl students, the cumulative incidence of infection was 40% by 24 months after first sexual intercourse. HPV 16 accounted for 10.4% of such infections.<sup>3,4</sup>

There is no known seasonal variation in HPV infection.<sup>2</sup> Communicability can be presumed to be high because of the large number of new infections estimated to occur each year. HPV is presumably communicable during the acute infection and during persistent infection. But this is difficult to confirm because of the inability to culture the virus.<sup>2</sup> Following initial HPV infection, the course of progression to cervical cancer depends on the type of HPV. Low-risk HPV types (such as HPV 6 or 11) have a negligible risk of progression but may persist.<sup>5</sup> Overall, the majority of HPV infections spontaneously clear within the first 24 months.<sup>6</sup> High-risk types (such as types HPV 16 and 18) are often associated with CIN 2 or higher lesions. The strong association of HPV 16 with CIN 2 or greater suggests that lesions caused by this infection evolve to CIN 2 without a prolonged



**Fig.1. Natural history of HPV infection**

period as CIN I. Fig.1 depicts the natural history of HPV Infection.

## Treatment

There is no specific treatment. Management depends on treatment of the specific clinical manifestation of the infection such as genital warts or abnormal cervical cell cytology. Anogenital warts may need excision for discomfort or cosmetic reasons. Recurrent laryngeal papillomatosis can require emergency excision for obstruction. Recurrence of warts may need repeated excisions.<sup>2</sup> Average number of surgeries required to remove warts and maintain an open airway in children suffering from juvenile onset recurrent laryngeal papillomatosis (JORRP).<sup>7</sup>

## Risk factors

Persistent infection with a high-risk HPV type is not the only factor for cancer since a large number of HPV infected women do not develop cancer.<sup>8,9</sup>

Various studies have shown the evidence of a number of cofactors helping in persistent infection.<sup>10</sup> Young age at sexual initiation less than 25 years, number of sex partners, lifetime history of sex partners, inconsistent condom use, number of pregnancies, genetic factors, smoking, lack of circumcision of male partner and oral contraceptive use helps in persistent infection.

Infection with one type of HPV does not prevent infection with another type; 5% to 30% have multiple types of the mucosal virus.<sup>2</sup>

Studies on prevention demonstrated a significant reduction in HPV infection among young women after initiation of sexual activity when their partners used condoms consistently and correctly.<sup>11</sup> However condoms cannot give absolute protection due to the transmission also

by non penetrative sex .Abstaining from sexual activity (i.e., refraining from any genital contact with another individual) is the surest way to prevent genital HPV infection. For those who choose to be sexually active, a monogamous relationship with an uninfected partner is the strategy most likely to prevent future genital HPV infections.

## HPV infection and cervical cancer

The natural history of cervical intraepithelial neoplasia (CIN) is in effect, the natural history of HPV infection in the cervix.<sup>12</sup> Transient genital HPV infections, both of high-and low-risk HPVs, are very common in young sexually active women with the lifetime risk for acquiring a genital HPV infection in the UK of the order of 70 to 80%. Most of these infections are transient and resolve.<sup>12</sup> If lesions develop, they are low-grade CIN1 and represent the infectious cycle of the virus and are, in fact, flat papillomas.<sup>12</sup> However approximately 10 to 15% of infected women develop persistent HPV infection, and fail to clear the virus possibly because of the failure to develop a strong cell-mediated immune response to HPV early proteins. These persistent infections with oncogenic HPVs are at risk for progression to the high-grade precursor lesion CIN2/3 and approximately 30 to 40% of CIN2/3 then progress on to invasive carcinoma.<sup>12</sup>

Low-risk HPV types, HPV 6 and 11 cause more than 90% of genital warts with minor types (HPV 42, 44) and some high-risk HPVs contributing to about 10%. High risk or Oncogenic HPVs in the genital tract are dominated by HPV16 and HPV18 which, with their close relative HPV types 31, 33, 35, 52, 58, 39, 45, 59, 56, 66 and 51, are the cause of cervical cancer.<sup>13</sup>

Thus in 99% or more of biopsies of invasive cervical cancer worldwide, HPV DNA sequences can be detected<sup>14</sup> and in the high-risk precursor



lesions, cervical intra-epithelial neoplasia (CIN 2, 3) approximately 80% contain the high-risk HPVs.<sup>13</sup> HPV Type 16 causes nearly 50% and together with type 18 about 70% of cervical cancers world wide. Overall, the malignant burden attributable to HPV infection is calculated to be 3.71% of all cancers. Human papillomavirus infection is not only the cause of invasive cervical cancer but HPV are also found in a proportion of anal, vulvar, vaginal, penile and head and neck cancers.<sup>15</sup>

### HPV and cervical cancer in India

Cervical cancer ranks the first most frequent cancer in women in India, and the first most frequent cancer among women between 15 and 44 years of age. India has a population of 365.71 millions women aged 15 years and older who are at risk of developing cervical cancer. As per IARC, Globocan 2002 data every year 132082 women are diagnosed with cervical cancer and 74118 die from the disease. The cumulative risk (%) of Incidence/ Death in India is approximately two times as compared to the world statistics. (Table I). Worldwide, HPV- 16 and 18 contribute to over 70% of all cervical cancer cases while many studies in India have

**Table 1. Cumulative risk of incidence/ death<sup>16</sup>**

Incidence/ Death	India*	World*
Cumulative risk (%) of Incidence. Age period 0-64 years	2.5%	1.3%
Cumulative risk (%) of death. Age period 0-64 years	1.4%	0.7%

\* Rates are per 100,000 women. Standardized rates have been estimated using the direct method and the world population as the reference. (Adapted from IARC, Globocan 2002)

also shown that HPV 16 and 18 accounts for around 76.7% of all invasive cervical cancer cases.<sup>16</sup> In a recent meta analysis by Bhatla, et al. published in 2008 aimed at determining HPV type-distribution and prevalence among women of South Asia in order to estimate the potential protection of a HPV-16/18 vaccine and to determine the additional HPV types that should be included in new vaccines for optimal protection against cervical cancer in this region shows that HPV 16 and 18 are responsible for approximately 87.8% in North India and approximately 76.2% in South India.<sup>17</sup>

### HPV – Anogenital warts

Genital HPV infection is the commonest viral STI (sexually transmitted infections) in the developed world, with an estimated 30 million new cases diagnosed annually worldwide.<sup>18</sup> Approximately 15% of the general population harbor sub clinical infection. The incidence and prevalence of clinical HPV genital infection have been steadily increasing since the mid-1960s, but the true prevalence of HPV anogenital infection in the community is unknown because of many factors.<sup>19</sup> The disease is symptom less and sub clinical infection is common. Most patients either do not seek help or consult general practitioners, and the disease is not notified to public health authorities.

Anal warts are a disease of young people. In men the peak is at 20-24years of age and is also significantly high till the age of fifty.<sup>20</sup> It is seen at peak in girls from 16-19 followed by 20-24 years of age and then gradually declines over years. This suggests that the young girls are more likely to be commercially exploited for sex and also undergo coercive sex.<sup>20</sup> Another probable explanation could be the tendency of female to engage with older males.

Current evidence suggests that over 50 % of sexually active adults (15–25 years of age)



have been infected with one or more HPV types.<sup>21</sup> The diagnosis of anogenital warts is mainly based on the history of exposure, clinical appearance, and epidemiological proof of the warts in the sexual contact.<sup>20</sup> The average time to development of new anogenital warts after infection with HPV types 6 or 11 is approximately 2–3 months.<sup>7</sup> 70% of individuals will suffer from anogenital warts within 3 months of having sexual contact with individual having anogenital warts.<sup>22</sup>

### **Indian scenario of ano-genital warts**

In India, the incidence of genital warts has been reported to vary from 2% to 25.2% among STI clinic attendees.<sup>18</sup> In a retrospective study determining the change in trends of the profile of STIs and HIV seropositivity in STD clinic attendees over a period of 15 years, there has been an increasing trend in prevalence of a genital warts over a period of time from 1990-2004 (Table 2) in the study.<sup>23</sup>

**Table. 2. Prevalence of genital warts in India.**<sup>23</sup>

Study Period	1990-93	1994-97	1998-01	2002-04
Percentage	5.8	11	10.5	18.1

### **HPV in HIV**

The incidence of warts is reported to be between 5 and 27 per cent in HIV infected individuals. In a prospective study, out of 912 HIV-1 infected patients, 21 per cent had common/plantar warts and 19 % had condyloma acuminata.<sup>20</sup>

### **Laboratory diagnosis of HPV**

So far HPV has not been isolated in culture. The infection is identified by the detection of HPV DNA from clinical samples. Assays for HPV detection differ considerably in their

sensitivity and type specificity. The detection rate can depend upon the anatomic region sampled and the method of specimen collection.<sup>2</sup>

Digene hybrid capture (hc2) high risk HPV DNA test is approved by FDA. This uses liquid nucleic acid hybridization and detects 13 high-risk types (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68). Results are reported as positive or negative and are not type-specific. The hc2 test is approved for triage of women with equivocal papanicolaou (Pap) test results (ASC-US, atypical cells of undetermined significance) and in combination with the Pap test for cervical cancer screening in women over age 30. The test is neither clinically indicated nor approved for use in men.<sup>2</sup>

**Serologic tests for HPV** are virus like particles (VLP) based enzyme immunoassays. They are not very useful as the laboratory reagents used for these assays may not be standardized and there are no standards for setting a threshold for a positive result.<sup>2</sup>

### **Cervical cancer screening**

Most cases and deaths from cervical cancer can be prevented through detection of precancerous changes within the cervix by cervical cytology using the Pap test. Currently available Pap test screening can be done by a conventional Pap or a liquid-based cytology. CDC does not issue recommendations for cervical cancer screening, but various professional groups have published recommendations e.g. the American College of Obstetricians and Gynecologists (ACOG),<sup>24</sup> the American Cancer Society (ACS), and the U.S. preventive services task force (USPSTF).

The use of HPV vaccine will not eliminate the need for continued Pap test screening, since 30% of cervical cancers are caused by HPV types not included in the vaccine.<sup>25</sup>

## HPV VACCINES

Recombinant technologies have allowed for the production of large amounts of the capsid structural protein L1.<sup>26</sup> This protein self-assembles into virus-like particles (VLPs) without any of the infective genetic components being present. When injected, these VLPs induce type-specific antibodies that have been shown to protect women from persistent infection and dysplasia.<sup>2</sup>

### Efficacy end points

The primary objective of vaccination is to reduce cervical cancer. Ethical and time considerations make it necessary to use a surrogate end point in clinical trials of vaccine efficacy.<sup>27</sup> The US food and drug administration (FDA) and its vaccines and related biologics advisory committee examined the natural history of cervical cancer to define surrogate markers for cervical cancer.<sup>28</sup> The only surrogate clinical condition is biopsy-confirmed CIN 2/3 or AIS. These lesions are the obligate precursor to invasive cervical cancer and are always treated.<sup>27,28</sup> Therefore, CIN 2/3 or AIS are strong surrogate markers for cervical cancer.<sup>28</sup> Hence while talking in context of the vaccines, it is worth while to focus on these end points rather than antibody titres.

**There are two vaccines available globally:** Quadrivalent HPV Vaccine, Gardasil<sup>TM</sup> (Merck & Co.) and Cervarix<sup>TM</sup> (GSK). Both vaccines are manufactured by recombinant DNA technology that produces non-infectious virus like particles (VLP) comprising of the HPV L1 protein, the major capsid protein of HPV.

Bivalent vaccine (Cervarix<sup>TM</sup>, GSK) that contains VLP for type 16 and 18 and quadrivalent HPV vaccine (Gardasil<sup>TM</sup>, Merck) which contains VLPs for 16 and 18 and also for types 6 and 11. The bivalent vaccine had used CIN 1, 2 and 3 as

its efficacy end points is thus approved for prevention against HPV 16 and 18 related cervical cancers. The quadrivalent vaccine (Gardasil<sup>TM</sup>, Merck) had efficacy end points against CIN 1, 2 and 3, AIS, VaIN 2/3, VIN2/3, warts and hence it is approved for prevention against HPV 6, 11, 16 and 18 related cervical cancer and in addition anogenital warts, vulval intra-epithelial neoplasia (VIN) and vaginal intra-epithelial neoplasia (VaIN)<sup>7,29,30</sup>

**Dose:** The schedule is IM injections at 0, 1 and 6 months for bivalent and 0, 2 & 6 months for the quadrivalent vaccine.

**Long Term Protection:** Both vaccines have good antibody titres and have shown to have protective titres around 5-6.4 years. Like any new vaccines, a study of the protective titers over next many years will determine the need for booster if any. Some vaccines induce long-term immunity, while others require booster doses. Vaccines that induce long-term protection are usually characterized by the generation of immune memory.<sup>31,32</sup>

### Vaccine storage and handling

HPV vaccine should be stored continuously at 35° - 46°F (2°–8°C) and should be protected from light. The vaccine should be removed from refrigeration immediately before administration. The vaccine must not be exposed to freezing temperature. Vaccine exposed to freezing temperature should never be administered.<sup>2</sup>

### Recommended age for the vaccine

Age of recommendation for routine vaccination in the United States is 11–12 years which is also endorsed by society of adolescent medicine (SAM) but can be given as young as 9 years age at the discretion of the clinician. Catch-up vaccination is recommended for females 13 through 26 years of age who have not been

previously vaccinated or who have not completed the full series. Various countries that have recommended the vaccine have different ages for primary and catch up groups between the ranges of 9-26 years. HPV vaccine is neither approved nor recommended for use among females younger than 9 years or older than 26 years of age. Studies with females older than 26 years of age are ongoing. There are no current completed studies among children younger than 9 years of age.<sup>7</sup>

### **What happens if the vaccine is given to older girls and young women up to 26 years of age?**

Participants infected with one or more vaccine HPV types prior to vaccination were protected against disease caused by the other vaccine types. However, prior infection with one HPV type did not diminish efficacy of the vaccine against other vaccine HPV types. There is no evidence that the vaccine protects against disease due to non-vaccine HPV types or provides a therapeutic effect against cervical disease or genital warts present at the time of vaccination.<sup>2</sup> However it is important to note that most HPV infections clear over a period of 2 years. Thus it would be worthwhile to give vaccine to a lady already infected with a vaccine type HPV as over a period of time her body might get rid of this infection and she might be protected against subsequent HPV infection due to that specific vaccine HPV type.

Currently only the quadrivalent vaccine is USFDA approved and hence ACIP recommendations are available only for the quadrivalent vaccine which is licensed by the food and drug administration for use among females 9–26 years of age.<sup>7</sup>

**Need for booster:** There is a very encouraging data from both Phase II and Phase III trials showing that serum antibody levels fall from the

peak levels achieved after the third immunization to a lower concentration that persists at the same level for at least 60-months post-vaccination.<sup>33</sup> The antibody concentrations in the plateau period in vaccinees are still 10 to 20 times that of natural infection. This data, combined with the evidence from large-scale population studies of naturally-infected individuals in which it can be shown that the antibody levels persist for at least 10 years after natural infection<sup>34</sup> leads to optimism that these vaccines will induce very long-lasting protection. The immune correlates of protection have so far not been established because all individuals in the trials appear to have sero-converted and there have been no evidence of vaccine breakthrough.

### **Male vaccination**

The males are a potential target for the vaccine for protection against warts, penile or anal cancer, and as a vector for transmission to females.<sup>35</sup> It is anticipated that in the future, the vaccine will be available for both of these groups. Immunogenicity bridging studies of antibody concentrations achieved after immunization in 9 to 15 year old girls and boys have shown that antibody levels after HPV VLP vaccination are higher in 9 to 10 year old girls than 13 to 15 year old girls, and higher in 13 to 15 year old girls than 16 to 23 year old women. The levels are higher in 9 to 15 year old boys than in 9 to 15 year old girls, suggesting that male immunization will be effective.<sup>36</sup>

Certainly if herd immunity against HPV is to be achieved and virus transmission interrupted effectively, then boys, as well as girls, should be immunized. However, all the efficacy trials have included women only and there is no efficacy data in men available although trials are ongoing. The arguments against vaccinating boys against the oncogenic HPVs are based on health economic considerations and cost effectiveness.

In a heterosexual population, the spread of HPV infection can be stopped entirely by complete protection of one sex alone and dynamic simulation models of HPV transmission show that if high coverage of females can be achieved, there is little to be gained in the additional reduction of cervical cancer by vaccinating males.

### **Issues of introduction of the vaccine in a developing country like India**

**Cost and delivery issues:** The current cost of over USD \$100 -120 per dose with three doses required to achieve full protection is prohibitive, but manufacturers have declared their willingness to tier prices for countries of different economic settings. There will also be the issue of vaccine delivery as this is an injectable vaccine and 3 doses are required to be given over a six month period.

**Social, religious and cultural issues :** Our social and cultural values will make it difficult to vaccinate young girls against a sexually transmitted disease though its main aim is to prevent cancer in women. Acceptability of the vaccine will be questioned by religious fundamentalists who feel that giving a vaccine against an STI will “give permission” for their children to become sexually promiscuous. They are also very confident that “their” children will not have sex before marriage, so do not need the vaccine. They have to be explained that 1) even virgins can be infected by their husbands soon after marriage 2) HPV can spread through nonpenetrative sexual intimacy 3) sexual abuse cannot be predicted.<sup>37</sup>

Rumors that TT is an anti-fertility vaccine since it is only given to young girls and women had a very negative impact on the mass immunization campaign in Mexico, Philippines and Uganda.<sup>38</sup> Similar rumors against oral polio vaccine has badly affected the polio eradication

program in countries as diverse as India and Nigeria.

**Parent education:** Educated parents will have many questions and one needs to deal with them in a scientific manner.<sup>39</sup> Most parents will worry that giving such a vaccine can amount to giving permission for their daughter to be promiscuous. As health professionals we have to allay their fears saying that this is just like the unjustified fear about giving sex education in schools that it will cause sexual experimentation .Parents have to be explained that this is not a vaccine against all sexually transmitted diseases but only those that cause cervical cancer that is a killer disease for Indian women .

### **Service delivery: SRH and AFHS centers**

Women who attend SRH ( sexual and reproductive health) services will have to be motivated to get their daughters for the vaccination.<sup>40</sup> AFHS (adolescent friendly health services) will have to play a major role in not just giving the vaccines but also giving sex education and safe sex practices.<sup>41</sup>

Vaccine delivery will need cooperation between the SRH community, the cancer prevention community and the Obstetrics and Gynecology specialists who are generally nonvaccinators with the traditionally vaccinating community ie, the pediatricians and the family physicians.

### **Resource material for HPV disease and vaccine**

There is a very interactive website for those who want to know more about the HPV vaccine HPV vaccine Global community of practice :at [http:// hpv-vaccine.net](http://hpv-vaccine.net)

WHO website has very good publications which can be freely downloaded 1) cervical

cancer and HPV and HPV vaccines. Key points for policy maker and health professionals.  
 2) Preparing for introduction of HPV vaccines. Policy and programs for countries.

### Points to Remember

- *HPV causes considerable disease burden in India. Cervical cancer is the leading cause of incidence and deaths in India.*
- *HPV types 16 & 18 accounts for approx. 76% of all cervical cancer cases in India.*
- *Cervical cancer is a preventable disease and vaccines along with screening play an important role in reduction of this disease.*
- *The quadrivalent vaccine will also reduce anogenital warts, VIN 2/3, VaIN 2/3. A lot of funding will be required to introduce the vaccine in our public health programs where it is most required.*

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**BOOK REVIEW**

Name : Radiologist talks to you

Editor : Dr.Elizabeth John

Review : The most popular articles published under the column of “Radiologist talks to you” serially in IJPP is now brought out as the “IJPP Series - I”.

Interpretation of X-ray has almost become a part of extended clinical examination. For clinicians having a vast knowledge in radiology is not sensible and a simple. It would be of immense help if salient and comprehensive practical guidelines to interpret skiagrams is given for day to day practice. This is a long felt need among pediatricians, which is being fulfilled by the “Radiologist Talks to you” as “IJPP series - I”. Normal X-rays and others that are likely to be missed in clinical Practice are covered in this series. The X-ray picture quality is good. This book apart from imparting radiological interpretation skill to the reader, will definitely serve as an important desk top reference for the busy pediatric practioner and will be a must have book for every pediatrician.

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<b>GENERAL ARTICLE</b>
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**GYNECOMASTIA****\*Anju Virmani**

**Abstract:** *Gynecomastia is abnormally large breasts in males, common in neonates, adolescents and the elderly. It is caused by altered balance of circulating estrogens and androgens or increased sensitivity of breast tissue to normal estrogen levels. Pathologic causes include conditions with increased estrogen, decreased androgen, medications, chronic renal or hepatic disease, etc. If breast development occurs before nine years or is present without other evidence of puberty, a complete work up is required. Physiological pubertal gynecomastia resolves spontaneously. In others, identifying and treating the underlying cause is important. Options of medical, surgical and radiation therapies are to be considered, depending upon the situation.*

**Key words:** *Gynecomastia, Etiology, Diagnosis, Treatment.*

Gynecomastia is the presence of abnormally large breasts in males, due to increased glandular tissue, and may be unilateral or bilateral; symmetrical or asymmetrical. It is a physiological event quite common in neonates, adolescents, and the elderly. In adolescent boys it can cause considerable psychological distress, even though it subsides spontaneously in 1-2 years. Physiologic gynecomastia can be diagnosed with

a good history and examination, and a few screening lab tests, and managed with reassurance. If persistent, it can be treated medically or corrected surgically. Rarely it may be due to hypogonadism or systemic disease or even rarer, due to malignancy or due to a tumor elsewhere. Treatment of the underlying condition is then required in them. Breast prominence due to increased adipose tissue is called lipomastia or pseudogynecomastia.

**Definitions**

Gynecomastia is abnormal enlargement (> 1 cm) of one or both breasts in men, with or without galactorrhoea, which is due to increased ductular tissue. If the breast tissue is more than 5 cm in size, it is called macromastia. Enlargement of breasts due to increased adipose tissue is called lipomastia or pseudogynecomastia. The two can usually be distinguished by careful clinical examination. Glandular breast tissue feels firm, rubbery and grainy, and may be very tender, while adipose tissue is soft. Often both adipose and glandular tissues are increased.

**Description**

The condition is fairly common<sup>1</sup>, and is almost always benign and temporary. It occurs in 60-90% neonates, due to the high levels of maternal estrogens, and subsides in a few weeks if left undisturbed. Similarly, during puberty, this physiologic phenomenon occurs in 3-70% males<sup>2</sup>. Typically, pubertal hypertrophy occurs at Tanner pubic hair stage 3-4, at ages 11-15 years; it is often tender and subsides spontaneously in a year or so<sup>3</sup>.

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## Pathophysiology

In males, estrogen (estrone and estradiol) comes mainly from conversion of androgens (testosterone and androstenedione) by the action of aromatase in muscle, skin, and adipose tissue<sup>4</sup>. Gynecomastia is caused by an altered balance of circulating estrogens and androgens, or by increased sensitivity of breast tissue to normal estrogen levels. The balance could be altered by increased serum estrogen level, decreased serum androgen level, or both. For example, during early puberty, serum estrogen levels may rise sooner than testosterone, leading to gynecomastia. This regresses as androgen levels rise later in puberty, restoring the normal androgen to estrogen balance<sup>5</sup>. Local tissue factors like increased local aromatase activity, decreased local estrogen inactivation, decreased local conversion of testosterone from androstenedione or changes in androgen or estrogen receptors absence of such receptors may also be important. Prolactin probably causes gynecomastia indirectly through hypogonadism. Several other hormones like progesterone, LH/hCG, growth hormone, IGF-1 and other growth factors, may have minor roles to play. Similar to female breast development, estrogen causes proliferation of ductules and stroma, with increased vascularity. In early stages, the ductular component is prominent, with loose stroma, where as in later stages, stromal fibrosis predominates, with few ductules. At this stage, medical therapy is unlikely to be effective<sup>6</sup>.

## Causes

Identifiable causes are found in less than 3% of boys, almost all being due to adolescent breast hyperplasia<sup>2</sup>. In recent years, increasing numbers of adolescents use anabolic steroids for body building (eg. androstenedione, used as a performance enhancing food supplement). These steroids are converted by aromatase to estrone and lead to gynecomastia. The clinician should

always tactfully check the possibility of steroid abuse with the adolescent because a history may not be directly available, and young boys are especially susceptible to estrogens, developing gynecomastia even with small exposures<sup>7</sup>. Various environmental factors can cause gynecomastia. Food<sup>8</sup>, ingestion of milk or meat from estrogen-treated cows, endogenous estrogens in foods (plant and animal sources), from parents' exposure (report of gynecomastia in children of a man working in a factory manufacturing estrogens, who absorbed the drug from their father's clothes<sup>9</sup>), or lavender and tree tea oils<sup>10</sup> have all been speculated to have estrogenic and antiandrogenic activities.

Potential pathologic causes of gynecomastia (Table 1) include conditions causing increased estrogen, decreased androgens, medications, chronic renal or hepatic disease, HIV and other chronic illnesses<sup>11</sup>. Medications which can cause gynecomastia include hormone treatment (estrogen, androgens, anabolic steroids, estrogen agonists, antiandrogens such as spironolactone and finasteride, or androgen-synthesis inhibitors), antibiotics (isoniazid, ketoconazole, metronidazole); anti-ulcer medications (cimetidine); cancer chemotherapeutics (especially alkylating agents); cardiovascular drugs (captopril, digitoxin); psychoactive agents (diazepam, tricyclic antidepressants); recreational drugs (alcohol, marijuana); and penicillamine. Usually stopping these medications rapidly leads to regression of the gynecomastia, but if it has been long standing, surgery may be required.

Klinefelter syndrome (KS) is the most common chromosomal disorder associated with hypogonadism and infertility in men; gynecomastia is seen in 50-70% cases<sup>12</sup>. KS is the only cause of gynecomastia in which there is a clearly established increase (20-fold) in the risk of developing breast cancer; compared with

**Table 1. Causes of gynecomastia****A. Estrogen excess**

1. Exposure to exogenous estrogens
  - a. Exposure to estrogens or drugs with estrogen like activity (eg. digitalis)
  - b. Accidental exposure to estrogens: dietary exposure (estrogen contaminated meats, phytoestrogens, soy, alcoholic beverages), occupational, estrogen containing cosmetics.
2. Increased endogenous estrogen production
  - a. Increased secretion of estrogens: from testis (Leydig cell tumors, hCG secreting tumors eg in lung, kidney, GI tract) or adrenals (feminizing adrenocortical tumors); drugs that enhance estrogen synthesis (eg. gonadotropins, clomiphene, phenytoin)
  - b. Increased aromatization of androgens to estrogens: aromatase excess syndrome, drugs (eg. androgens, ethanol), obesity, hyperthyroidism, hCG-secreting tumors, Peutz-Jeghers syndrome.

**B. Androgen deficiency**

1. Primary hypogonadism
  - a. Klinefelter syndrome
  - b. Congenital anorchia
  - c. Testicular infections (eg. mumps orchitis, leprosy), trauma or radiation
  - d. Destruction or inhibition of Leydig cells (chemotherapeutic/cytotoxic agents eg. alkylating agents like vincristine, methotrexate, nitrosoureas, cisplatin, imatinib)
  - e. Disordered enzymes of testosterone biosynthesis: drugs (eg. ketoconazole, spironolactone in high doses, flutamide, finasteride and dutasteride, etomide,

metronidazole, cimetidine), or inherited defects in androgen biosynthesis.

f. Kallmann syndrome

2. Secondary hypogonadism

- a. Pituitary/hypothalamic disease/surgery/radiation
- b. LHRH agonists/antagonists
- c. Possibly highly active anti retroviral therapy (HAART)

**C. Altered serum androgen/estrogen ratio**

1. Puberty
2. Aging
3. Refeeding after starvation
4. Renal failure and dialysis
5. Hepatic cirrhosis
6. Hyperthyroidism
7. Drugs
8. Chronic illnesses, eg HIV, leprosy

**D. Decreased androgen action**

1. Drugs (eg. spironolactone, ketaconazole, cimetidine)
2. Androgen receptor (AR) defects: absent or defective ARs (complete and partial androgen insensitivity syndromes); or expansion of CAG repeats in AR gene (Kennedy disease).

**E. Miscellaneous**

Increased serum prolactin (eg antipsychotics, metoclopramide, possibly calcium channel blockers) or unknown mechanisms (INH, methyl dopa, busulfan, antidepressants, diazepam, amphetamines, HAART, growth hormone, amiodarone, penicillamine, omeprazole, phenothiazines, ACE inhibitors, alcohol, marijuana, and heroin)

normal men<sup>13</sup>, so these boys and men should be encouraged to perform periodic breast self-examinations to look for any suspicious breast masses. In normal males, breast carcinoma is rare, peak incidence being in the age group 50-60 years<sup>14</sup>.

### **Clinical evaluation**

A thorough clinical history is important (Table 2). The age of onset and duration of breast enlargement and presence of discharge or change of shape of nipples should be documented. Any history of mumps, testicular trauma, alcohol or drug abuse, use of local applications or drugs (eg. prescription medications or over-the-counter medications), or history suggestive of hypogonadism, and family history of gynecomastia should be asked for.

Tanner pubertal staging, including thorough breast examination (size, consistency, mobility from underlying tissues, nipple discharge, axillary lymphadenopathy) and testicular examination (size, consistency, presence of nodules, asymmetry) are needed. True gynecomastia must be distinguished from lipomastia. If the examiner puts thumb and index finger on each side of the breast and slowly brings them together, glandular tissue is felt in true gynecomastia. Evidence of feminization (including body hair distribution and eunuchoid habitus), chronic liver disease, thyroid disease, or renal disease should be looked for.

### **Diagnosis**

A newborn with breast enlargement should be followed up closely; no investigations are needed if the breast tissue regresses spontaneously in the first few weeks. Similarly, a boy with age-appropriate physical and sexual development and no suspicious clinical features does not need further evaluation, and should simply be followed up and reassured that

spontaneous regression is likely<sup>15</sup>. If breast development occurs before the age of nine years or is present without other evidence of puberty, a complete workup is required (Table 2). If enlargement is tender, progressive, hard or fixed to underlying tissue, there is a bloody discharge, breast size is >5 cm or there is lymphadenopathy, a mammogram or ultrasound followed by a fine needle aspiration or tissue biopsy should be done. Serum chemistry may be done to look for renal or liver disease. If feminization syndrome is suspected, serum testosterone, leuteinizing hormone (LH), estradiol and dehydroepiandrosterone sulfate should be done. If hyperthyroidism is suspected, TSH and T4 should be done. If a testicular neoplasm is suspected, a testicular ultrasound and further workup should be done.

### **Differential diagnosis**

1. Male breast cancer: This condition is fortunately very rare<sup>16</sup>, except in those with an inherited germline BRCA2 mutation (100 times greater risk), KS (10-20 times greater risk), or family history of breast cancer in female relatives (2.5 times greater risk). It should be suspected only if there is a hard eccentrically located asymmetric mass, fixation to the skin or underlying structures, ulceration, axillary lymphadenopathy, or a bloody nipple discharge. A suspicious mass should be biopsied (Table 2).

2. Diabetic mastopathy: This has been described with long-standing type 1 diabetes<sup>17</sup>. It may be unilateral or bilateral, painless or painful, discrete mass or diffuse nodularity, especially in the subareolar region. The exact mechanism is unclear, though autoimmunity is suspected to play a role, as lymphocytic infiltration of the mammary ducts and lobules, with varying degrees of fibrosis and vasculitis is seen. It may regress spontaneously, but often persists and may recur after excision.



**Table 2. Workup of gynecomastia**

<b>A. History</b>	d. Signs suspicious for breast cancer
1. Breast related	2. Genital examination
a. Duration of breast enlargement	a. Testes: size, presence of masses
b. Presence of breast pain	b. Phallus size; pubic hair, Tanner staging
c. Change in nipple shape; bloody discharge.	3. General
2. Puberty related	a. Degree of virilization: facial and body hair, muscular development, voice
a. Presence and duration of pubic, axillary, facial hair	b. Body proportions: normal or eunuchoid
b. Gonadal changes, libido, erections	c. Evidence of chronic hepatic/ renal disease
3. Evidence of systemic illness	d. Evidence of hyperthyroidism
a. Recent rapid weight loss or weight gain	e. Abdominal masses
b. History of chronic hepatic, renal or thyroid disease	<b>C. Investigations</b>
4. Use of drugs	1. Liver and kidney function tests, TSH
a. Performance enhancers including over-the-counter food supplements	2. Serum testosterone, LH, FSH, estradiol, prolactin: if indicated
b. Prescription drugs	3. Adrenal androgens (DHEA-s or urinary 17 ketosteroids): only if indicated
c. Recreational drugs	3. Tumor markers for germ cell neoplasms ( $\beta$ hCG, $\alpha$ -fetoprotein): only if indicated
d. Dietary or accidental exposure to estrogen, eg. cosmetics used by or occupation of family members or patient	4. Mammogram/ breast ultrasound and biopsy/ FNAC of breast tissue: only if breast malignancy suspected
<b>B. Examination</b>	5. Ultrasound of testis and biopsy: only if testicular malignancy suspected
1. Breast examination	6. Abdominal CT scan: only if adrenal malignancy suspected
a. True gynecomastia or lipomastia	
b. Tenderness	
c. Size of tissue	

3. Dermoid Cyst,
4. Hematoma,
5. Lipoma,
6. Lymphangioma,
7. Neurofibroma

### Prognosis

Pubertal gynecomastia is not a medical problem by itself, with over 90% cases resolving spontaneously in few weeks to 2 years. There may be pain, and often social and psychological difficulties. Gynecomastia due to an underlying

treatable cause usually responds well to treatment or removal of the cause. Rarely, it indicates a dangerous underlying condition, which will require treatment. Macromastia does not resolve completely, and requires surgical correction.

## Treatment

Physiologic pubertal gynecomastia is a benign problem which resolves in 1-3 years in almost 90% cases. However, affected boys may become anxious about teasing and become aloof and anti-social, or try to hide the chest by avoiding T-shirts, swimming and activities involving exposure. They may not be willing to discuss the problem with parents or peers, so empathy and communication are important to tackle the situation. In most cases just reassurance to the adolescent and parents that it will regress spontaneously, and regular follow up, may be enough. Mild pain can be reduced with paracetamol.

Identifying and treating an underlying cause is important, because this usually causes regression. For example, if the cause is a prescription drug, it can be substituted; if a recreational drug (alcohol, marijuana, heroin) or a drug being abused for so called enhancement of performance (anabolic steroids), its use should be discouraged; if an environmental factor is found, its exposure stopped.

If the cause is primary or secondary hypogonadism, parenteral or transdermal testosterone replacement therapy is needed, which will cause resolution of gynecomastia. Testosterone enanthate can be given intramuscularly every 2-4 weeks in the dose of 200-300 mg. Transdermal patches used once daily may be scrotal (4-6 mg) or nonscrotal skin patches (5 mg). Occasionally testosterone exacerbates or causes gynecomastia by being aromatized into estradiol. To avoid this, nonaromatizable androgens like DHT have been

tried, systemically and topically (DHT gel applied to the breast)<sup>18</sup>. If Klinefelter syndrome is diagnosed, appropriate counseling about future risk of breast cancer and need for regular followup should also be provided.

If obesity is present, this gives an excellent opportunity to counsel weight loss with regular exercise and avoidance of junk foods and other high calorie foods. Losing weight does not reduce the glandular breast tissue but can improve appearance along with improving general health and self-esteem. Care should be taken to counsel against massive weight loss, which can result in sagging and drooping chest tissues.

If the boy has a high level of anxiety and social stress, or marked pain and tenderness, medical therapy can be attempted. Treatment basically can aim to block estrogen effect (selective estrogen receptor modulators (SERMs) that act as estrogen receptor antagonists at breast tissue eg. tamoxifen, raloxifene, clomiphene), decrease estrogen production (aromatase inhibitors eg. testolactone, anastrozole), counteract estrogen effect (androgens). Medical intervention is likely to be effective only in the initial 1-2 years; with time as fibrosis increases, tissue becomes less amenable, and surgery (liposuction, gland excision, skin sculpture, reduction mammoplasty, or a combination of these techniques) remains the only option. Radiation therapy to prevent gynecomastia prior to estrogen therapy, and compression garments to camouflage chest deformity and stabilize bouncing tissue are also options which have been offered.

**Medical treatment** : 1. Tamoxifen, an estrogen antagonist, in doses of 10-20 mg twice a day for 3-9 months, is effective in upto 90% recent-onset and tender gynecomastia. It is well tolerated, nausea and epigastric discomfort being the main side effects<sup>19</sup>. If gynecomastia recurs on stopping

the medication, a second course of therapy may be attempted.

2. Raloxifene in a dose of 60 mg/d for 3-9 months, has been reported to be more effective than tamoxifen in adolescents<sup>20</sup>.

3. Clomiphene, in a dose of 50-100 mg per day for up to 6 months, has been used earlier, giving partial reduction in about half the patients, and complete reduction in 20%. Side effects are rare, and include visual problems, rash, and nausea.

4. Danazol is a synthetic derivative of testosterone, which suppresses gonadotropins, and thus decreases testicular estradiol production. It can cause complete remission in less than a quarter patients, in a dose of 200 mg twice daily. Adverse effects include weight gain, acne, muscle cramps, fluid retention, nausea, and abnormal liver function test results.

5. Testolactone, an older peripheral aromatase inhibitor, was used in doses of 150 mg 3 times per day for 6 months. It is less effective than tamoxifen, and can cause nausea, vomiting, edema, and worsening of hypertension, epilepsy and migraine.

**Surgical treatment** : Medical therapy is more likely to fail in long-standing gynecomastia, as the stroma becomes more fibrotic. Surgery is the preferred treatment in such adolescents, as well as in those who do not tolerate medical therapy. Surgery, usually done on an outpatient basis under general anaesthesia, involves excision of the glandular tissue by means of a periareolar incision, with or without suction lipectomy<sup>21</sup>.

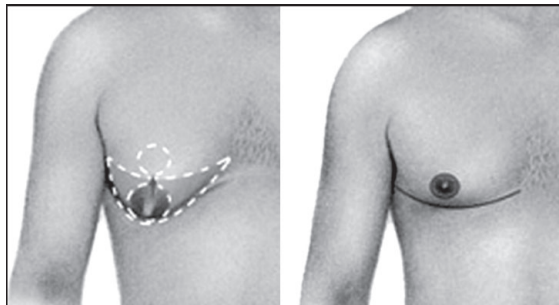
1. Reduction mammoplasty can be advised to patients with macromastia, long-standing gynecomastia, or those with failure of medical therapy.

2. Liposuction may be needed in patients with lipomastia.

3. Excision and repositioning of the nipples may also be needed in patients with excessive sagging of the breast tissue due to marked weight loss (Fig.1).

Complications of surgery include bleeding excessively, scarring, healing poorly, nerve, skin or muscle damage, sensations of skin changes and the sensation of the nipple loss.

**Radiation therapy** : Radiation therapy to the breast, used in men with prostate cancer before starting antiandrogen therapy, was also tried in the past to treat pubertal boys with gynecomastia, but the longterm risk of breast cancer after radiation exposure is a significant concern.



**Fig.1. Excision and liposuction**

### Points to Remember

- *Gynecomastia is a common asymptomatic finding in the newborn and adolescent.*
- *Only reassurance is required in majority as spontaneous regression is the norm.*
- *Emotional disturbances may occur in adolescents.*
- *Early onset of breast enlargement, unusual clinical findings and large breast size are the indications for further evaluation with lab investigations.*
- *Medical or surgical therapy may be required in appropriate situations.*

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## DERMATOLOGY

### SCABIES AND PEDICULOSIS IN CHILDREN

\* **Vijayabhaskar C**

**Abstract:** *Scabies and pediculosis are common infestations seen in day to day practice. These two conditions do not respect any socio economic status. When there is a classical presentation there is no difficulty in diagnosis. But scabies does not always present in the classical way. "Eyes does not see what the mind does not know". Hence one should always remember to rule out scabies in any child presenting with itching and rule out pediculosis if recurrent impetigo occurs in the scalp. Topical permethrin and oral ivermectin has revolutionized the treatment of scabies and pediculosis. General measures such as the treatment of all contacts and washing of linen in hot water play an equally important role as application of the scabicide.*

**Key words:** *Scabies, pediculosis, itching, permethrin, ivermectin*

In this article we will deal with the most common conditions we see in our office practice, ie. Scabies and Pediculosis.

#### SCABIES

Human scabies caused by mite *Sarcoptes scabiei* var. *hominis* is highly contagious. It is an obligate parasite to humans.

Scabies spreads due to intimate personal contact or sharing of inanimate objects<sup>1</sup>. Dogs

and cats may be a source of human infestation<sup>2</sup>. This disease is not a disease of the poor and does not respect any socioeconomic status.

The adult mite is 0.5mm long and has a flattened oval body with wrinkle like, transverse corrugations and has eight legs.

Infestation occurs when a fertilized female mite arrives on the skin surface. Within an hour, the female excavates a burrow in the stratum corneum. It can extend from few millimeters to a few centimeters. Eggs are laid in the burrow averaging 2 to 3 per day along with scybala which are the fecal pellets. This scybala may be responsible for some of the itching. Larva hatches and matures in 14 to 17 days. The adult mite copulates and the cycle is repeated. The itching is initially mild and localized and as the load of the mite increases it becomes intense and generalised.

At any given time, the number of mites may vary from half a dozen to one and half dozen. Mite can survive away from human skin for more than a week.

Transmission occurs during direct skin to skin contact with an infected person. Patient starts scratching which aids in destroying the burrows and removal of mites providing initial relief. Scratching can spread the mites to other areas and after 6 to 8 weeks patient may develop intense generalised itching.

#### Clinical manifestation

Primary lesion in scabies is burrows which are easily noticed in the web spaces and mites

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are seen in them or at the edge of vesicles. Most of the primary lesions get destroyed during scratching. Burrows are linear, curved or S shaped and may vary from 2 to 15mm in length. At the end of the burrow one can see a slightly elevated vesicle. Vesicles or pustules are seen over the palms and soles in case of infants. Common sites of burrows are finger webs, wrists, sides of hands and feet, penis, buttocks, scrotum and palms and soles of the infants. Sometimes papules are seen which are discrete and rarely contains mite in it and it is due to the hypersensitive reaction.

Lesions of scabies are typically found in the finger webs, wrists, extensor surface of the elbows and knees, sides of the hands and feet, axillary areas, buttocks, waist area and ankle areas. In males the penis and scrotum and in adolescent females the breast including the areola and nipple may be infested.

In infants, the lesion may be slightly different from adults or adolescents. In infants infestation occurs over the face and scalp. Vesicles are common over the palms and soles which is a highly characteristic sign of scabies. Secondary eczematization and impetiginization are common but burrows are difficult to find. Nodules may be seen on the diaper area and axillae.

The initial symptom in scabies is itching, particularly at night. When itching prevails for certain time and if not identified and treated it can lead to secondary impetiginization, erosions, excoriations and crusting of skin.

As discussed earlier, itching is classical. When a person comes in contact with mite for the first time, the itch may take weeks to develop due to the hypersensitivity reaction to the mite, fecal pellets and eggs. This is one of the reasons why all family members may not develop the itching at the same time.

If a person who is treated for scabies gets reinfected, then the itching may appear within a few days as his or her body is previously sensitized to the mite and other products.

Mostly, in male children the genitals are invariably involved with small papules. Even if a single papule over the genitals it is more in favour of scabies.

In most of the cases, other family members may be suffering from itching but if no other family member suffering from itching it still does not rule out scabies.

## **Types of scabies**

**Classical scabies:** The above mentioned features fit into the classical scabies.

**Clean man scabies:** Here itching would be the only symptom but there may not be any secondary impetiginization as they are very clean. No scabetic lesions are seen. Strong suspicion and itching in other family members will aid in the diagnosis of scabies.

**Scabies of infants and newborn:** One may not see the burrows but involvement of face and scalp will be present. Palms and soles will show vesicles and pustules.

**Scabies incognito (in disguise):** There is a tendency to use steroids for relief of itching if the cause is not found. This can aggravate the scabies but the itching may be masked and the lesions may change its morphology. Once steroids are stopped the lesion may appear in a severe form.

**Norwegian scabies or Crusted scabies:** Here the lesions tend to involve the hands and feet with asymptomatic crusting rather than the typical inflammatory papules and vesicles. There may be thick subungual keratotic material and nail dystrophy. Grey scales and thick crusts may be

seen over trunk and extremities. Hair may be shed profusely<sup>3</sup>. It occurs in those with neurologic or mental disability. In children, it is commonly seen in Down's syndrome, leukemia and in children with immunosuppression. Itching may be absent or very severe. Lack of immunity and indifference to pruritis may be the cause for this condition. In contrast to the classical scabies, the number of mites in the body may be in millions.

**Animal scabies:** This is a disease transmitted from pet animals like dogs and cats. They are caused by different species. Papules are seen over the areas of contact with pet animals like forearms, abdominal and thigh region. These mites may not survive for long in human skin.

**Nodular scabies:** Brownish, itchy, deep seated nodules may be seen over the male genitalia and inner aspect of thigh. These are resistant to treatment.

## Diagnosis

It is mainly a clinical diagnosis with typical symptoms, characteristic lesions and distribution.

### Identification of burrows

To enhance burrows for better visualization the surface of web spaces can be touched with a drop of mineral oil or blue or black ink. Then area is cleaned with alcohol swab. If there is a burrow, it absorbs the ink and is highlighted as blue or black line. These areas may be scraped away with a curved #15 scalpel blade and transferred to a slide for microscopic viewing<sup>3</sup>.

## Differential diagnosis

**Papular urticaria:** Here lesions are seen mostly over the exposed areas like the extremities and the covered areas are spared.

**Atopic Dermatitis:** History and associated features will aid in the diagnosis of atopic dermatitis.

## Treatment

It should be compartmentalized as treatment of the condition, complications and general measures.

Some of the medicines like crotamiton, 25% benzyl benzoate have not been dealt as better drugs are available now.

First and foremost the advice is to apply the medicine to all the family members and contact persons irrespective of their itching status.

### For infants below 2 months of age

Only sulfur ointment may be used. It can be prepared by a chemist. 3 to 5% precipitated sulfur in petrolatum or a cold cream base is applied to the entire body below the neck once each day for three days. Baby is given bath every 24 hours after each application and it is highly effective and safe. The sulfur preparation is messy, stains the clothes, stings and has an unpleasant odor and cause dryness<sup>4</sup>.

### For infants above 2 months, children and adolescents

**5% Permethrin cream:** The dermal cream of choice for treatment of scabies in children. One application is said to be effective but a second application one week later is recommended. It should be applied below the neck all over the body and in case of lesions present over the face, may be applied over the face (avoid application over eyes and mouth). The nails should be cut short and medication applied under them vigorously with a toothbrush. It should be washed after 12 hours of application. In case of infants, it should be washed 8 to 12 hours after the application. Inform the parents that the infestation may disappear with the first application of medication but the itching may persist for 2 weeks or rarely more than that due to the hypersensitivity. In infants and young children,

use of socks may be advised to prevent finger and toes sucking. Prescribe antihistamines for more than 2 weeks and reassure the parents.

**1% Gamma benzene hexachloride:** It is a central nervous system stimulant that produces seizures and death in the scabies mite. It has to be applied in the same way as permethrin but has to be avoided in children below 2 years of age. Approximately 10% of gamma benzene hexachloride is absorbed through intact skin and can accumulate in fat and binds to brain tissue if used for prolonged period<sup>3</sup>. If there are secondary impetiginous lesions it is better to avoid this drug or to treat the impetigo before application of the drug. The application of this medicine is same as for Permethrin except that it should not be used over the face.

### Oral therapy

**Ivermectin:** This drug can be used alone or in combination with topical preparation. It should be used in children weighing above 15 kgs or above 5 years of age with a dose of 0.2mg/kg body weight on day 1 and day 15<sup>5</sup>. The itching starts improving within 48 hours of treatment. In case of crusted scabies, treat with topical permethrin and oral ivermectin.

**Management of secondary infections:** Treat the impetiginous lesions with appropriate topical and systemic antibiotics.

**Post-scabetic pruritis:** After successful anti scabetic treatment, continue oral antihistamines. If inflammatory lesions are still present topical steroids can be used along with anti histamines. If itching is intractable, short course of systemic steroids will definitely help<sup>3</sup>. Kindly do not use steroids before the anti scabetic therapy<sup>3</sup>.

**Nodular scabies:** Persistent nodular lesions over the scrotum after successful treatment of scabies are treated with intralesional steroids

(triamcinolone acetonide 10mg/ml)<sup>3</sup>. These nodules may persist for months together if not treated.

### General measures

All clothes and bedding in contact with the patient should be washed in hot water or put in a hot dryer at the time of application of medicine.

### PEDICULOSIS

**Definition :** It is active infestation of the hair on scalp and eyelashes by the parasite *Pediculus humanus capitis*.

### Incidence and prevalence

Incidence is higher in children compared to adults and more prevalent in the developing countries. Peak age group is between 4 and 11 years. High incidence of infestation is seen in longer and medium hair. M:F ratio is 1:2. Kindly note that pediculosis also does not respect any socio economic status.

### Pathogenesis

It is an eternal parasite with obligatory blood feeding habit. The life cycle starts with eggs which are attached to the hair shaft by gel secreted by the female louse. The egg hatches in 6 to 10 days, goes into nymph stage, molts 3 times, matures in 9 to 14 days and becomes an adult. Adult louse mates as soon as it matures and lays eggs within 1 to 2 days and lays up to 100 eggs in an average lifespan of 30 days. Within half a minute it can get transmitted from head to head. It can survive in water for 4 hours in a dormant stage.

### How does the transmission occur?

Transmission is by prolonged head to head contact. It is found predominantly in the occiput and this area in the scalp is called as louse pit. It can also be found on the eyelashes.

Transmission occurs in crowded living conditions. This louse is not responsible for any human disease<sup>6</sup>. There is no evidence of poor personal hygiene aggravating the disease.

## Symptoms

In most cases particularly in the initial stages, there are no symptoms. Pruritis can start 12 weeks after the infestation. Scratching can lead to secondary bacterial infection. If there is severe louse infection for one to one and half years it can cause general systemic reaction of malaise and generally feeling “lousy”. Generalized itching of scalp and nape of neck with intense itching is present at night.

## Signs

- Visualization of nit found within ¼ inch of the hair from the scalp.
- Visualization of adult louse.
- Presence of pruritic papules on the nape of the neck or around ears.
- Look at the eyelashes for the parasites.

## Diagnosis

It is mostly clinical. Identification of eggs, nymphs and lice with naked eye or magnifying glass is possible.

## Treatment

1% Permethrin and 1% Lindane may be used.

**1% Permethrin** is available as crème rinse. It is a neurotoxin to lice but less toxic to humans as absorption rate is very low. Initially clean the hair with shampoo and dry with towel. Apply the lotion over the hair, behind the ears and over the nape of the neck. Leave it on only for 10 minutes and rinse with water. Comb with fine toothed

comb to remove dead lice, eggs and nits from hair. Repeat the application after 7 days. All family members are advised to apply the medicine on the same day. Do not use in infants below 2 months of age.

### **1%Gamma benzene hexachloride lotion:**

Use when permethrin is not available. It is a pediculocide and not ovicidal. Do not use in children less than 2 years of age. It is neurotoxic to pediculi. Apply to dry hair 30 ml for short hair, 45 ml for medium hair and 60 ml for long hair and the contact time is for 4 to 5 minutes only. Massage the hair with little amount of water and then rinse the hair. Dry the hair with towel and use comb with fine tooth to remove the dead lice and the eggs.

### **Combination of 1% permethrin with cotrimoxazole:**

When there is resistance to treatment, a combination of topical permethrin crème rinse with oral cotrimoxazole for 10 days is used<sup>7,8</sup>. Cotrimoxazole is not a pediculocide directly but as blood is sucked by the parasite it enters the gut and kills the bacteria in the gut of the parasite which has symbiosis with the parasite thus killing the pediculi.

### **Oral Ivermectin:**

Ivermectin for children weighing above 15 kgs or above 5 years of age can be used with a dose of 0.2mg/kg/dose on day 1 and day 10.

Treat the secondary impetigo with appropriate antibiotics and if itching is severe, anti histamines can be used.

### **Non pharmacological therapy:**

Remove the nits using nit combs for 2 weeks. Mechanical removal of lice with a wet comb is an alternative. Add olive oil over the hair and comb the hair. Do it every 4 days for several weeks. Hair saturated with vinegar and water in 1:1 ratio applied and removed within 15 minutes may help to unglue nits.

Petrolatum jelly like vaseline when applied to the hair and left overnight with a shower cap may kill the lice due to suffocation of the lice. But it will not kill the eggs hence it has to be repeated weekly for 4 weeks.

### Eye infestation

Vaseline is taken on the fingertips and rub the petrolatum slowly into the lids and brows 3 times each day for 5 days. Ask the child to close the eyes before the application.

Baby shampoos can be applied to the eyelashes and eyebrows with a cotton swab three times each day for 5 days.

In older children, if they demand removal, it could be done by making the patient recline and asking the child to close the eyes the lice can be plucked from the eyelashes with a forceps.

Fluorescein drops (10% to 20%) applied to the lids and eyelashes has immediate toxic effect on the lice.

Both scabies and pediculosis though common sometimes are difficult to diagnose unless we have a close watch on the lesions. We have to reassure the parents and our job does not end in writing the prescription but explaining them thoroughly to follow the prescription.

### Points to Remember

- *Rule out scabies in a child with itching unless proved otherwise.*
- *Think of pediculosis in recurrent impetigo of the scalp in a child.*

- *Appropriate medicines and mode of application to be taught to the parents.*
- *Treat all contacts in both the conditions.*
- *Reassure the patient and parents that the itching may last over a period of 2 to 4 weeks.*

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**PICTURE QUIZ**



Can you spot the diagnosis?

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**Answer on Page: 375**

## RADIOLOGIST TALKS TO YOU

### NEURAL TUBE DEFECTS

*\* Vijayalakshmi G*

*\*\* Elavarasu E*

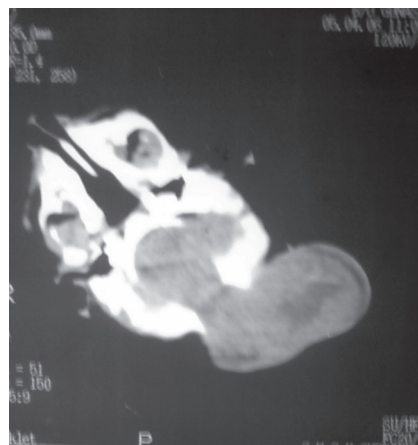
*\*\*\* Vijayalakshmi M*

*\*\*\* Venkatesan MD*

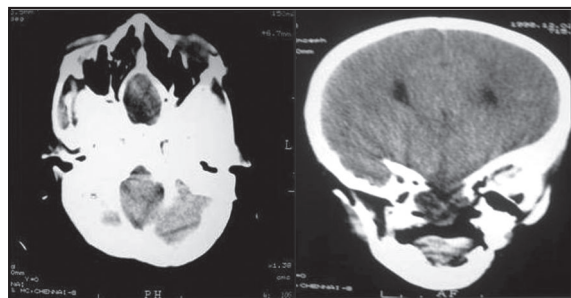
The early central nervous system begins as a simple plate which folds to form a groove and then closes to become a tube. Failure of this closure results in neural tube defects. Normally the brain and spinal cord are covered and protected by the skull and vertebrae.

Neural tube defects consist of gaps in this protective covering that leave the neural tissue open to damage.

When the neural tube fails to close at the head, the result is anencephaly where brain is not formed at all. When there are gaps in the skull, parts of the brain and its meninges bulge out. Fig 1 is an encephalocele diagnosed postnatally. There is a large gap in the occipital bone through which a part of the brain has herniated. Cranial ossification is complete by 10 weeks after which the skull defect and sac can be demonstrated by ultrasound. The majority of encephaloceles are occipital. A few may be frontoethmoidal or sphenoidal. Fig 2 is a trans-sphenoidal



**Fig 1. Occipital encephalocele**



**Fig 2. Trans-sphenoidal encephalocele**

encephalocele. There is a large gap in the sphenoid bone with neural tissue bulging through it into the nasopharynx.

When there is an opening in the spine, the meninges and the CSF can balloon out of the spinal canal to form a meningocele. The spinal cord is in its normal location. If the spinal cord also enters the sac then it is called a myelomeningocele.

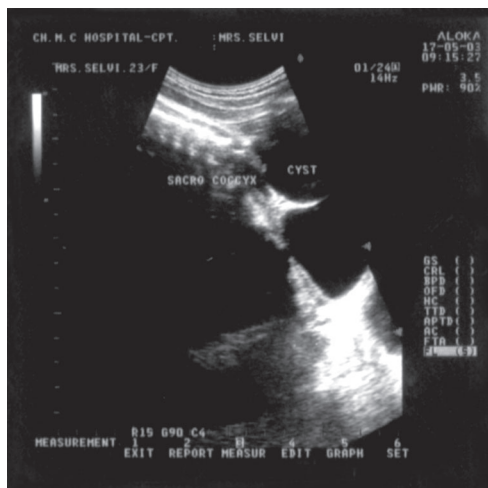
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\* Associate Professor

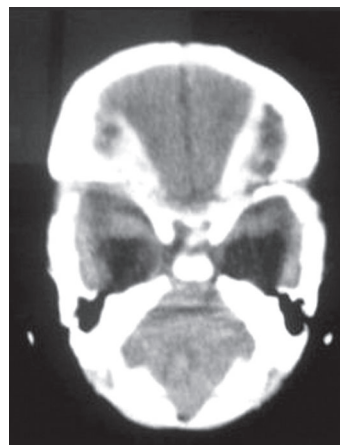
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\*\*\* Professor

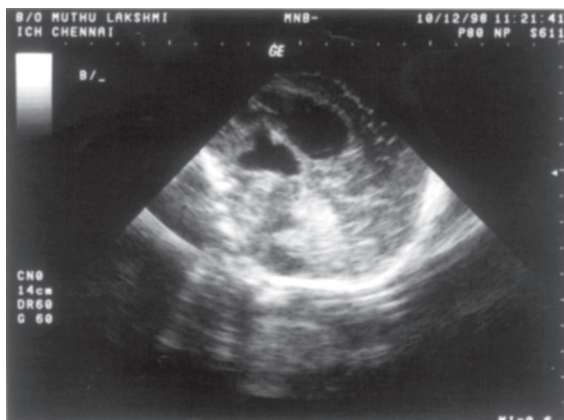
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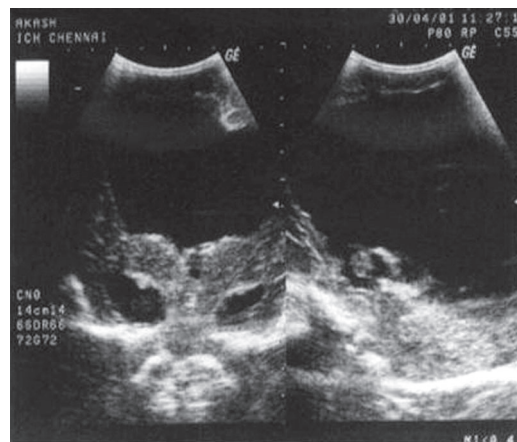
**Fig 3. Sacro-coccygeal teratoma**



**Fig 4. Arnold Chiari malformation. The 4<sup>th</sup> ventricle is not seen. Dilated temporal horns are seen**



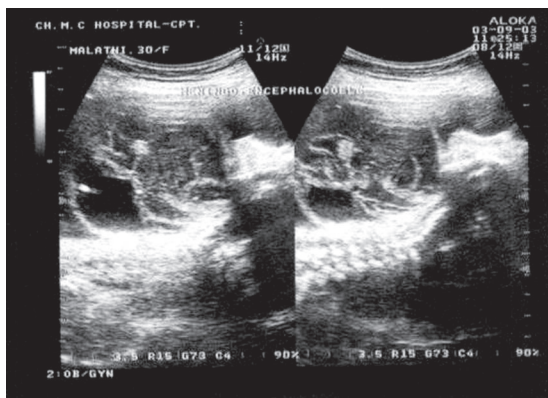
**Fig 5. Normal midsagittal view. Note the cisterna magna at the base**



**Fig 6. Arnold Chiari malformation. Cisterna magna is not seen. Note dilated 3<sup>rd</sup> and lateral ventricles**

Fig 3 shows a multilobulated cystic lesion in the sacro-coccygeal area. This is actually a cystic sacro-coccygeal teratoma diagnosed antenatally. A meningocele appears just like this but it is located higher in the spine, commonly lumbosacral. In addition, the spine appears different. In the longitudinal scan of a normal spine the ossification centres of the two pedicles

appear as two parallel echogenic dotted lines. (Fig 3 and Fig 7). The ossification centres of the vertebral bodies are seen as a third dotted line. In meningocele there is a splaying of the parallelly placed echogenic dots, ie. the pedicles are widely spaced. The soft tissue defect and the cystic meningocele or meningomyelocele will also be seen.



**Fig 7. Arnold Chiari malformation Type 3**

Those with meningocele may also have Arnold Chiari malformation where the cerebellum protrudes into the upper spinal canal because the posterior fossa is too small. The 4<sup>th</sup> ventricle is not visualized (Fig. 4). because it is thinned, elongated and partly displaced into the cervical canal. In ultrasound the normal cisterna magna is seen as a triangular black

shadow in a midsagittal section (Fig.5). This is absent in the Chiari malformation as the cerebellum dips down compressing and obliterating that cistern. (Fig 6).

Hydrocephalus is a frequent accompaniment as is seen in the same figure and in Fig 4. The lateral and third ventricles are grossly dilated.

Fig 7 is an antenatal scan of a high cervical encephalomeningocele into which, the medulla, 4<sup>th</sup> ventricle and cerebellum have been pulled. This is a Type 3 Chiari malformation.

These malformations that we saw are disorders of dorsal induction which is the first stage in the formation and closure of the neural tube. They are therefore very early events and are complete by 28 days of conception. With the advent of ultrasound, this problem acquired significance because these conditions can be diagnosed in utero and termination of pregnancy is possible thus reducing long term morbidity.

**Answer to Picture Quiz :** Cleidocranial Dysplasia

### NEWS AND NOTES

**International Association for Study of Obesity  
Organizes**

**5<sup>TH</sup> ASIA OCEANIA CONFERENCE ON OBESITY (AOCO)**

**Renaissance Convention Centre, Mumbai.**

**February 6<sup>th</sup> – 8<sup>th</sup>, 2009**

**Special Focus : CHILDHOOD OBESITY**

**Internationally Accredited Obesity Certificate Course – 5<sup>th</sup> & 6<sup>th</sup> Feb, 2009**

**Specialist Certificate of Obesity Professional Education (SCOPE) Course – 6<sup>th</sup> Feb, 2009**

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**Organizing Committee :** Dr.K.Ramamoorthy / Dr.Ramen Goel

**Scientific Committee :** Dr.H.B.Chandalia

**Conference Office :** AOCO – 2009

125, MRC Building, Bombay Hospital, New Marine lines, Mumbai – 400020

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<b>CASE STUDY</b>
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**BRAIN STEM  
ACUTE DISSEMINATED  
ENCEPHALOMYELITIS IN  
CONGENITAL  
AGAMMAGLOBULINEMIA  
IN A CHILD**

\* **Riaz Ahmed**

Acute disseminated encephalomyelitis (ADEM) is a monophasic fulminant demyelinating illness of the CNS, days to weeks following viral infections or immunization, with high morbidity and mortality. MRI brain study is one of the mainstay in the diagnosis.<sup>1</sup> This illness is said to be immunologically mediated and so intravenous immunoglobulin and /or steroids are sometimes used in the treatment with varying results.<sup>2</sup> Although circulating immune complexes are thought to play a role in the pathogenesis of ADEM, no specific type of immunological dysfunction or the mediators have been described so far.<sup>3</sup> A wide variety of neurological illnesses including demyelination secondary to invasion of central nervous system is a well known phenomenon with human immunodeficiency virus (HIV1) infection<sup>4</sup>. Severe congenital humoral and cellular immunological disorders could present with a picture of chronic encephalitis with gliosis of brain-stem rarely resembling demyelination<sup>5</sup>. Common variable immunodeficiency disorder causing sub acute spinal cord degeneration had also been reported in an adult<sup>6</sup>. Congenital

B cell deficiency disorder is characterized by hypo gammaglobulinaemia with absence of circulating B cells, presenting at early age with frequent infections by extracellular pyogenic organisms and enterovirus invasion<sup>4</sup>. Demyelinating illness of the CNS is not reported in this disorder and we are presenting a boy with the above illness with evidence of acute brain-stem demyelination.

**Case Report**

A six year old boy, presented with inability to move and speak while he woke up from sleep. He was suspected to have primary B-cell deficiency disorder in early infancy as he had suffered from recurrent episodes of pyogenic infections, including meningitis. The diagnosis was confirmed by serum protein electrophoresis and quantitative assay of immunoglobulins; since then, he was on regular monthly immunoglobulin injections. On examination, he was conscious but could not communicate clearly and the voice also became faint, unintelligible. His neurological status revealed bilateral 6<sup>th</sup> and 7<sup>th</sup> Nerve paresis (LMN), and involvement of 9,10,11 and 12<sup>th</sup> cranial nerves. He had features of decorticate posturing and bipyramidal signs. The primary care physician who saw him first, diagnosed as brain-stem tumor and referred him to neurosurgery department as the CT brain revealed hypodense lesion in the pons. MRI brain showed hyperintense T2 signals in both pons, midbrain, bilateral thalamus and left cerebellum. HIV screening was done and was found to be non reactive. Lumbar puncture was not performed initially because of the primary care physician's concern of possible pontine

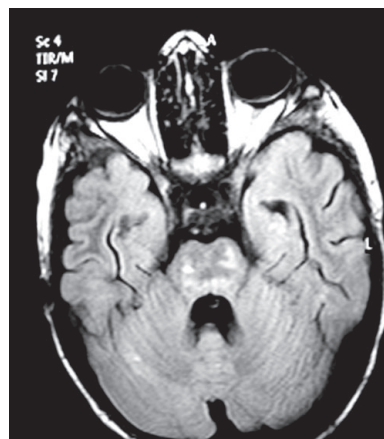
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**Fig. 1. T2 weighted axial view showing ADEM lesion in pons with pseudo hypertrophy**



**Fig. 2. T1 axial view showing clearing of demyelination area from pons.**

tumour, but by the time MRI yielded a diagnostic clue and treatment was started. On the basis of clinical as well MRI findings, ADEM was considered and was given intravenous immunoglobulin (0.4 Gm/Kg) infusion daily, for 5 days. On day 7, a repeat MRI brain showed marked clearing of the above lesions in all extra pontine areas. His neurological status showed only mild improvement; he remained in bed with bilateral pyramidal tract involvement but the cranial nerves showed some recovery. The follow up revealed considerable improvement after 3 weeks and he was able to walk with support and could speak with dysarthria.

## Discussion

In the absence of CNS infection, clinical features and MRI findings of white matter are sufficient to establish the diagnosis of ADEM<sup>3</sup>. Although ADEM affects subcortical whitematter predominantly, brain stem involvement has been reported in few cases<sup>7,8</sup>. Acute demyelination of central and peripheral nerves occurs in many viral infections of central nervous system especially

in HIV1 infection<sup>4</sup>. Congenital B cell deficiency disorder presents primarily with recurrent pyogenic infections including life-threatening sepsis and so regular monthly immunoglobulins is the standard modality of prophylaxis in such patients<sup>5</sup>. These patients are prone to develop lymphoreticular malignancies in the 4<sup>th</sup> or 5<sup>th</sup> decade of life. ADEM as a manifestation, is rare in this disorder and no case of primary brain stem demyelination has been reported so far. The extensive T2 signal in the brain MRI in both pontine and extra-pontine lesions almost rules out brain-stem malignancy, vascular lesions and the repeat MRI did show significant improvement<sup>6</sup>. Though IV immunoglobulins (IVIg) and high dose steroids could modify or cure the disease, IVIg is preferred especially in children because of its equal efficacy, safety and with the advantage of preventing the theoretical exacerbation of viral infections with steroids<sup>7-10</sup>. With our previous experience of treating ADEM patients in our institute, we preferred IVIg than high dose steroids because of the above reasons as well as to avoid steroid induced side effects. The anti-inflammatory effects of these agents are



suggested to contribute to the clearing of CNS lesions, as well as to the clinical response.

## Conclusion

Isolated brain- stem involvement in ADEM is a rare entity in children and no such cases have been reported in patients with congenital agammaglobulinaemia. Our patient though diagnosed late, did show improvement after IVIG in the MRI images and follow up study revealed improvement in clinical status. This case is presented for its rarity of the occurrence.

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## NEWS AND NOTES

### X1th National Conference of Pediatric Infectious Diseases

#### X1th NCPID – 2008

Organized by : Indian Academy of Pediatrics, Varanasi.

22<sup>nd</sup> & 23<sup>rd</sup>, November 2008

Venue: Hotel Ramada, Varanasi.

Registration Fee: Rs.2000/-till 31<sup>st</sup> July 2008

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<b>CASE STUDY</b>
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## **VALPROATE INDUCED REVERSIBLE HYPER-AMMONEMIC ENCEPHALOPATHY**

**\* Sai Sampath K Natuva**

**\*\* Badri V K**

Valproic acid (VPA) is effective in the treatment of seizure disorders, bipolar disorder, migraine headache prophylaxis, neuropathic pain, restless legs syndrome, dementia-related agitation, and social anxiety disorder among other conditions. Hyperammonemic encephalopathy (HE), with or without hepatic failure, is a rare but serious adverse effect of valproate therapy<sup>1,2</sup>. Children younger than two years, those with urea cycle defects or carnitine deficiency and those on multiple AED's are predisposed to valproate-induced HE with hepatic failure<sup>2</sup>. However, hepatic dysfunction is notably absent in majority of patients with valproate-induced HE<sup>3,4</sup>. The typical presentation of VPA-induced hyperammonemic encephalopathy (VHE) is acute onset of impaired consciousness, confusion, lethargy. These initial signs may progress to ataxia, stupor, and coma. Although the incidence of VHE is unknown, mild and reversible elevations in ammonia have been described in 16-52% of patients receiving VPA<sup>5</sup>. Here we depict a case report of VHE in a 8 yr old boy, with no history of underlying liver disease with

normal VPA levels. Because of the wide spectrum of symptoms associated with VHE, physicians should consider hyperammonemia in the differential diagnosis of any patient taking VPA who shows changes in behavior, cognition, or orientation.

### **Case Report**

A 8 year old male child, born to non consanguineous parents and with normal birth and developmental history, had idiopathic generalized epilepsy since the age of 6 years. He was on phenytoin 50mg bid for two years. His seizures had been well controlled with phenytoin without any adverse affects. As he developed fixed drug eruptions (Phenytoin induced), therapy was switched over to VPA 200mg once daily. Six weeks after the institution of the VPA patient presented to the neurology department, with recurrent episodes of vomiting, refusal of food, irrelevant talk, fearfulness, abusing attendants, resisting parents and family members. There was no history of fever, exanthematous lesions, trauma, recent vaccination, toxin and anesthetic exposure.

On examination child was irritable, resisted examination, with ill sustained attention. He had no pathological reflexes and no meningeal irritation. His fundi were normal, pupils were symmetrical and reacting to the light. His vital signs and rest of the neurological examination was normal. Results on initial investigation, including complete blood picture, serum electrolytes, liver and renal function tests and ultrasound abdomen were normal. Peripheral smear did not reveal any hemoparasites or

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malignant cells. Creatinine and albumin levels were normal. CSF analysis showed 2 lymphocytes, proteins 35 mg/dl and glucose 55 mg/dl. The results of chest x ray and MRI brain were unremarkable. The patient's sodium valproate level was within therapeutic range. An electroencephalogram (EEG) showed diffuse slowing of background activity consistent with metabolic encephalopathy. Subsequent tests revealed elevated venous ammonia level [158 (normal 12-47)  $\mu\text{mol/L}$ ]. His liver function tests were normal, thus valproate-related hyperammonemic encephalopathy was suspected. Valproate therapy was immediately discontinued, and patient was started on Topiramate 50 mg bid. Subsequently over the three days, the child became oriented, playful, well attentive, and cooperative. Ammonia declined to normal level ( $38\mu\text{mol/L}$ ). EEG showed normalization of the background activity.

## Discussion

Patients with VHE present with varying degrees of cognitive and behavioral dysfunction. They may also be asymptomatic. One case report described a young man with increased aggressiveness<sup>6</sup>. Elderly people may present with worsening dementia. Others may become comatose. Seizure activity may increase and three deaths have been reported<sup>7</sup>. Other anticonvulsants may potentiate the effects of VPA. Phenobarbital, phenytoin and topiramate may increase ammonia levels in people taking VPA<sup>8,9</sup>. Patients with VHE may have no other laboratory derangements other than an elevated serum ammonia. VPA levels may be normal and do not necessarily correlate with the degree of hyperammonemia or the severity of symptoms. Electroencephalograms show generalized slowing and increased epileptiform discharges.

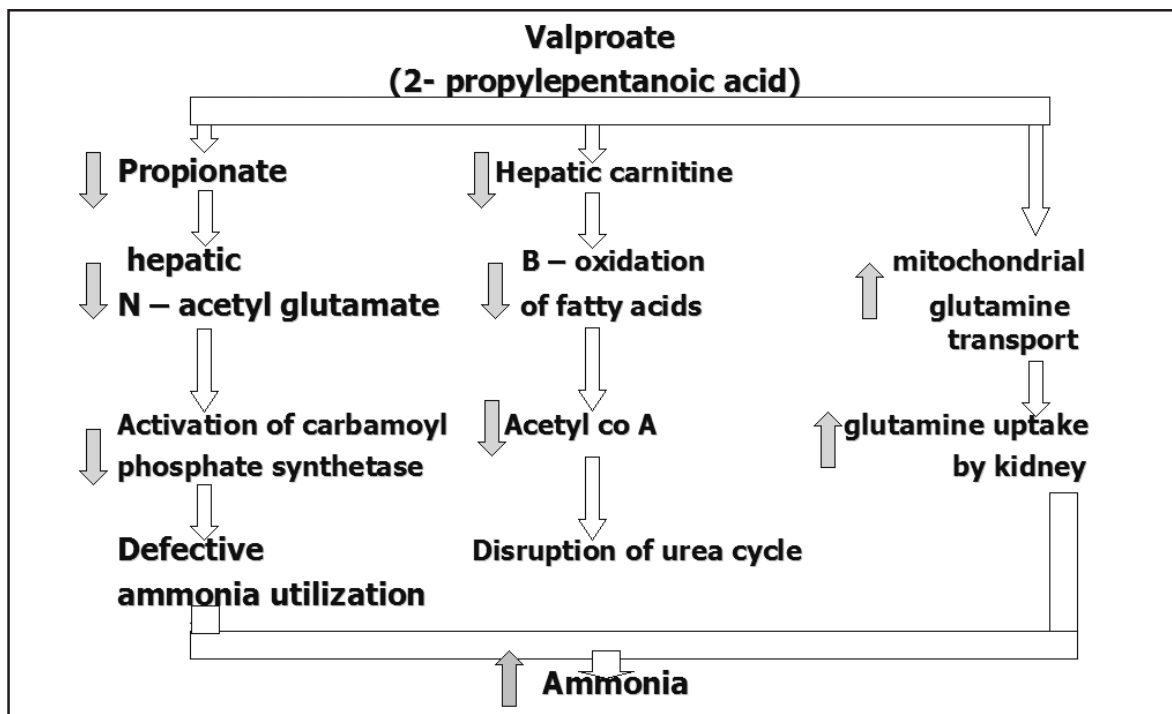
**Table 1. Non-hepatic causes of hyperammonemic encephalopathy**

<b>Inherited defects of enzymes in the urea cycle</b>	<b>Drugs</b>
<ul style="list-style-type: none"> <li>• Ornithine carbamoyltransferase deficiency</li> <li>• Carbamoyl phosphate synthetase deficiency</li> </ul>	<ul style="list-style-type: none"> <li>• Valproate</li> <li>• 5-fluorouracil</li> <li>• Asparaginase</li> <li>• Salicylate</li> <li>• Halothane</li> <li>• Enflurane</li> </ul>
<b>Defects in fatty acid oxidation</b>	<b>Other metabolic causes</b>
<ul style="list-style-type: none"> <li>• Systemic carnitine deficiency</li> <li>• Acetyl coenzyme A dehydrogenase deficiency</li> </ul>	<ul style="list-style-type: none"> <li>• Hyperinsulinemic hypoglycemia</li> <li>• Distal renal tubular acidosis</li> <li>• Organic aciduria</li> <li>• Congenital lactic acidosis</li> </ul>
<b>Hematologic disease</b>	<b>Other</b>
<ul style="list-style-type: none"> <li>• Multiple myeloma</li> <li>• Acute myeloblastic leukemia</li> <li>• Hematologic disease from allogeneic bone marrow transplantation</li> </ul>	<ul style="list-style-type: none"> <li>• Parenteral nutrition</li> <li>• Reye's syndrome</li> <li>• Urinary tract infection</li> <li>• Portosystemic shunt</li> <li>• Idiopathic</li> </ul>

The primary treatment for VHE is the withdrawal of VPA. Complete recovery generally occurs over a period of 1 day to a few days. VPA causes decreased serum levels of carnitine<sup>10</sup>, which leads to increased levels of ammonia (Fig 1). L-carnitine has also been shown to be effective in reducing ammonia levels and in improving symptoms of hyperammonemia in VPA related toxicities<sup>11</sup>. It is generally safe and may be given orally or intravenously at a dose of 50 to 100 mg/kg/day.

Physicians often attribute encephalopathy and elevated levels of serum ammonia to liver failure. However, other conditions, including valproate-related hyperammonemic encephalopathy, must be considered (Table 1). Unfortunately, few physicians are aware of this rare condition. In our case, the clues to the correct diagnosis were the patient's normal hepatic function and the use of valproate therapy.

Although its pathogenesis is not completely understood, this condition appears to be more frequent among patients with carnitine deficiency and those with congenital enzymatic defects in the urea cycle<sup>5</sup>. VPA induced hyperammonemia may arise because of increased renal ammonia production due to reduced glutamine synthesis. The condition may also be due to the inhibition of carbamoyl phosphate synthetase or the reduction of hepatic ammonia metabolism owing to decreased carnitine availability, which leads to suppression of fatty acid  $\beta$ -oxidation (Fig 1). Collectively, these actions of VPA provide the basis for the development of clinically significant hyperammonemia and offer an explanation for the palliative effect of administered L-carnitine. VHE is seen in both children<sup>12</sup> and adults<sup>9</sup> and it develops within days to weeks after initial treatment. There are many risk factors which increase the valproate toxicity (Table 2).



**Fig. 1. Proposed mechanisms for VPA induced hyperammonemia.**

**Table 2. Risk factors which increase valproate toxicity.**

- Underlying urea cycle enzyme deficiency which increases valproate toxicity<sup>15</sup>
- . Concomitant AED therapy; particularly topiramate increases the risk<sup>16,17</sup>
- . Underlying liver disease<sup>10</sup>
- . High initial dose<sup>11</sup>
- . Longterm valproate therapy<sup>12</sup>
- . Salicylates<sup>12</sup>
- . Strict vegetarian<sup>12</sup>
- . Ureterosigmoidostomy<sup>13</sup>
- . Disorders with reduced albumin synthesis<sup>14</sup>

The mental status change associated with hyperammonemia is not fully understood. However, a likely mechanism is that hyperammonemia stimulates increased glutamine synthetase activity, causing increased production of glutamine in astrocytes. Cerebrospinal fluid and blood levels of glutamine may be elevated in conjunction with hyperammonemia<sup>13</sup>. Glutamine in astrocytes causes an osmotic shift of fluid into the astrocytes, producing astrocyte swelling and cerebral edema<sup>14</sup>.

So VHE is a potentially serious consequence following the use of VPA; physicians should consider this possibility when there is a change in mental status in patients treated with VPA. The primary treatment is withdrawal of VPA; L-carnitine supplementation may decrease ammonia levels which improves the patient's clinical condition.

### Points to Remember

- *VPA can lead to hyperammonemic encephalopathy in children.*
- *VHE may have no other laboratory derangements other than an elevated ammonia.*

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## NEWS AND NOTES

### APLS: The Pediatric Emergency Medicine Course (As per Guidelines of American College of Emergency Physicians) 6-7th December 2007

**Venue: Sir Ganga Ram Hospital, New Delhi**

Registration Fee: Rs 2000/- in favor of 'Ambulatory Pediatrics' payable at Delhi  
(Registration limited to 40 delegates, No Spot Registration)

**Contact: Course Director:** Dr Suresh Gupta, Senior Consultant, Pediatric Emergency Medicine, Dept. of Pediatrics, Centre for Child Health, Sir Ganga Ram Hospital, Rajender Nagar, New Delhi 110060, Phone: 9811426628, 28312656. 28323591

## LETTER TO EDITOR

The recent article “Hematinics in Children” is an eye-opener<sup>1</sup>. The incidence of anemia 50-70% under 15 years & 75% under 5 years is alarming-more so because sufferers have a lower quality of life<sup>1</sup>.

Among factors affecting Iron (Fe) absorption, one more factor needs to be considered. Aluminium (Al) is known to bind to transferrin<sup>2,3</sup>, and thus may affect delivery of dietary supplemental Fe to hemopoietic tissue.

In most Indian kitchens, Al utensils are extensively used for cooking, and this Al enters food<sup>2,3</sup>. Al has been classified as one of the non-essential micronutrients<sup>2</sup>, and while FAO/WHO committee established maximum weekly intake at 7mg/kg body wt, we often ingest 10-100 mg/day<sup>3</sup>. The conviction that this element is harmless for humans, and is quickly excreted with urine<sup>3</sup> may not be true<sup>3</sup>. Studies of environmental toxicology indicate that Al could be a cause of many diseases in humans, animals and plants<sup>3</sup>. Al is readily absorbed in blood and accumulates in brain, bone and erythroid tissue, causing malaise, memory loss, dementia, asterixis, twitches, seizures and encephalopathy<sup>4</sup>. Also it causes muscular pains, osteomalacia, fractures<sup>4</sup>, cardiac toxicity<sup>2</sup> anemia<sup>2,3,4</sup>. Al toxicity results from replacing Mg<sup>++</sup> & Fe<sup>+++</sup> by Al<sup>+++</sup><sup>3</sup>. Al forms phosphates, hexokinase, cholineacetyl transferase, ferrooxidase, etc<sup>3</sup>.

On the other hand, cooking food in Fe utensils is said to increase Fe content of food though debatably<sup>5,6</sup>.

So, while treating Fe deficiency anemia, if instructions are given to parents not to cook/store food in Al utensils, (stainless steels can be used), there will be some improved absorption and utilization of dietary and supplemental Fe.

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