MANAGEMENT OF CHILDHOOD PSYCHIATRIC DISORDERS

Section Editor & Contributor

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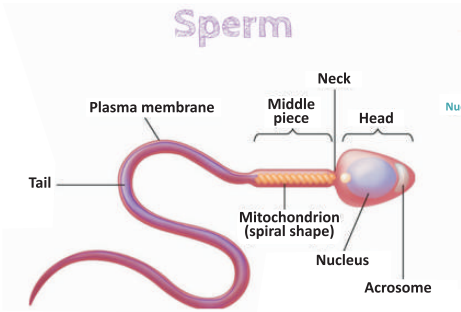
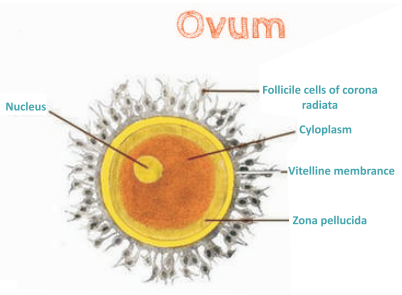
1. CHILD'S GROWTH AND DEVELOPMENT



Structure of Mature Human Spermatozoan



Structure of Human Ovum

Development is a process by which the individual becomes fully functional, acquire knowledge and skills to survive and look after all his needs. These include intellectual, emotional and social skills to live in harmony in the society.

The growth and development of a child occurs in several stages:

1. **Prenatal Stage (Conception to birth of the child)**:

   This stage lasts from 270 to 280 days which occurs in the mother's womb. A new born child is a miniature human being. It weighs 3 to 3.5 kg. All the internal organs start functioning. Pre – mature delivery, low birth weight may negatively affect the growth and development of the child.

   - Genetic Factors
   - Mother's health – ill-health during pregnancy
   - Internal atmosphere in the mother's womb
   - Nutrition of the mother
   - Easy or difficult delivery process resulting in birth trauma

   decide the growth and development of the child. Every school should get information about pre – natal stage of development of the child.

2. Infancy and Toddler State (birth to 3 years):

60% of brain growth takes place during pre – natal state. The brain weighs 300 gms. After birth, there is rapid growth of the brain. The neuronal networking develops at a rapid speed. The child learns to register light / sound / touch. Its starts recognising mother, father, siblings, and differentiate between known / unknown people. It tries to understand what it sees or hears or experiences. It adjusts him/herself to the environment, and fights against disease producing organisms. It learns to sit, stand, walk and talk! It helps him/herself to eat, bathe, acquire control over bowel – bladder movement (urination – defecation), dress – undress him/herself, and avoid common – simple dangers!

3. Childhood Stage 3 to 10 years:

This stage is further divided into:

Early Childhood 3 to 5 years

Middle Childhood 5 to 7 years and

Late Childhood 7 to 10 years

There is physical growth and learning. His/her height and weight keep increasing, language improves. He/She may learn more than one language, learn to read and write and grammar. He/She learns to express emotions in a socially acceptable manner. He/She understands good and bad, right and wrongs. He/She follows social – ethical norms. He/She competes with age-mates and gets motivated to do better than others. He/She takes care of his/her needs.

Intellectual – Cognitive development: During childhood specially middle and late childhood, the child learns to think, analyse, reason it out, understands the concepts, logic *v/s* illogical thinking, reality *v/s* imagination, concrete *v/s* abstract thinking, pros and cons, problem solving and decision making.

4. Adolescence 11 to 18 years:

It is further divided into early adolescence 11 to 15 years, late adolescence 15 to 18 years. This period is vital because the child grows into maturity / adulthood during this period. It is a transactional period between ignorant

childhood and responsible adulthood). Adolescence is considered to be a period of rapid changes in physical, emotional, intellectual, social and ethical growth of the individual. During adolescence, the following issues are considered to be important which influence the development of the individual.

A – Autonomy *v/s* Dependency

Adolescent boys and girls want to be independent and autonomous. They want to do things and behave according to their choices and conveniences. This may lead to friction and resentment between parents and children.

D – Desires and disappointments

Adolescents have innumerable desires, want money, materials, luxuries, entertainments – unlimited! They expect immediate fulfilment of these desires.

O – Old *v/s* /new style of living

They prefer new / modern ways of living with no constraints.

L – Learning Skills and abilities are not properly made use of. They may not be motivated to learn academic subjects or they may lack the ability to learn the chosen subjects or subjects of the course. Poor performance and failure in exam lead to low self-esteem and confidence.

E – Emotionally sensitive, crude in emotional expressions. They may develop a lot of negative emotions like fear, anger, jealousy and depression.

S – Increased interest in Sex: Indulge in excess sexual expressions / act including sexual crimes.

C – Confusion and lack of clarity regarding many issues including goal of education and career.

E – Egoistic: Each adolescent may think that he / she knows everything. - doesn't listen to others views and may show arrogance.

N – Negative attitudes towards the family, education system and society.

T – Targets: They may have un-realistic, high targets or ambitions or no target / ambitions. They live for the day and drift. No commitment to reach the targets.

Parents should monitor the growth and development. Keep checking the height and weight once in 3 months and note it in a notebook. If the child is under-weight or over-weight, it should be corrected.

Weight and Height chart of a growing child	
Weight	
At birth	3 kg
6 months	7 kg
1 year	9 kg
2 years	12 kg
5 years	18 kg
10 years	28 kg
15 years	40 kg
Formula Ex:	Age x 2 + 8 kg 6 yrs x 2 = 12 + 8 = 20 kg 8 yrs x 2 = 16 + 8 = 24 kg 12 yrs x 2 = 24 + 8 = 32 kg
Height	
At birth	50 cms
6 months	66 cms
12 months	75 cms
2 years	85 cms
5 years	105 cms
10 years	140 cms
Formula Ex:	Age x 7 + 70 cms 8 x 7 = 56 + 70 = 126 cms 12 x 7 = 84 + 70 = 154 cms 15 x 7 = 105 + 70 = 175 cms
Head - Circumference	
At Birth	34 cms
6 months	42 cms
2 years	48 cms
5 years	50 cms

2. Emotional disturbances in children

Emotions are natural reaction to a stimulus. When a need or desire is satisfied, child becomes happy. When a need / desire is not satisfied child becomes sad / angry. Appreciation and rewards bring joy and happiness. Comments, punishments result in sad mood. Imagined or real danger creates anxiety and fear. Separation from parents or known environment leads to anxiety. Discrimination, bad behaviour of others, insults result in anger and resentment. Children express their emotions freely.

Some children are emotionally sensitive and over react. They keep showing emotions for a longer time than others. Some children cannot control their emotions and express them in such a way that they suffer and make others to suffer also. Many do not openly talk about the causes of their emotional reactions. They are afraid to talk and reveal who and what made them to develop a particular emotional reaction. Emotional disturbances lead to trouble some – abnormal behaviour and also lead to poor learning and academic performance.

Emotional disturbances are more common in early and late adolescents.

Sadness and depression

10 to 30% children suffer from sadness and depression. The child who is depressed may show the following features:

1. Child becomes inactive, dull and withdrawn.
2. Loses interest in studies, hobbies, may become irregular to the class and school.
3. Inattentive in the classroom, does not react, does not comprehend, gets confused, and seems to be lost.
4. Crying spells moves to tears easily.
5. Forgetfulness, loses personal belongings and items such as pen, books, money, bag or valuables.
6. Poor learning, memory, performance in tests and examination
7. Remain isolated, does not mix with other children, and does not play.
8. No smile or expression of happiness when appreciated or rewarded.
9. Sometimes remain fearful / anxious

10. Sometimes irritable, sulking, bouts of anger if disturbed by others or when their needs are not met with or when people force him / her to be active.
11. Expresses ideas of hopelessness, worthlessness. Child may say he / she is a burden to the family.
12. Complains pain, weakness easy fatigability. The child may be taken to the doctor with repeated headache, pain in abdomen, chest pain, painful limbs and giddiness. Doctors on examination do not find any damage or defect in the body.
13. Absconding from home, wandering away.
14. Death wishes, self-harming / suicidal ideas / attempt

Causes

- Any loss, separation, failure, frustration, death, rejection, discrimination, needs / desires are not attended to / fulfilled, any negative life event in the family, ill-health / injury.
- Low dopamine / serotonin neurotransmitter in the brain
- Low thyroxine level in the blood

Counselling

Talk to the child, parents, and friends of the child to find out the causative stress factor. Let the child ventilate himself / herself.

Bring these issues to the notice of the parents.

Do not allow the child to be alone. Let someone be with the child all the time.

Reassure the child that you will do everything to solve the problems. Make him / her to feel better by repeated reassurances.

Divert the child's attention towards hobbies, sports, music, dance and other creative activities.

Medicines

Prescribe Anti-depressant drugs which have to be given for 2 or 3 months. Tell the parents to supervise the medication. Generally, these drugs are safe, non-habit forming and no serious side effects.

Involve a professional counsellor if and when it becomes necessary especially if suicidal ideas and deliberate self-harming present.

Fear and Anxiety

Fear and anxiety are very common in children because of their insecurity and lack of physical and mental strength to face common / uncommon dangers. Many situations make them anxious. They are afraid of:

1. Darkness
2. Loneliness, when they have to be alone.
3. Insects / animals
4. Police / police station
5. Strict teachers and parents or guardians
6. Test and examination
7. After making a mistake / breaking the rule
8. Spirits and ghosts
9. Authoritative persons or people who give threats
10. Doctors, injection, hospital
11. Heights, water, fire
12. Taking part in competitions, fear of losing / failing
13. Bullying age mates / school mates

The following children are more prone for anxiety

- Very strict and punitive parents / guardians
- Single parent
- Rejecting and non-loving parents
- Rural families and parents with no / less education
- Lower – socio economic status and lower class groups
- Ill and disabled parents
- Pampered children
- Children who are subjected to physical, sexual, emotional abuse in the past.

- Children with disability either physical / mental
- Children who have diseases which carry social stigma (fits, skin lesions, white patches on the skin)
- Poor performance and failure in examination
- Children who have seen threatening people or exposed to traumatic events like accidents, murders, violence, suicide.

Counselling

Find out when, how and why child feels anxious. Explain to the child the degree of danger and how to feel safe and secure. Each child has to be taught about self-defence and when and how to call for help.

Teach the child simple relaxation- Deep breathing exercises.. Instead of being alone, let the child be with someone.

Tell the child to avoid negative thinking like:

On making a mistake / breaking the law, let the child confess it in front of elders or concerned people. Let him not try to hide it or blame others for the same.

Fearful objects

If they are not dangerous, show it to the child. If they are dangerous, what precautions to be taken like going away, self-defense. Discuss every situation of anxiety and fear with the child and show how to face them.

Medication

There are medicines like tab Propranalol at doses between10mg to 40mg a day for 4 to 8 weeks to combat anxiety

Take the help of a professional counsellor when it is necessary. In severe cases refer to a Psychiatrist.

Anger

Out of all the negative emotions, anger is very troublesome and even dangerous emotion both in children and adults. Anger appears to be commonly seen in adolescents as their frustration tolerance is low and their expectations are more!

Counselling

- Listen to the child and ask him to explain why he is angry, with whom he is angry and what are the issues.
- Avoid making any value judgement about the child or his behaviour
- Ask him to hold on, not to react immediately
- Explain to him that he was to plan to show and exhibit anger in a socially acceptable manner, to avoid causing pain, distress, resentment and anger in others mind
- Tell that his anger is justifiable but exhibiting anger may create more problems for himself and others
- Ask him to count from 1 to 50

  To chant the name of God

  To imagine the picture of God / idol in the mind

  To sing a song

  To draw a picture

  To go out and expose himself to fresh air

  To walk up and down in the garden or whatever he is

  To read a book of his choice

  To write what he feels and his experience
- Allow him to talk to the individual (parents, sibling, friends, teachers or anybody on whom he is angry and has complaints
- Arrange for joint session in which the child and family members exchange their views and opinions
- Prescribe Tranquilizers like RISPIRIDONE 1 to 4mg which will help to reduce anger
- Take professional counsellors help.

Stubbornness

Some children who are pampered at home develop stubbornness. They would like to do what they want. If they are restricted or forced to change they become very angry. They show lot of resentment, show temper and tantrums.

They disobey, give back answers, irritate others, and misbehave. They could blackmail, stop going to school, stop eating, threaten to call the police etc.

Management: Limit setting and love and ignore

Set limit to their demand. Refuse to accept or carry out his demands. Explain to him that his need or demand is unreasonable and you are not going to fulfil it. When he threatens, ignore his threats. Tell him 'I will love you. I will care for you. But we don't like your demands and tantrums'. Stop him firmly if he becomes aggressive / violent.

Give attention, love and fulfil his reasonable demands. Cut down all extra care, luxuries and say you will give extra care if he is not stubborn. Consistent firm handling is required by all concerned. Teach and train him to be satisfied with what he get and let him learn to postpone his needs.

3. Childhood Disorders

There are many common disorders seen in children. They have to be identified and referred to a Child Specialist / Psychiatrist.. The causative factors are related to

a) Genetic Factors
b) Damage to brain / arrested / poor development of the brain
c) Parental separation
d) Wrong and bad parenting, single parenting
e) Under nutrition and nutritional disorders including obesity
f) Severe illnesses like Brain Fever / Fits
g) Physical / sexual abuse and any other traumatic life events
h) Frequent change of school
i) Very strict / punitive teachers and school system
j) Living in a hostel / boarding school / in a relative's house
k) Repeated failures and frustrations
l) Severe negative emotions
m) Mental disorders like Schizophrenia, Bipolar Disorder, Autism

1. **Attention Disorder Hypersensitive disorder (ADHD)**

   Common features are:

   - Very short attention span
   - Not concentrating on any task / activity, easy distractibility
   - Not completing any task, shifts from one task to another
   - Jumping from one activity to the other
   - Falling behind in school and do not participate in school activities
   - Unnecessary behaving in a troublesome manner; do not sit or stand in one place, keep moving around. Keep climbing stairs. Keep displacing articles or even destroying them.
   - High levels of anger, aggression
   - React immediately. Run around carelessly. Walk on the road dangerously. Come in the way of vehicles.
   - No one can predict what they will do next minute
   - Throw away or break articles, or poke others. They do not realise they are spoiling the articles
   - Unnecessarily laugh loudly, talk loudly, cause disturbance
   - They pay no attention to their security. Hence they injure themselves often.

Treatment

1. **Medical treatment:** Atomoxetine, Clonidine, Methylphenidate, Risperidone etc. Any one of these medicines has to be taken for 6 to 12 months, or sometimes for a longer term. These are safe to take. Parents need not worry about giving them to the child.

   These medicines have to be continued even if the child has fever, cough, nausea, loose motions.

2. **Recommend activities to increase concentration and interest**

   Find out what activity interests the child or can hold its attention, do that activity more often. Some examples include:

   - Drawing

- Filling colours in drawings
- Play in sand and water
- Make clay figures and dolls
- Sing and dance
- Play games
- Cancel one specific alphabet in printed sheets
- Separate the grains or coloured beads in a bowl
- Remove the various parts of the toys and reassemble them again
- Water the plants, remove the weeds

With age, symptoms of ADHD reduce. They develop like normal children. Around 5% of children continue to suffer from ADHD and show some troublesome behaviour in adulthood like anger, impulsive behaviour, aggression etc.

2. Conduct Disorder

Some children have conduct disorder from childhood, which continues in teenage and do various degrees of mistakes or commit crimes, shows anti-social behaviour.

- Hiding the truth or telling lies for selfish reasons, or for bad reasons.
- Stealing in their house or in other houses [money, valuables, materials]
- Cheat others, commit forgery
- Hurting others by physical attack or aggression or verbal abuse
- Using vulgar words
- Breaking the rules of the family, school or the society
- Sexual misconduct and crimes
- Teasing other students, or people and feeling happy after insulting them, enjoying destructive acts
- Causing damage to articles at home or outside
- Forming gangs and causing trouble to people, behave like rowdy

- Violence on birds or animals or insects
- Joining local rowdies or anti-social elements. Taking part in their activities and helping carry out such activities
- Chain snatching or robbery, selling stolen goods
- Use and abuse of tobacco, alcohol, ganja and opiates, selling these substances.
- No repentance for these activities

There are many reasons for conduct disorder. More than one reason might cause the child to do such activities

1. Brain damage
2. Mental retardation, not knowing right from wrong
3. Too much love or too much discipline from parents
4. Parents or family members neglecting them
5. No love and affection from family, feeling rejected
6. Being teased by classmates. Stopping going to the school after failing.
7. Parents or others having bad habits or criminal tendencies
8. Neighbours or locality having bad habits or indulging in crimes
9. Joining those who commit crimes for money or for recognition, power and status
10. Parents having material discord and fights

Treatment

Such children have to be corrected with love.. Parents have to be more attentive and try to reform the child. Reward them when they are not naughty. Appreciate them if they behave nicely. Keep them away from friends who commit mistakes. Use the help of those whom the child trusts, to improve the behaviour of the child. Take the help of medicines prescribed by a doctor, for anger, depression or fear.

If the child has dropped out of school or failed, try to see if the child can continue education further. If it is found that the child lacks intelligence or

interest for studies the child has to be admitted for vocational training. Train the child how to behave towards others with courtesy and good manners. Psychiatrist's help may be needed.

3. Autism Disorder

'Autism' is a rare, unusual 'mental disorder' caused by the lack of development of the brain.

Main symptoms

1. Qualitative impairment of reciprocal interaction of the child.
2. Qualitative impairment in verbal and non-verbal communication and imaginary activity.
3. Markedly restricted repertoire in activities and interests of the child.

Some characteristics of Autism include:

- Do not talk, no communication with parents, families, other children.
- Do not pay attention to presence of any others.
- Stay by themselves, get involved in themselves.
- Repetitive pronunciation of some words, sentences. Other words, or something heard from TV serial or advertisement is repeated suddenly.
- Talk with the child, show some toys, but the child will not look at your face. It might stare at your hands or the articles held by you.
- Do not react to others' laughter, cry, fear or anger or any emotion.
- Look for hours together at their hands, fingers or toy they like. Stay serious or laughs to themselves.
- Pull the mother by hand to the kitchen to denote hunger. Touch fruit / food, but does not stay that they are hungry.

Possible causes of Autism could be hereditary, or irregular development of brain [reason not known], or someone in the family might have schizophrenia, or similar diseases.

Solution and treatment

- There is no effective or simple remedy for autism. Tranquilizers like Risperidone might help.

- Counselling and Training: child needs training. It should be taught communication and social skills, and come out of self-involvement, and mingle with others. This skill has to be imparted by trained teachers to parents, and other family members. This is a long term process. We have to wait and watch how much the child improves. Child shows improvement but slowly.
- Contact agencies who help in training autistic children.
- Interact with other families having autistic child.
- Autism is a handicap, contact Dept. of Disabilities for help and guidance.

4a. Eating Disorders

1. Anorexia Nervosa

Feeling that "I will get fat, I have to reduce weight" makes the person stop eating. Low weight leading to extreme malnourishment. If forced to eat, she will eat and then vomit, or take medicines for diarrhoea. This leads to depression, disturbance or cessation of menstrual cycle, anaemia, body becoming skin and bone. There is no clarity on the reason for this disorder. This might arise more in those girls who admire slenderness, or joining the group of very slim girls, who wish to participate in beauty contests, or who wish to join modelling, acting professions.

Treatment: Admission to hospital, nourishment, behavioural therapy will be useful. Antidepressants also will help. The girl has to be encouraged to eat and enjoy the food. She needs counselling regarding her body image and health.

2. Bulimia

Too much eating, untimely intake of high calorie diet [cake, pastry, ice cream, chocolate, sweets, and fried snacks]. The main aspect of this disorder is eating unlimited. This leads to heavy weight, and fatty body.

Feeling of being unappreciated, extreme emotional swings, being the target of extreme punishment or neglect from caregivers, mental pressures, etc..may lead to bulimia.

Treatment: Psychiatric care, behavioural therapy, anti-depressants, tranquilizers or mood stabilizers will help.

3. Pica

Pica is a desire to eat harmful items that should not be eaten. This is manifested mainly in children, teenagers, pregnant women. This causes the person to eat mud, sand, paper, plastic, cotton, cloth, pencil, chalk, cement, hair, wood, leaves, uncooked rice, grains etc. this causes many health issues.

Extreme emotional swings, insecurity, inferiority, supressed aggression or insult causes Pica.

Treatment: Psychiatric care, behavioural therapy, antidepressants will help.

Some girls show symptoms of anorexia nervosa for some time, thereafter bulimia manifests. They need mood stabilizing medicines.

Some children have time periods of not eating specific fruits or eatables or vegetables. At other time periods they avoid not eating some other fruits / vegetables / food items. This is a common occurrence.

Children have to be educated about the benefits of eating fruits / vegetables / home cooked food, and the dangers of eating outside food often. Tell them how hotel and roadside food is unhygienic, may contain chemicals and leads to ill health. Ask your doctor also to advise them. Also, parents and other family members should be role models to the children. They should eat fruits, vegetables and avoid street food / hotel food, so that the children emulate them.

• **EAT MORE** Fruits, vegetables, sprouting beans, egg, fish
• **EAT LESS** Sugar, salt, spices, sweets, creams, fried food, red meat
• **DO NOT EAT** All junk and prepared foods, Cool drinks, Road-side, uncovered foods **DO NOT EAT** in dirty places
Carry home-made food and water when you go out. Avoid hotel food. Wash your hands before you eat.
• Eat along with family and friends. Eat slowly chew well.

4b. Sleep Disorders

Sleep is essential for physical and mental relaxation. Energy is saved during sleep. Growth hormone is secreted during sleep in children.

- Below the age of 5 years children sleep for more than 10 hours
- Between 6 to 10 years, they sleep for 9 to 10 hours
- Between 11 to 15 years they sleep for 8 to 9 hours
- After 15 years they sleep for 7 to 8 hours

Many children do not follow sleep hygiene.

Some children have the following disturbances during sleep.

- They are afraid to sleep alone.
- Take long time to get unto sleep (Insomnia)
- Sleep lightly and waking up frequently during night
- Talk, express emotions, grind teeth, and pass urine during sleep
- Walk during sleep (Somnambulism)

- Have 'Night mares' and 'Night terrors'

  Wake up with fear and appears to be disturbed
- Adolescent boys may have 'Discharge of semen' during sleep
- They may not feel fresh when the get up from sleep
- They may sleep for a long time; wake up very late in the morning
- Sleep during day time.

Teach them sleep hygiene

- Fix the time of sleep in and sleep out time
- Sleep in: 10 to 10.30pm Sleep out: 6 to 6.30AM
- Take easily digestible food items for dinner
- Avoid excess eating
- Relax for 30 minutes before you go to bed. Take bath if you are tired.
- Let the place / room of sleeping be comfortable and clean. Change the bed sheets / pillow covers frequently
- Let the child sleep with some-one else sleeping in the room. Let him sleep with other children or grandparents.
- Light a lamp or put a bed-light in the room
- Let the child avoid seeing horror films or serials where ghosts / dracula (monsters are shown. No serial / film which depicts violence
- Let there be beautiful dolls. Wall hangings, pictures of God / Goddess in the room.
- Play soft music in the room
- Keep comic books, light literature books for reading incase there is delay in getting into sleep.

5. Bed Wetting and Urinary Incontinence

Normally, children learn to control passing of urine between 3 to 5 years of age; however some children do not learn this capacity. Some children learn to control and later, lose the capacity. At night, without knowing, they pass urine, and feel ashamed and cause inconvenience to themselves and to family members. When they go out, if they pass urine in relative's house, it irritates everyone.

There are many reasons for bed wetting:

- Small size of the bladder
- Weak nervous system
- Mental retardation
- Infection of urinary system (urinary tract or urinary bladder).
- Feelings of insecurity
- Anxiety or inferiority complex
- In the evening, drinking lot of water or other liquids along with food, and not passing urine before going to sleep at night.
- Having to sleep alone, separation from loved ones, fear of darkness or ghosts or any evil force
- New place or environment. Thoughts of not being safe
- Being angry with parents, or having a desire to trouble them
- Problems at school: learning issues, lack of cooperation by classmates or bullying, punishment by teachers and the resulting
- Toxins in the body
- Communicate one's anger, resentment in this way.
- Embarrassment, other unpleasant experiences.

Treatment and prevention

- Test the urine and check for infection; if there is infection take treatment for it.
- Comfort and reassurance: the child and the parents should be assured that this is a temporary problem. They need not think that this is a serious problem and they should not worry about this.
- Make the child have dinner by 7 or 7:30 pm; do not give water or fluids before bed-time, and ask the child to pass urine before sleeping.
- Your child should not be told scary stories, ghost / Dracula stories at bed-time; do not allow him to watch scary TV / video programs; rather they should see pleasant movies.

- If your child has to sleep alone, let there be someone with her and a small light to make her feel secure.
- In the middle of the night, make the child get up and pass urine.
- Next day, make a blue ink mark in the calendar if the child has not passed urine. If the child has passed urine, make a red ink mark in the calendar. If the child has not passed urine, show appreciation. Give a reward, if the child has not passed urine on all seven days of the week. If the child had passed urine, inform him / her that there would be no reward. To ensure winning the reward, the child will start controlling herself from passing urine in bed.
- In the daytime, if there is urgency to pass urine, tell the child to control for 5 to 10 minutes. This will train the urinary bladder to hold more fluid, for longer time.
- After 3 to 4 weeks training, there will be better control on urine passing.
- Do not punish or humiliate, or make fun of the child for bed wetting
- Tab Imipramine 25 mg tablet, at 8pm every night for 3 months may be recommended
- If there is a need, take the child to a psychiatrist.

6. Suicides and Para-suicides in Children/Adolescents

More and more children and youngsters are turning their faces towards death all over the world. India has the world's largest youth population – 36 crores. Higher suicidal deaths are being reported from several Indian studies. National crime report bureau (NCRB) says 34.4% of all suicides during 2014 were between 15 to 29 year olds. Suicide of students has risen from 5.5% of all suicides in 2010 to 6.2% in 2014.

Academic pressures, poor performances in examination, frustrations of various kinds, interpersonal relationship problems, the wide gap between desires - expectations and ground hard realities of life appear to push the students with one parent and those whose mothers are working are at a higher risk for suicidal behaviour pointing towards the importance of parents' emotional support and their availability for ensuring the students' capacity to prevail over difficulties and frustrations of life. Parents should

cut down their unrealistic – over expectations about their children in academic and non-academic achievements. Insults, humiliation through open criticisms and punishments have to be avoided both by parents and teachers. When students spend more time with mobiles, TV, internet, friends, recreational activities, parents naturally object to that with anger. Students perceive this as an encroachment into their autonomy. They get angry and use suicidal behaviour as a method of protest and to 'bend' the parents who have control over them. Thus, **para-suicides where adolescents try to communicate their anger and frustration are on the rise**. Wrist-slashing, consuming some available tablets or cleaning agents like Harpic, Dettol or half-hearted hanging are common methods. Parents get scared and are forced to listen to the student.

TV serials, cinema, print media giving wide publicity for suicides and para-suicidal behaviours of celebrities and others appear to motivate youngsters to tread the same path.

***Factors gaining momentum in influencing suicide in children**:*

1. **Alcohol use and abuse** is increasing in youngsters who think that alcohol beverages are a must to enjoy life. More than 50% of them start consuming alcohol. Alcohol increases depression and anger and takes away the wisdom of discriminating good, bad, danger and safety.

2. **Need and greed for luxurious life**:

   Youngsters are after items which are considered to be luxurious including sex. They want to enjoy every minute of their life at any cost. Costly food, fashionable clothes and ornaments, costly vehicles; only a few get them, making the majority to develop jealousy and frustration.

3. **Increased family discords and decreased family size and support**.

   Now a day, more than 70% of families are nuclear families with an average size of 3 to 4 people only. Disputes and discords are on the rise among the parents, and between parents and children. Cooperation is dwindling and confrontation is increasing. Thus many youngsters spend time outside the family and do not get emotional support within the family. They do not share their feelings with their parents.

Domestic violence is on the rise, women and children are subjected to physical, emotional, intellectual abuse. Divorce rates are increasing and leading to emotional distress in youngsters.

4. **Social disorganisation and insecurity**:

All social evils are on the rise. For example:-

- Gap between rich and poor.
- Sex-class-caste-religion-regional discrimination and exploitation
- Corruption, cheating, crimes of all kinds.
- Selfishness among rulers, leaders, celebrities.
- Dwindling moral, ethical values.
- Importance given to money, power, status.
- No protection to common people.
- Misleading mass media.

5. **Increasing ill health**: both physical and mental diseases are on the rise. More than 20% of the population is suffering from depression and anxiety disorders.

***Prevention of suicidal behaviour**:*

- Improve parenting skills, they should show adequate love, support, inculcate discipline in children.
- Schools and colleges, teachers are to be student – friendly. In addition to academic performance, enough emphasis on life-skills education.
- Growing children should be made to select healthy hobbies and recreation.
- Every child must learn to manage frustrations and disappointments. He or she should be trained to understand and adapt to reality.
- Counselling and guidance services have to be arranged in every school / college through teachers and counsellors
- Objective of education should not stop at 'getting a job'. **Goal of education is development of Healthy Personality**.

4. Child Counselling

The child is given advice and suggestions to bring a qualitative change in its:

- **Thinking**: Negative thinking is changed to positive thinking,
  - To become optimistic and develop positive approach,
  - Child is encouraged to think with logic.
  - Think to understand its problems / difficulties,
  - Think appropriately to make right decision,
  - Think what is good, what is bad for him,
  - Think realistically, understand the

  Difference between reality / truth and

  Un-real – fantasy / myth
  - Think rationally and scientifically
  - And avoid superstitions
- **Attitudes**: Attitudes develop over a period of time depending on knowledge, experience and what is taught by others. Negative attitudes are changed to positive attitudes in counselling. Attitudes towards parents, family, teachers, classmates, school, education following norms of the society, work and responsibilities, living style, following ethics and value are changed for better.
- **Emotions**: Negative emotions like anger, fear, sadness, jealousy are identified. They are reduced and child is trained to express these emotions openly in a social acceptable manner. The child is made to avoid crude expressions of negative emotions. The child is encouraged to develop and experience positive emotions like love, friendship happiness and tolerance. Emotional excitements have to be avoided. Emotional equilibrium has to be established. Child is made to feel comfortable with its emotional experiences and expressions.
- **Academic Studies**: Improve his learning, memory and performances in examination by improving:
  i. Concentration
  ii. Motivation

iii. Study techniques

iv. Confidence to face examination

v. Writing and communication skills

vi. Avoid examination fear

To choose and select the appropriate course of career

- **Improve relationship with**

  i. Parents – siblings – other family members

  ii. Classmates - schoolmates

  iii. Teachers and other staff of the school / college

  iv. Significant others in the surroundings / society

- **To develop and get motivated in healthy habits like**

  i. Sports / gym / any physical activity

  ii. Art – music, dance, drawing – painting, decoration, handicraft, creativity, cultural activities

  iii. Yoga – meditation – breathing exercises

  iv. Travelling

  v. Competitions: Debate, essay writing, drama, poetry recital.

- **To give up bad habits like**

  i. Excess use of gadgets (mobile – TV – computer)

  ii. Ragging and bullying others

  iii. Smoking, drinking, doping, gambling, video games

  iv. Gossiping / spreading rumours, making false changes on people, scaring others

  v. Causing damage to property and valuables

  vi. Eating junk foods

  vii. Cheap and unhealthy entertainments

  viii. Watching porno and sex films

- **To develop healthy life style**

  i. Food intake – eating habits: What to eat, when and where to eat, how to eat

  ii. Sleep: To follow sleep hygiene

  iii. Personal and environmental hygiene

  iv. Exercise – physical activities

  v. Stress free and peaceful life

  vi. Mental Equilibrium

- **Goals and objectives**

  Short term, long term and life time goals have to be selected. Honest attempts to reach these goals.

- **Follow ethics and moral values**

  To know right – wrong, good – bad

- **Life skills education**: WHO has recommended the following life skills for every growing child.

  1. Creative thinking
  2. Critical thinking
  3. Problem solving
  4. Decision making
  5. Effective communication
  6. Maintain relationship with others
  7. Self-awareness
  8. Empathise with others
  9. Effective management of emotions
  10. Effective management of stress

NEWBORN AND ANTENATAL SCREENING

Section Editor

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Inborn errors of metabolism are a wide spectrum of disorders that are present since birth. Many o them are debilitating to the new born and some are fatal. Some of these metabolic disorders require certain foods to be avoided, while some require a specific type of diet to be followed, in order to achieve optimal growth and development. These require to be identified at birth, so that the necessary interventions can be initiated early.

The screening of newborns using Tandem Mass Spectroscopy (MS / MS Technology)allows for the detection of more cases as compared to clinical methods of diagnosis alone. This is a powerful technique that has a significant role in the newborn screening programs[1].It permits the detection and quantification of many errors of the amino acids, urea cycle disorders, organic acid and fatty acid oxidation defects. It is possible to do multiple metabolite analyses for the detection of numerous metabolic disorders in a single analytical run.[1]

MS/ MS technology can assist in diagnosing metabolic problems during the newborn period that were previously only diagnosed after becoming symptomatic[2]. This allows for treatment to be initiated when the infant is healthy and also assists in defining the spectrum of clinical disease related to the condition. The technique of tandem mass spectrometric analysis of dried blood spots was first proposed for newborn screening in 1990 by Millington et al [3] .Initially it was used for the screening of numerous inherited fatty acid oxidation and organic acid disorders by a single procedure, but was subsequently extended to amino acids including phenylalanine, and other amino acid . This is done from a single punch of dried blood spot and is capable of detecting several inherited metabolic disorders.

Extent of the problem

Inborn errors of metabolism are higher in children born to consanguineous marriages, those with a positive family history of similar problems or an unexplained death in the family [1]. This could reflect the recessive autosomal trait that is responsible for most IEM's . The lack of early detection as well as lack of parental counselling could result in more than one sibling in the family affected.

Being a phenotypically and genetically heterogenous group of disorders, caused by a defect in the metabolic pathway, leading to a malfunctioning metabolism and or accumulation of toxic intermediate metabolites. The cumulative incidence has been shown to be over 1 in 800, present amongst all ethnic groups and age[4]. To date, more than 1000 different IEM's have been identified. However, with the use of MS technology, it is possible to inexpensively detect over 30 different metabolic disorders with one single blood spot specimen. The sensitivity and specificity pf this method may extend from 99% and 99.95% respectively.

The Inborn errors of metabolism

There are over 1000 inborn errors of metabolism that have been diagnosed to date. The initial screening tests include multi component analysis of body fluids in suspected cases[5]. The list of these errors is mentioned in Tables 1-4 below. The final diagnosis depends on the demonstration of specific enzyme defects and can be further confirmed by DNA studies.

Table 1: Qualitative tests for inborn errors of metabolism

Test	Result	Compound detected	Disorder
Odor	Musty	Phenylacetate	Phenylketonuria
	Maple syrup	2-Oxoisocaproate, 2-oxo-3-methyl valerate	Maple syrup urine Disease (MSUD)
	Sweaty feet	Isovalerate	Isovaleric acidemia
	Cat urine	3-Hydroxyisovalerate	3-Methylerotonyl glyeinuria
Ferric chloride test	Blue-green color	Phenylpyruvate	Phenylketonuria
		Imidazole pyruvate	Histidinemia
		Xanthurenic acid	Xanthurenic aciduria
	Transient blue-green	Homogentisate	Alkaptonuria
	Green-gray	Branched-chain oxaacids	MSUD

Test	Result	Compound detected	Disorder
	Green color	p-hydroxyphenyl pyruvate	Tyrosinemia, types 1&2
Dinitro-phenyl hydrazine (DNPH) test	Golden yellow precipitate	Phenylpyruvate 2-Oxoisovalerate 2-oxoisocaproate 2-oxo-3-methyl valerate 4-Hydroxyphenyl pyruvate Pyruvate	Phenylketonuria MSUD Tyrosinemia, types 1&2 Lactic acidosis
Cyandie Nitro-prusside test	Magenta color	Cystine Homocystine	Cystinuria, hyperarginemia, Homoeystinuria
Bendediet's test	Brick red precipitate Brown ppt	Glucose Galactose Fructose Xylose 4-Hydroxypheny pyruvate Oxalic acid Homogentisate	Diabetes, Fanconi synd Galactosemia Fructose intolerance, Essential fruetosuria Pentosuria Tyrosiemias, types 1&2 Hyperoxaluria Alkaptonuria
Strip test for ketones (Ketostix)	Positive	Accione, butanone, accloacclate, 2-methy lacetocetate	3-Oxothiolase defect, popionic acidemia, methylmalonic acidemia
Berry spot test	Purple ring	Mueopolysaceharides	Mueopolysaceharidoses

Table 2: Metabolic disorders detectable in newborns aged 1-5 days by using tandem mass spectormetry

Disorder	Primary metabolic indicator
Amino Acids	Phe
Phenylketonuria	Leu/Ile, Val
Maple syrup urine disease	Met
Homocystinuria (cystathione synthase deficiency)	Met
Citrullinemia	Cit
Argininosuccinic aciduria	Cit
Tyrosinemia, type I	Tyr
Fatty Acids	
Medium-chain acyl-CoA dehydrogenase deficiency	C8, C10, C10:1, C6
Very-long-chain acyl-CoA dehydrogenase deficiency	C14:1, C14, C16
Short-chain acyl-CoA dehydrogenase deficiency	C4
Multiple acyl-CoA dehydrogenase deficiency	C4, C5, C8:1, C8, C12, C14, C16, C5DC
Carnitine palmitoyl transferase deficiency	C16, C18:1, C18
Carnitine/acylcarnitine translocase defect	C16, C18:1, C18
Long-chain hydroxy acyl-CoA dehydrogenase deficiency	C160H, C18:10H, C18OH
Trifunctional protein deficiency	C160H, C18:10H, C18OH
Organic Acids	
Glutaric acidemia, type I	C5DC
Propionic acidemia	C3
Methylmalonic acidemia	C3
Isovaleric acidemia	C5
3-hydroxy-3-methylglutaryl CoA lyase deficiency	C5OH
3-methylcrotonyl CoA carboxylase deficiency	C5OH

Notes : The list of primary metabolic indicators is not all-inclusive and serves only as a guideline. It is based on results obtained from laboratories experienced in tandem mass spectrometry technology and that serve as diagnostic metabolic laboratories in the United States and other countries. The identified disorders have been detected from analyses of dried blood-spot specimens collected during the newborn period. Certain disorders require complex metabolic profiles and intermetabolic relation to detect disease with low false-positive and not false-negative rates.

Fig. 3 Enzymes in the diagnosis of lysosomal storage disorders

Disorder	Affected Enzyme	Tissue
Sphingolipidoses		
GM_1 gangliosidosis	b-Galactosidase	S, L, F
GM_2 gangliosidoses-Tay Sach Sandhoff	b-Hexosaminidase A	S, L, F
Metachromatic leukodystrophy	Arylsulfatase A	S, L, F
Krabbe leukodystrophy	Galactoccrebrosidase	L, F
Fabry disease	a-Galactosidase A	S, L, F
Gaucher disease	Glucoccrebrosidase	L, F
Niemann-Pick disease, A & B	Sphingomyelinase	L, F
Farber lipogranulomatosis	Ceramidase	L, F
Mucopolysaccharidoses		
Hurler disease (MPS I-H)	a-L-iduronidase	S, L, F
Scheic disease (MPS I-S)	a-L-iduronidase	S, L, F
Hunter disease (MPS II)	Iduronate 2 - sulfatase	L, F
Sanfilippo, A (MPS IIIA)	Heparan N-sulfatase	L, F
Sanfilippo, B (MPS IIIB)	a-N-Acetylglucosaminidase	L, F
Sanfilippo, C (MPS IIIC)	Acetyl CoA : a-glucosaminide acetyltransferase	L, F
Sanfilippo, D (MPS IIID)	N-Acetylglucosamine-6-sulfatase	L, F
Morquio, A (MPS IVA)	N-Acetyl galactosamine-6-sulfatase	L, F
Morquio, B (MPS IVB)	b-Galactosidase	L, F
Maroteaux-Lamy (MPS VI)	N-Acetylgalactosamine 4-sulfatase	L, F
Sly syndrome (MPS VII)	b-Glucuronidase	S, L, F

Disorder	Affected Enzyme	Tissue
Glycoproteinoses		
a-Fucosidosis	a-Fucosidase	S, L, F
a-Mannosidosis	a-Mannosidase	L, F
b-Mannosidosis	b-Mannosidase	L, F
Sialidosis, type I	a-Neuraminidase	L, F
Galctosialidosis	a-Neuraminidase & b-Galactosidase	L, F
Schindler disease	a-N-acetylgalactosaminidase	L, F
Aspartylglueosaminuria	Aspartylglucosaminidase	L, F
I-cell disease & Pscudo-Hurler Polydystrophy (Mucolipidosis, II & III)	All lysosomal enzymes elevated in plasma except b-glucosidase	S, F
Other storage disorders		
Wloman disease	Acid csterase	L, F
Pompe disease	Acid maltase	Muscle

Abbreviations : ***S:*** *Serum;* ***L:*** *Leukocytes;* ***F:*** *Fibroblasts*

New-born Screening for Hearing Impairment

Out of every 1000 children born in India, at least 5-6 may have some hearing impairment with no other indicators[8] .Congenital or acquired hearing loss in infants is linked to life long deficits in speech and language acquisition, poor academic performance, personal- social maladjustments and emotional difficulties. Early identification of hearing loss and appropriate intervention within the first six months of life have been demonstrated to ameliorate many of these adverse consequences. Universal hearing screening as well as periodic screening of the hearing until adolescence is recommended for every child[7].

Causes of hearing loss in infants

There are many causes of hearing loss in the new-born infants/. Congenital infections like toxoplasmosis, measles, rubella, cytomegalovirus infection etc

during pregnancy have an adverse effect on the developing fetal hearing. Exposure to ototoxic drugs like Streptomycin, and chemicals can be associated with damage to the hearing. Defective structural development of the inner ear may be associated with impaired hearing. Genetic disorders may be associated with impairment in the infant's hearing. Post natal infections like meningitis, sepsis, and head injury may result in damage to the hearing. Sometimes, congenital tumors may occur, which are associated with disturbances and impediment in the infant's hearing . Genetic factors are believed to cause about 50 percent of congenital hearing loss. Preterm babies are at increased risk of hearing loss.

Types of hearing loss

Conductive hearing loss occurs when something interferes with sound passing through the outer or middle ear. A blockage in the ear canal, damage to the eardrum, or fluid or an infection in the middle ear (called otitis media) are examples of conditions that can cause a conductive hearing loss. This type of hearing loss is usually temporary and can often be corrected with medication or surgery. z Sensorineural hearing loss usually occurs when the hair cells in the inner ear cannot detect all incoming vibrations or when neural impulses are not transmitted to the brain. Prenatal infections, lack of oxygen at birth, or genetic factors can cause this type of hearing loss, which is generally permanent. However, many children can be aided with devices that amplify sound. Sensorineural hearing loss also can result from damage to the brain's auditory center. Mixed hearing loss occurs when a child who has a sensorineural hearing loss also has a conductive loss (such as fluid in the middle ear). It is very important that children with permanent hearing loss be monitored and treated for middle ear problems so hearing is not further reduced.

Methods of screening

The auditory function can be either peripheral (Cochlear) or central (brainstem) and techniques are available to distinguish between them [8].

Some of the methods of screening include Auditory Brainstem response (ABR), otoacoustic emissions (OAE's) and automated ABR (AABR) are used in new born hearing screening programs [9].

No single test can detect all failure patterns in auditory stem, hence a two stage sequential testing can be done to detect the hearing impairment. The less invasive and cheaper to perform OAE test is performed first. Those who screen positive for this test are followed up with the ABR test. Which has a greater sensitivity and specificity [8].

The OAE is performed by placing a plastic probe containing the transmitter and a microphone is inserted into the infant's ear. The transmitter sends down sounds into the inner ear and the microphone picks up the response vibrations of the hair cells. The ear normally echoes the sounds that are heard, and this is detected by the OAE machine.

The ABR is an electrophysiologic measurement that is used to assess the auditory function from the 8th nerve through the auditory brainstem[9]. Small ear phones deliver a click stimulus to the infant's ear , with attenuation of the background sound, and the waveform is then noted. This is compared with the normative infant data that is used as a comparator. In the AABR, the entire process is automated. This screening tool can be used in infants below 6 months of age.

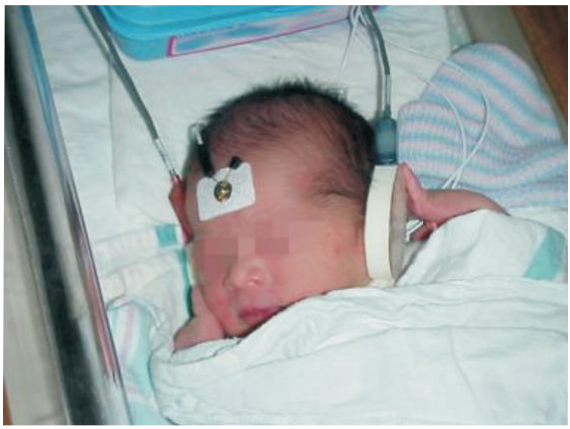
Timing of Screening

The Early hearing Detection and Intervention (EHDI) guidelines from the American Academy of Pediatrics mentions the following:

- A hearing screening no later than 1 months
- A diagnosis no later than 3 months of age
- Entry into early intervention no later than 6 months of age.

The National Program for the Prevention and Control of Deafness that is piloted by the Indian government recommends the following of this same pattern of 1-3-6 to screen, confirm diagnosis and initiate intervention before 6 months , in order to achieve the best results [8]. Screening of every infant born in a health facility must be undertaken before discharging the mother and infant.

Fig. 1: An infant's hearing is screened by measuring the automated auditory brainstem response (AABR).



Pulse Oximetry Screening

Congenital heart disease is present in approximately 800 per 100, 000 births[10]. About one fourth of these may have critical congenital heart malformations, which must be detected and assessed early. Early diagnosis is crucial for CCHD because any delay increases the morbidity, mortality and disability. Some studies have shown that the deaths from unrecognized CCHD occurred at a rate of 4.6/100,000 live births[12]. Critical congenital heart diseases are those that cause death or require major invasive intervention within 28 days of birth. Major congenital heart diseases are those that result in death or require major invasive intervention within 12 months after birth [13].

Conditions that require early management

Several congenital heart diseases are missed in the early neonatal periodand result in morbidity and mortality unless they are managed surgically within the first year of life. Some of these are listed in the table below[12].

Table 1: CHD's that can be detected by early screening

Most consistently cyanotic

- Hypoplastic left heart syndrome
- Pulmonary atresia with intact ventricular septum
- Total anomalous pulmonary venous return
- Tetralogy of Fallot
- Transposition of the great arteries
- Tricuspid atresia
- Truncus arteriosus

May be cyanotic

- Coarctation of the aorta
- Double outlet right ventricle
- Ebstein's anomaly
- Interrupted aortic arch
- Defects with single ventricle physiology

Role of Pulse oximetry as a screening tool

Pulse oximetry POS is a safe, non-invasive easy to perform and widely available screening tool. Ultrasound done antenatally and postnatal clinical examination may often miss the diagnosis of a congenital heart disease. POS which are designed with probes for the newborns must be used as a screening device. It is desirable to use an oximeter that provides a wave form, as it provides more accurate tracking or the oxygen saturation.

According to the American Academy of Pediatrics (AAP) guidelines, it is essential to maintain a log of the exact pulse oximeter results for every baby that is screened.[14]. This will ensure that the results whether the infant has passed or failed the screen test, and if failed, the description of the subsequent evaluation and final specific diagnosis.

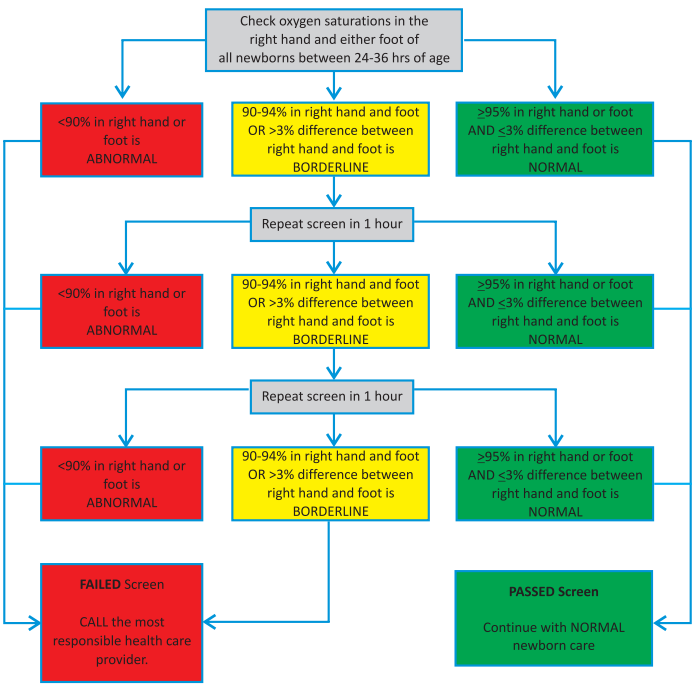
Currently CCHD screening using POS is considered to be a part of the routine nursery care, and the overall consent for managing the baby is sufficient to carry out this screening investigation[14]

Reports of studies done in USA and UK in asymptomatic newborn babies has shown that the POS screening is a neutral to cost effective way of detecting CCHD[12]

Timing of screening

POS can be done at any time after birth , but is recommended to be doe between 24 to 36 hours after birth[12]. This timing allows for flexibility of conducting the screen. All late preterm and term infants should be routinely screened .

Fig2 : Algorithm for newborn screening for CHD[12]



The results should be > 94% saturation in any limb. Testing using the right hand and one foot minimises the false negative rates. New-borns who fail this screening test should undergo a complete clinical evaluation blood pressure measurement , with chest x-ray, echocardiogram and referral to the cardiologist.

Effectiveness of the POS Screening test

In the Swedish study on which the recommended pulse-oximetry screening protocol is based, 25% of babies with a failed screen had CCHD, 47% had another disease process such as pulmonary pathology or sepsis, and 28% were well. Data from New Jersey demonstrates that in asymptomatic babies with a failed CCHD screen, 10% had CCHD, 23% had another disease process causing hypoxemia, and 67% had non-critical congenital heart defect or were well. The differences between these two studies may be in part related to age at screening and a much higher prenatal detection rate of CCHD in New Jersey than in Sweden. The false positive rates have been shown to be very low. It is important to recognize that a baby with a failed screen can look completely well on exam but have a significant underlying medical problem.

Antenatal Screening

Screening for Hypothyroidism

Thyroid disease affects approximately 5% of women in the reproductive age[15]. This is associated with complications in pregnant women and the new- born. Overt hypothyroidism affects 1% of all pregnancies, but subclinical hypothyroidism is estimated to affect 3-15% of pregnancies.

Effect of thyroid hormones on Pregnancy

Maternal thyroid dysfunction is associated with adverse outcomes in the mother and fetus[16]. The pregnancy is adversely affected by hypothyroidism in the mother. It can result in miscarriage, preterm delivery, eclampsia, pre- eclampsia and placental abruption. The fetus is affected by the low maternal thyroxine and there is adverse neurological development with reduced IQ of the infant. These infants may also develop hypothyroxinemia, thyroid peroxidase antibody .

Thyroid hormones variations in pregnancy

Several changes occur in the maternal levels of thyroid hormone during normal pregnancy. The serum thyroid stimulating hormone TSH has been found to alter during pregnancy. In the first trimester, there is a decline in the level of TSH due

to the effect of human gonadotropic hormone hCG which is a weak stimulator of TSH receptors.As there is a variation in the amount of TSH produced during the different trimesters, it is important to evaluate the levels against the reference levels:

First trimester	: < 2.5 mIU/L
Second trimester	: <3 mIU/L
Third trimester	: <3mIU/L

Levels of T3 and T4 are also altered during pregnancy due to the increased thyroid binding globulin TBG levels. In early pregnancy, the levels of T3 and T4 start increasing due to higher TBG levels, such that it is 1/5 times that of the upper limit of non pregnancy levels. Free T4 assays are unreliable due to interference by high TBG level.

Hypothyroidism

The estimated prevalence of hypothyroidism in India is said to be 2-3 % with 1/10 of these being overt hypothyroidism and 2-2.5% being the subclinical cases of hypothyroidism[17]. This is dangerous, as it may be missed and lead to undesirable complications.

Overt hypothyroidism is defined as an elevated TSH level with a decreased level of free TSH. This occurs commonly with associated chronic autoimmune thyroiditis, endemic iodine deficiency, prior radioactive iodine therapy or thyroidectomy[16]. It is important to recognize overt hypothyroidism and mandatory to treat it , so as normalize the TSH values to within trimester specific pregnancy reference range. Overt hypothyroidism OH is diagnosed with the serum TSH is > 2.5-3 Miu/l with ;low FT4 levels or TSH is > 10 m IU/L irrespective of the FT4 levels[17].

Subclinical hypothyroidism is defined as an elevated level of TSH with a normal level of circulating free T4 level.

TSH levels between 2.5- 10 m IU/L with normal FT4 concentration is considered as subtle hypothyroidism SH [17] .The symptoms of hypothyroidism remain subtle and if unrecognized could result in adverse maternal outcomes like eclampsia, placental abnormalities preterm labor and low birth weight. The American thyroid Association has recommended that women with subtle hypothyroidism who are TPO Ab positive should be treated with levothyroxine replacement[16].

Risk factors for Hypothyroidism

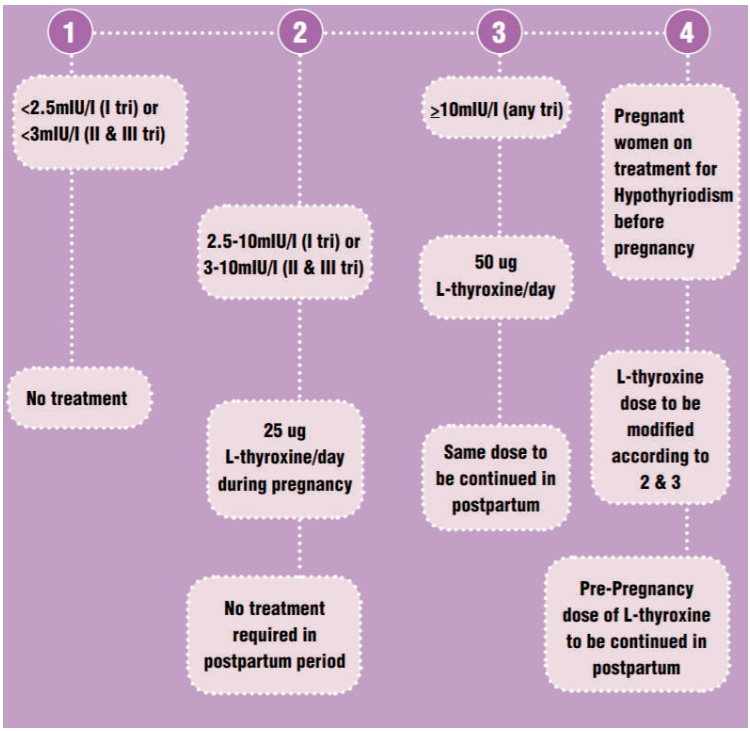
Presence of certain factors may point towards a suspicion of hypothyroidism. These are important for prenatal screening and treatment[17].

Fig 3: Risk factors

High risk factors for hypothyroidism

- → Residing in an area of known moderate to severe iodine insufficiency (according to area mapping)
- → Obesity (pre-pregnancy/first trimester Body Mass Index (BMI) ≥30kg/m2) [BMi= weight in kg/height in m2]
- → History of prior thyroid dysfunction or prior thyroid surgery
- → Symptoms of thyroid dysfunction or the presence of goiter
- → History of thyroid dysfunction in first degree relative (parents/sibilings/ children)
- → History of diagnosed mental retardation in family/previous births
- → Known case of autoimmune disease like Type I diabetes/Systemic Lupus Erythematosus (SLE)/Rheumatoid Arthritis (RA)/Addison's disease/ Coeliac disease, etc.
- → à History of recurrent miscarriages, pre-term delivery, intrauterine demise, pre-eclampsia/eclampsia, abruptio placentae
- → History of infertility (inability to conceive after one year of unprotected intercourse)
- → Use of amiodarone or lithium, or recent administration of iodinated radiologic contrast.

Fig 4: Management of hypothyroidism based on the TSH values in pregnancy and post-partum period



Screening for thyroid dysfunction and treatment of all pregnant women with SH is desirable , in order to improve the pregnancy outcomes [16].

Screening for gestational diabetes mellitus

Gestational diabetes mellitus GDM,is defined as diabetes that is diagnosed during pregnancy without overt signs [18]. This helps to differentiate the condition from those with pre existent Diabetes Mellitus DM, which may have been diagnosed and well controlled. GDM is still diagnosed in the late second or early third trimester due to the lack of appropriate guidelines for assessment in the first trimester.

Asians have a high prevalence of DM as well as a genetic predisposition to develop metabolic syndrome, and hence there is a high likelihood of developing GDM and its complications[19] .It is known to affect 7% of all pregnancies, while in India it ranges from 6-9% in rural population and a high of 12-21% in the urban community [19]. This implies that the Indian population is at a higher likelihood of developing DM and impaired glucose tolerance teste GTT.

Occurrence rates

GDM is diagnosed in 16.3% of those below 16 weeks of gestation, 22.4% between 17-23 weeks of gestation and 61.3% after 23 weeks of gestation. The HAPO study has shown that maternal hyperglycemia at levels below that diagnostic of DM is associated with increased birth weight and macrosomia.

Effects on pregnancy

Hyperglycemia in pregnancy is associated with both maternal and fetal complications[20,21]:

Table 2: Effects of hyperglycemia in pregnancy

Maternal complications	Fetal complications
Hypertension	Macrosomia
Pre-eclampsia, shoulder dystocia	Neonatal hypoglycaemia
Increased likelihood of Caeserean delivery	

Timing of the screening

The Screening test is recommended at ≥24-28 weeks of pregnancy, with 75 gm of glucose as the test. This is the recommendation of several international organizations, including the American Diabetes Association (ADA), The International Workshop-Conference on Gestational Diabetes Mellitus screening, International Association of Diabetes and Pregnancy Study groups (IADPSG). All pregnant women, even without a previous history of diabetes must be screened.

Risk factors

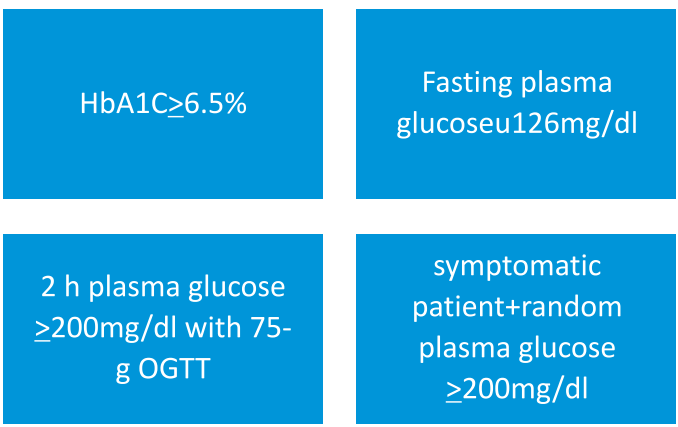
Women with a higher risk of developing gestational diabetes must be screened at the first pre-natal visit . The risk factors include[20].

- Increased weight (BMI≥ 25)
- Decreased physical activity
- First degree relative of a diabetic
- Prior history of GDM /delivery of abay> 9 pounds
- Metabolic abnormalities- hypertension, HDL<35 mg/dl, Triglyceride > 250 mg/dl
- Polycystic ovarian syndrome
- HbA1C ≥
- Impaired GTT/ impaired glucose testing in the past
- Evidence of insulin resistance (severe obesity/ acanthosis nigricans)
- History of cardiovascular disease

The diagnosis of GDM is confirmed with a minimum of one abnormal value.

Criteria for diagnosis of GDM

Fig5: Diagnosis of GDM



Any pregnant woman who meets these above criteria are considered to have overt Type 2 Diabetes mellitus.

Anemia in Pregnancy

Anemia is a frequently encountered problem especially in pregnant women [22,23] .The incidence and etiology varies depending on the socio-economic status in different countries. However, iron deficiency anemia has been found to be prevalent globally and the World Health organization ranks IDA as one amongst the top 20 causes of disability adjusted life years lost, ahead of tuberculosis [23].

Prevalence of iron deficiency anemia

According to data available, there are about 400 million non pregnant women worldwide who suffer from iron deficiency anemia. The prevalence of pregnant women with iron deficiency anemia stands around 41.8% [23].Racial and ethnic discrepancies do exist. In the United States of America itself, the prevalence of IDA amongst pregnant women is around 18.6%. The UK prevalence rate is around 24% according to recent reports [22] .The prevalence of IDA was reported to be highest amongst Indian pregnant women at 29%while it was around 16% amongst Black Caribbean women [22].

Indian studies have reported anemia in 78% of pregnant women in urban slums of Delhi [24].South Indian studies have shown more than 50% of pregnant women to be anemic.

Contributory factors

Specific dietary factors play a role in the development of IDA . Vegetarians have lower iron stores but show no differences in the haemoglobin indices compared to those who consume a non- vegetarian diet.

Pre-existent anemia due to various causes, especially excessive menstrual loss would predispose the development of IDA during pregnancy.

Classification of anemia (WHO definition)

The definition of anemia as recommended by the CDC is a haemoglobin or a hematocrit value that is less than the 5th percentile of the distribution in a healthy reference population based on the stage of pregnancy[25].

- Ist Trimester- Hb < 11gm/dl
- 2nd Trimester – Hb< 10.5 g/dl
- 3rd Trimester- Hb< 11gm/dl

All pregnant women must be screened for anemia, and the extent of the anemia must be documented.

Classification of anemia

Table 3: Severity of anemia

Severity of anemia	Hb in g/dl
Mild	10-10.9
Moderate	9.9-7
Severe	6.9-4
Very severe	<4

FOGSI Recommendations[25]

- All pregnant women must be screend for anemiauring the first ante natal visit
- Investigations to be done include complete blood count, with peripheral smear, RBC indices(MCV, MCH, MCHC) , reticulocyte count, blood films for malaria parasite and stool examination (for ova, cyst, occult blood)
- Further confirmation of IDA requires teste like TIBC, serum iron level, transferrin saturation. Soluble transferrin receptors, zinc protoporphyrin and eryhthrocyte protoporphyrin wherever these are possible to be done.

- In case of microcytic and hypochromic anemia, serum ferritin and C-reative protein help to differentiate IDA from other causes like thalassemia trait or anemia associated with chronic disease.

Serum ferritin levels of 15mcg /l defines iron deficiency and has a specificity of 987% and sensitivity of 75% for frank IDA [22] .The gold standard for confirming the diagnosis is a bone maroow aspirate , which may not be acceptable to most pregnant women.

Clinical outcomes associated with IDA [22]

Maternal-

- Infection during pregnancy
- Ante partum haemorrhage
- Placental abruption
- Premature rupture of membranes
- Postpartum haemorrhage
- Postpartum depression
- Lactation failure

Fetal-

- Low birth weight
- Preterm delivery
- Very low birth weight
- Neurodevelopmental delay
- Neonatal death
- Small for gestational age
- Still birth
- Congenital anomaly

References

1. Al Riyami S, AlManey M, Joshi SN et al. Detection of inborn errors of metabolism using tandem mass spectrometry among high risk Omani patient. Oman Med J 2012;27(6):482-5.

2. Hannon WH, Grosse SD et al. using tandem mass spectrometry for metabolic disease. Recommendations and reports 2001; 50(RR03):1-22.Available at www.cdc.gov/mmwr/preview/mmwrhtml/rr5003a1.htm

3. Sweetman L. Newborn screening by tandem mass soectrometry. Clin Chem 2001;47(11):Available at http://clinchem.aaccjnls.org/content/47/11/1937

4. Mak CM, Lee HC, Chan AY, Lam CW. Inborn errors of metabolis, and expanded newborn screening: a review and update. Crit Rev Clin Lab Sci 2013;50(6):142-62. Available at /www.ncbi.nlm.nih.gov/pubmed/24295058

5. Elshaari FA, Sheriff DS, Agela AE et al. Screening for inborn errors of metabolism . Int J Biomedicin2013;3 (3):211-4.

6. Wirth M, Jellimann JM, Jellimann S et al. Neonatal diabete mellitus : improved screening and early management of an underestimated disease. Clin Case Rep 2018;6(1):18-22.

7. BuzHarlor AD Jr. Hearing assessment in infants and children: recommendations beyond neonatal screening. Peaditr 2009;124(4). Available at http://pediatrics.aappublications.org/content/124/4/1252

8. Garg S, Singh R, Khurana D. Infant hearing screening in India: current status and way forward. Int J Prev Med 2015;6:113

9. Delaney AM.Newborn hearing screening. Medscape 2018. Available at

10. Peacock G. Hearing loss in newborn: the '1-3-6 ' guidelines. Available at https://www.medscape.com/viewarticle/895191.

11. Basco WT. Does screening newborns for congenital heart disease save lives? Available at https://www.medscape.com/viewarticle/896697

12. Narvey M, Wong K, Fournier A. Pulse oximetry screening in newborns to enhance detection of critical congenital heart disease. Pediatr Child Health 2017;22(8):494-8

13. Ewer AK, MiddletonLJ et al. Pulse oximetry screening for congenital heart defects in newborn infants: a test accuracy study. Lancet 2011;378(9793): 785-94. Available at https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)60753-8/abstract

14. American Academy of Paediatrics. Program to enhance the health and development of children. Available at

15. Levenson D. The debate over universal TSH screening in pregnancy continues. https://www.aacc.org/publications/cln/articles/2015/september/the-debate-over-universal-tsh-screening-in-pregnancy-continues. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3671674

16. Chang DLF, Pearce EN. Screening for maternal thyroid dysfunction in pregnancy: a review of the clinical evidence and current guidelines. J Thyroid Res 2013; Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3671674.

17. Ministry of Health and Family Welfare, Government of India. National guidelines for screening of hypothyroidism during pregnancy 2014. Available at http://www.nrhmorissa.gov.in/writereaddata/Upload/Documents/National_Guidelines_for_Screening_of_Hypothyroidism_during_Pregnancy.pdf

18. Huhn EA, Fischer T et al. Screening of gestational diabetes mellitus in early pregannacy by glucose tolerance test and glycosylated fibronectin: study protocol for an international prospective, multicentric, cohort trial. BMJ Open. Available at https://bmjopen.bmj.com/content/6/10/e012115

19. Rani PR, Begum J. Screening and diagnosis of gestational diabetes mellitus, where do we stand/ J Clin Diagn Res 2016;10(4):QE01-04. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4866200/

20. Patel SJ. Gestational diabetes testing protocol. Available at https://emedicine.medscape.com/article/2049380-overview

21. Kuo CH. Chen S-C, Fang C-T et al. Screeningh gestational diabete mellitus: the role of maternal age. Plos one 2017. Available at https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0173049

22. Rukuni R, Knight M, Murphy MF et al. Screen in for iron deficienct and iron deficiency anemia in pregnant: a structured review abd gap analysis against UK national screening criteria. BMC Preg Childbirth 2015;15:269. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4618150/

23. Marcewicz LH, Anderson BL, Byams VR et al. Screening and treatment for iron deficiency amnemia in women.:results of a survey of obstetrician-gynaecologists. Matern Child Health J 2017;21(8):1627-33. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5759051/

24. Sinha M, Panigrahi I, Shukla J, Saxena R . Spectrum of anemia in pregnant Indian women and importance of antenatal screening. Indian J Pathol 2006;49(3):373-5

25. FOGSI recommendations. Good clinical practice recommendations for iron deficiency anemia in pregnanacy(IDA) in India. J ObstetGynecol India. 2011;61(5):569-71. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3257335/pdf/13224_2011_Article_97.pdf

MALADIE d' ALZHEIMER

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MALADIE d' ALZHEIMER

Introduction

Alois Alzheimer, Physician practicing at Frankfurt, Germany came across in 1907 a patient aged 51 years, with the problems of progressive memory loss and disorientation, who in the course of 4 years deteriorated and became incontinent, incoherent and immobile. Alzheimer was puzzled by her peculiar illness and examined her brain on her death. He found neurofibrally tangles (NFTs) and senile plaques in the brain (1). This form of dementia has been named after Alzheimer as *Maladie d'Alzheimer* (Alzheimer's disease).

The condition was thought to be of two types based on the age of onset. The term Alzheimer's disease was restricted to those in whom the disease occurred at a relatively young age less than 65 years of age. It was considered a type of 'presenile' dementia. It was referred to as senile dementia of the Alzheimer's type when it occurred in elderly individuals over 65 years of age. Later it has been shown Alzheimer's disease does not have a bimodal age of onset. Now the condition has been considered as a single entity with a prevalence that increases sharply after age 65 (2). It doubles every 5 years from those between 65 and 85 years of age.

Definition

Alzheimer's disease (AD), the most common cause of dementia, is a progressive and fatal neurodegenerative disorder characterized pathologically by atrophy of the cerebral cortex and hippocampus, with intraneuronal neurofibrillary tangles containing abnormally phosphorylated *tau* protein, extracellular amyloid plaques, and neuronal cell death, and clinically by gradual impairment of memory (3). The patient becomes progressively impaired in both cognitive and functional capacities. The loss of intellectual abilities is of sufficient severity to interfere with social and occupational functioning.

There is mental deterioration with loss of intellectual abilities of sufficient severity to interfere with social and occupational functioning. There is a progressive impairment of activities of daily living. The patient manifests a variety of neuropsychiatric symptoms and behavioural disturbances.

AD is the leading cause of dementia in persons more than 65 years of age. The incidence of AD increases with age. This progressive degenerative disease accounts for 50-70% of all dementia (4). It places enormous burdens on the patient, on the family and on caregivers. AD may be familial or sporadic. It may also have an early age of onset.

Aetiology

The aetiology of AD remains undetermined. Advancing age, genetic predisposition and environmental factors appear to be important factors in the development of the disease. A positive family history of dementia suggests a genetic cause of AD. Genetic predisposition has been identified in the early onset of the disease and appears to be inherited as an autosomal dominant trait with relatively complete penetrance. 4 different genes have been identified to involve in the heritable form of the disease. The presence of the appolipoprotein E4 allele found on the long arm of chromosome 19 increases the likelihood of development of AD (5). Apolipoprotein E4 genotype appears to enhance amyloid beta-peptide aggregation or decrease its cleavage. Patients with Down's syndrome (trisomy 21) who are more than 30 years old often present with progressive dementia and pathologic changes similar to AD. Chromosome 21 harbours a gene responsible for AD. Mutations of presenilin-1 gene located on chromosome 14 may lead to an early onset autosomal dominant AD (6). Rarely the mutations of the preseniline-2 gene on chromosome-1 may cause autosomal dominant AD with an earlier onset of the disease and a shorter more rapidly progressive course than the disease caused by mutations in presenilin-2 (7).

Other risk factors identified are (3):

- Advancing age
- female gender
- head injury
- low serum levels of folate and vitamin B12
- raised plasma levels of homocysteine
- family history of AD or dementia
- low socioeconomic status

Oestrogen deficiency and exposure to aluminum and depression may probably act as risk factors.

Pathology

AD is associated with destruction of more than 100 billion neurons and their associated 100 trillion connections. There is progressive loss of cortical neurons and formation of amyloid plaques, intraneuronal neurofibrillary tangles and accumulation of a beta-amyloid in arterial walls of cerebral blood vessels (amyloid angiopathy). Beta-amyloid is the major component of the plaques, whereas hyperphosphorylated *tau* protein is the major constituent of the neurofibrillary tangles. The pathological process of atrophy begins in the hippocampus and spreads to involve diffuse areas of temporal, parietal and frontal lobes of the cerebral cortex. Brain shows atrophy with widened sulci and narrowed gyri. There is symmetric enlargement of the third and fourth ventricles. The loss of neurons, especially in the nucleus *basilis* causes a relative deficiency of acetylcholine to result in different clinical manifestations.

Pathogenesis and Pathophysiology

A cascade of events pertaining to amyloid underlies development of AD (8). The process is initiated from production of beta-amyloid peptide from the amyloid precursor protein (APP) by the enzymes beta and gamma secretases (9). It progresses through different steps such as oxidation and lipid peroxidation of cell membranes, glutamatergic excitotoxicity, beta-amyloid aggregation, inflammation and *tau* (a microtubule-associated protein) hyperphosphorylation, and cause neurotoxicity, neuronal cell death and neurotransmitter deficit. The aggregation of beta-amyloid and inflammation cause neuritic plaques with microglial activation and *tau* hyperphosphorylation leads to formation of neurofibrillary tangles.

Excessive amounts of neuritic plaques and neurofibrillary tangles in the brain areas, that are associated with cognition and behaviour spread to other cortical areas as the disease progresse. More tau tangles are seen in the brain as the disease advances. There is also reduction in synaptic density, loss of neurons, and degeneration in hippocampal neurons. There is a specific degeneration of neurons concerned with maintenance of specific transmitter cysteins and result

in deficits of acetylcholine, norepinephrine, and serotonin (11). Though plaque formation arrests, tangles continue to proliferate and their proliferation correlates with the progress and severity of dementia.

Clinical features

AD begins gradually and is characterized by functional and behavioural disturbances. AD presents with multiple cognitive deficits manifested by impaired memory (impaired ability to learn new information and to recall previously learnt information) and any of the cognitive disturbances such as loss of orientation, deterioration of language, impaired ability to carry out motor activities despite intact motor function (apraxia), inability to recognize or identify objects despite intact sensory functions (agnosia) and disturbances in executive functioning such as planning, organizing, sequencing and abstracting (12). Immediate and recent memory is the first to decline (last learnt, first lost). These symptoms manifest even early in the course of the disease with apathy and diminished interest and reduced concern. There are non-cognitive changes such as personality changes, decreased judgment ability, aimless wandering, psychosis, mood disturbances, agitation and sleep abnormalities. The patients find difficulty in adjustment with the changes of environment.

Memory, learning, attention, concentration, analysis of problem, orientation, speech and ability to find way are affected. The person finds difficult to carry out his occupation and social interactions become improper (13)

The earliest manifestation of AD is impaired memory. The person finds difficulty in recalling the names of relatives and friends or recent events. In the early stages of the illness, the things learnt last are first to be lost and the remote memory is preserved in the early stage of the disease ('last learnt first lost').

Memory and concentration are affected in the early stages of the disease. There is difficulty to perform simple tasks. They find difficulty to solve simple arithmetic problems and difficulty in making routine decisions and are confused. The mood and behaviour are affected.

As the disease advances the patient requires continued supervision. The basic activities such as use of toilet, eating and grooming are affected as the disease advances. Patients become dependent on others for all activities of daily living.

Mood changes and apathy are noted early in the course of the disease and persist. Agitation and psychosis are commonly noted with the progress of the disease. Behavioural disturbances progress over the course of illness.

Diagnosis

AD is characterized by progressive decline and ultimately loss of multiple cognitive functions including both: memory impairment-impaired ability to learn new information or to recall previously learnt information and at least one of the following; loss of word comprehension ability (aphasia), loss of ability to perform complex tasks involving muscle coordination (apraxia), loss of abililty to recognize and use familiar objects (agnosis) or loss of ability to plan, organize, and execute normal activities.

AD has to be distinguished from other common causes of dementia in elderly patient. AD may coexist with vascular dementia. Vascular dementia has a sudden onset and sometimes follows a cerebrovascular accident along with symptoms like headache, dizziness and focal neurological deficits may be present. AD must also be differentiated from dementia with Lewy bodies, Parkinson's disease with dementia, frontotemporal dementia, and reversible dementias.

Coexistence of thyroid disorders and vitamin B12 deficiency should be looked into, as they are reversible with treatment.

Neuroimaging helps in excluding vascular and intracranial causes of dementia. In the early stages of the disease, there may not be any abnormalities. With the progression of the disease, CT or MRI scans demonstrate hippocampal and cortical atrophy and ventricular enlargement in AD. CSF and plasma levels of amyloid are higher even before the manifestations of the illness. A positron-emission tomography (PET) scan shows reduced glucose metabolism in the parietal and temporal lobes (14). Unfortunately, it may not always differentiate symptomatic AD from asymptomatic controls with amyloid plaques. The EEG is normal or there may be nonspecific slowing.

Neuropsychological tests to assess various components of intellectual functions such as memory, naming objects, simple calculations, problem solving, judgment, are to be undertaken. Patients with mild cognitive impairment and in early stages of AD exhibit reduced levels of beta-amyloid peptide and increased levels of total *tau* and *tau* phosphorylated as threonine 181 in cerebrospinal fluid (16,17).

Diagnosis is definite where there is histological confirmation of clinical diagnosis, probable if there is no histologic confirmation of the clinical diagnosis and possible if there are atypical features (18).

Prognosis

AD is relentlessly progressive, despite all available therapy. AD progresses slowly with loss of 3 to 4 points per year on a standard instrument (the Mini-Mental State Examination) (19).Initial insidious memory impairment converts, over time to disorientation, personality and judgment dysfunction, speech abnormalities and apraxias. The patient loses the ability to take care of one's self. The patient lives for 8 to 10 years after they are diagnosed to have AD (20). They slowly terminate into a vegetative stage. The following conditions may be associated with AD at death: septicemia, pneumonia, and upper respiratory tract infections, nutritional disorders, pressure sores, fractures and wounds (21).

Treatment

The aim of treatment of AD is to achieve an improvement in cognition and to minimize disturbances in behaviour (depression, agitation, anxiety, insomnia and psychosis). The treatment consists of support, use of cholinesterase inhibitors, antidepressants and psychotropic agents.

Cholinesterase inhibitors

The neurotransmitter, acetylcholine (Ac) is necessary for clear thinking. It gets destroyed by the enzyme acetylcholinesterase (ChE). The loss of cholinergic function has been found to be closely related to cognitive dysfunction (22). Since acetylcholine deficiency has been observed in AD, ChE inhibitors have been used to block the action of ChE so as to increase the cerebral concentration of acetylcholine essential for synaptic transmission. They are orally administered. Donepezil, rivastigmine and galantamine (ChE inhibitors) facilitate an increase in the level of acetylcholine (23).

Absorption of donepezil is not affected by food unlike rivastigmine and glantamine. Donepezil exhibits longer serum half-life (70-80 hours) and greater protein binding capacity (96%). These agents show improvement in global function and reduce cognitive disturbances in mild-to-moderate AD. There is reduction in behavioural disturbances and temporary stabilization of activities of daily living (24)

Cholinesterase inhibitors

Agent	initial dose (mg)	frequency	duration (weeks)	maximal dose (mg)
Donepezil	5	onceat bed time	4-6	10 mg a day
Rivastigmine	1.5	twice	4	3 mg a day every 4 of 12 mg weeks to a maximum
Galantamine	4	twice	4	4 mg a day every 4

These agents show improvement in global function and reduce cognitive disturbances and improve cognitive function. There is reduction in behavioural disturbances and temporary stabilization of activities of daily living (26). If there is no response over a period of six months, these agents are to be discontinued. The drugs will exhibit better effects in the early stages of the disease when the destruction is minimal.

Side effects may occur in the form of nausea, vomiting, diarrhoea, abdominal distress, weight loss, insomnia, muscular cramps, fatigue, bradycardia and syncope. Typically these agents are started at low does to minimize side effects. The dose is then titrated up to the maximum tolerated dose.

The duration of treatment is not conclusively established. The patients continue to exhibit benefit from therapy for two to three years (29). Administration of more than one cholinesterase inhibitors is not advised but memantine and vitamin E can be administered together as they act by separate mechanisms on neurotransmitter system (30).

Memantine

The symptoms of AD are thought to be due to persistent activation of central nervous system N-methyl-D-aspartate (NMDA) receptors by the amino acid glutamate. Glutamate acts as the main excitatory neurotransmitter substance Being an excitatory neurotransmitter in cortical and hippocampal neurons, glutamate is implicated in neurodegenerative disease. Glutamine synthetase is oxidized in the brains of individuals with AD, resulting in excess accumulation of glutamate. Memantine, an NMDA receptor antagonist acts either by interfering with glutamatergic excitotoxicity or by providing symptomatic improvement through effects on functions of hippocampal neurons (31).

Memantine is useful in moderate-to-severe AD. The treatment is initiated at a dose of 5 mg daily and increased to 5 mg twice a day and then to 10 mg in the morning and 5 mg in the evening and ultimately 10 mg twice a day at the end of week 8. Food has no effect on its absorption. It shows cognitive improvement, reduced decline in activities of daily living and a reduced frequency of new behavioural symptoms (32).

Memantine is well tolerated. Confusion, headache, diarrhoea, myasthenia, fatigue and bradycardia may occur as side effects.

Unlike cholinesterase inhibitors, which are used only for treatment of early and intermediate stages of AD, memantine is recommended for the treatment of advanced stages of AD. It is advised to start therapy with a cholinesterase inhibitors, and then switch over to another agent in the same class if the initial agent is ineffective or if intolerable side effects have been noted (34).

Antioxidants

During excitotoxicity, an excess amount of calcium enters the neurons which activate the enzymes that produce free radicals and cause destruction of cells. Oxidative stress has been considered an important pathogenic process associated with aging and AD. It is reduced with administration of antioxidant agents such as alpha-tocopherol (vitamin E, 1000 IU twice a day) or selegiline 5-10 mg daily every morning to counteract an increase in free-radical formation (35).

Hormonal replacement therapy

Oestrogen increases cerebral blood flow, prevents atrophy of cholinergic neurons and reduces oxidative stress (36). It may even reduce neuronal injury by decreasing formation Oestrogen- (hormone)-replacement therapy may delay the onset of AD.

Anti-inflammatory agents

Anti-inflammatory agents (steroidal or non-steroidal anti-inflammatory drugs) have not shown much success (37). Anti-inflammatory drugs are tried with a hope of limiting phosphoration of *tau* protein and reduction of the incidence and slower rate of progression of AD (38).

Antipsychotics and mood stabilizers

Antipsychotics, antidepressants and antianxiolytics are useful for patients with behavioural disturbances. These are very common in the patients with AD and they may be controlled with antipsychotics. Mood stabilizers like carbamezapine may reduce behavioural disturbances and agitation (39, 40). Depression can be treated with new antidepressants like selective serotonin reuptake inhibitors (sertraline) and tricyclic antidepressants (34) that have anticholinergic side-effects.

Psychotropic agents

agents to control different symptoms	initial dose of the agent (mg)	final administered orally (mg)
Psychosis, agitation		
Resperidone	0.5	1
Olanzapine	2.5	5
Haloperidol	0.25	2
Agitation, mood stabilization		
Carbamezapine	200 (twice daily)	400 (twice daily)
Depression, anxiety		
Citalopram	10	20
Sertraline	25	75
Depression		
Nortriptyline	10	50
Mirtazapine	7.5	15

New approaches to therapy

Efforts are made to find treatment to slow or halt the memory destroying disease following better understanding of the molecular events that appear to trigger this disorder. Many drugs are under various stages of clinical trials and there are some promising preliminary results (41).

Amyloid plaques and tangles

A cascade of events pertaining to amyloid, underlie development of AD (42). Amyloid cascade hypothesis is based on the fact that plaques and tangles of proteins in the cerebral cortex and limbic system deleteriously affect the higher functions of the brain. The plaques are deposited outside the neurons and are composed of a small protein called amyloid beta (A-beta).

This hypothesis has led to the efforts of developing drugs to inhibit the production of A-beta and *tau*, and thus stop the harmful effects of them on the neurons.

Neuritic plaques have a central core of insoluble deposit of amyloid beta-peptide surrounded by astrocytes, microglia and dystrophic neuritis consisting of paired helical filaments (37). Neurofibrillary tangles are made up of paired helical filaments of abnormally filled and phosphorylated *tau* protein in the neuron and its dendrites. More *tau* tangles are seen in the brain as the disease advances. There is also reduction in synaptic density, loss of neurons, and degeneration in hippocampal neurons. There is a specific degeneration of neurons concerned with maintenance of specific transmitter cysteines and result in deficits of acetylcholine, nor-epinephrine, and serotonin (38). Though plaque formation arrests, plaque formation of tangles continues. It correlates with the progress and severity of dementia.

Genetic predisposition

Members of the families having a high risk of getting AD at a relatively young age, carry rare genetic mutations that encode APP specifically affecting the areas of the protein in and around the A-beta region. Genetic predisposition appears to be inherited as an autosomal dominant trait with relatively complete penetrance. 4 different genes have been identified to be involved in the heritable form of the disease. This makes them susceptible to develop the disease at a relatively young age. It has been shown persons with Down's

syndrome (trisomy 21) exhibit much higher incidence of AD in middle age. This is due to the fact chromosome 21 contains APP gene. There is an increased production of A-beta from birth, and consequently an increased amyloid deposit beginning from young age.

Mutations in two related genes called presenilin 1 and 2 lead to occurrence of severe form of AD very early in life The mutations increase amount of A-beta that is prone to clumping Mutations of presenilin-1 gene located on chromosome 14 may lead to an early onset autosomal dominant AD (6). Rarely the mutations of the presenilin-2 gene on chromosome-1 may cause autosomal dominant AD with an earlier onset of the disease and a shorter, more rapidly progressive course.

Protease inhibitors

It is not clear how A-beta destroys the neurons. Aggregates of A-beta found outside the neuron can initiate a cascade of events that can bring about an alteration of the *tau* protein inside the cell. A-beta aggregates are likely to bring about changes in the kinases that add phosphates onto proteins. Thus A-beta plays the pivotal role in the initiation of AD. In this background, drugs are being produced targeting the proteases (protease inhibitors) that produce A-beta, and to inhibit their activity.

Inhibitors of aspartyl proteases could block gamma-secretase cleavage of APP in cells. Gamma-secretases like beta-secretases contain a pair of aspartic acids essential for catalyzing the protein-cutting reaction. Presenilin protein appears to be an unusual aspartyl protease attached to the cell membrane. Two aspartic acids in presenilin lie within the membrane. They are very essential to the gamma-secretase cleavage to produce A-beta. Inhibitors of gamma-secretase bind directly to presenlin. High doses of gamma secretase inhibitors cause toxic effects in mice by disrupting the Notch signal. Molecules have been identified that modulate gamma secretes so that A-beta production is blocked without affecting cleavage of Notch (39). Attempts have been made to produce inhibitors that can curtail the creation of A-beta or create a shorter peptide that does not clump easily. Such a preparation called, Flurizan has shown promising results

Immunization

The second strategy is to clear the brain of toxic assemblies of A-beta after its production by active immunization. It involves recruiting the patients own immune system to attack A-beta. Injection of A-beta into mice genetically engineered to develop amyloid plaques stimulated an immune response that prevented the plaques from forming in the brain of young mice and cleared plaques already present in older mice (43)

Immunization with selected parts of A-beta instead of entire peptide can stimulate the antibody producing B-cell of the immune system without triggering T-cells involved in the occurrence of encephalitis.

Non-immunological strategy

Non-immunological strategy to stop aggregation of A-beta compounds has been attempted. The compounds interact directly with A-beta to keep the peptide dissolved in the fluid outside brain neurons preventing formation of harmful clumps. Alzhemed, a small molecule apparently mimicking heparin binds to A-beta and reduces peptide aggregation and shows some improvement in cognitive functions of patients with mild AD.

Targetting Tau

The *tau* filaments cause neuronal tangles, and they are a promising target to prevent degeneration of neurons. Inhibitors could block the kinases that place an excessive amount of phosphates onto *tau*, which is an essential step in filament formation. No success has been seen in production of such a drug.

Reduction in production of APP

Cholesterol lowering agents (statins) used to cut risk of heart disease could become a treatment for AD. Epidemiologic studies have shown people taking statins have a lower risk of acquiring AD By lowering cholesterol these drugs may reduce production of APP or perhaps affect the creation of A-beta by inhibiting activity of the responsible secretases. Statins may not be able to reverse neuronal degeneration once it has occurred (DM).

Cell-based therapy

Cell therapy is another approach in the treatment. The gene encoding a large protein such as nerve growth factor (NGF) was inserted into the skin biopsies

obtained from patients with mild forms of AD. Such genetically modified cells were implanted surgically into the forebrain of the patients, with a view that the implanted cells would produce and secrete NGF, thus preventing the loss of acetylcholine producing neurons and improve memory. The treatment was associated with slowing down of cognitive decline.

Nutraceuticals

Many chemical substances of natural dietary origin, called nutraceuticals have shown to possess neuroprotective properties. They appear to protect the nerve cells from free radical damage and moderate acetylcholinesterase activity, associated with β-amyloid plaques and neurofibrillary tangles .They have been tried as complementary and preventive therapy in neurodegenerative disorders Curcumin, a polyphenol derived from turmeric herb has shown in vivo and in vitro studies to reduce aggregation of amyloid beta plaques, and attenuate the hyperphosphorylation of tau. It holds promise as a therapeutic agent for AD with superior effectiveness and safety (44).). *Crocus sativus* (saffron) may inhibit the aggregation and deposition of amyloid beta in the brain and it has shown to improve cognitive function (46)

Family support

The family plays a vital role in giving support to the patients and in ensuring adherence to treatment regimens. Psychological support to the patient would include helping them to maintain a daily routine, maintenance of nutrition, hydration, body weight, exercise, hygiene and cleanliness, and conditioning of food and bowel habits.

The persons who live with and provide care for patients with AD are in great emotional stress and they require proper counseling and support. Although the patient has the disease, it is the family that suffers the most.

The care givers should be specifically trained in patient care. Following diagnosis of AD, the patient must be made to follow a daily routine. In early stages of the disease the patients are able to adapt to necessary changes. It is necessary to manage the patient in his familiar surroundings. Any change in layout of patient's room, shifting the patient's bed room or moving the patient to another home creates a tremendous amount of confusion in the patient and it is deleterious (48).

The patient should be given a well balanced diet, rich in proteins, high in fibre, and adequate amount of calories. Care should be taken to avoid accidents caused by tripping over furniture, falling down the stairs or slipping in the bath room. Sufficient fluid should be given for drinking during day. Sleep patterns must be maintained as sleep disturbances are extremely distressing to the family.

Mood changes are controlled by keeping a clean calm environment with a fixed daily routine. The patients should not be questioned repeatedly or given too many choices. The patients lose their geographic orientation and can get lost even in familiar surroundings. They are found wandering aimlessly either in the neighbourhood or far away. They should have some identification and the doors of the house should be securely locked and the patient has to be accompanied by someone while on walk or visiting some places.

In early stages of AD, an individual may retain enough mental functions to be legally permitted to make a will. It becomes important for the physician to advise the family and the patient in a sensible manner to take action for drawing up of will before the progression of intellectual impairment to such a degree that it is too late to help.

Prevention

Low education level has been considered a risk factor in the development of AD. Ramon Cajal had noted the role of axons in keeping our mental functions. He said that there is sprouting of collaterals from axons by rigorous mental activity ('*gymnastique cerebrale*').

Stages

AD passes through 3 stages as follows:

1. Stage of asymptomatic cerebral amyloidosis: It exhibits high amyloid retention on PETS and a low level s of beta amyloid in CSF
2. Stage of amyloid positivity+ evidence of synaptic dysfunction and/or early neuronal degeneration exhibiting neuronal dysfunction on FDG PET/MRI, high *tau*/p-*tau* in CSF and MRI imaging showing cortical thinning, and hippocampal atrophy

3. Stage of amyloid positivity+ evidence of neurodegeneration+subtle cortical degeneration. There is poor performance on more challenging cognitive tests, yet it does not meet criteria for MCI.

Some individuals may not progress beyond the stage 2. Individuals in stage 3 are postulated to be more likely to progress to MCI and AD dementia.

The working group has recommended inclusion of the biomarkers to enhance the certainty that the underlying disease is AD, and to estimate the likelihood of progression to the subsequent stages of illness. Since there is no uniformity in the standardized techniques, or the levels between laboratories for CSF amyloid beta or *tau*, the use of biomarkers are restricted only for research purpose, and not for clinical purpose.

References

1. Alzheimer A. Uber eine eigenartige Erkrankung der Hirnrinde. Allg Zeits Psychiatry Psychisch YGerichtlich Med. 1907: 64; 146-8
2. Lipsky M, Castellani RJ, Rolston RK, Smith MA. Alzheimer disease. DM 2010: 56; 479-546
3. Cummings JL, Cole G. Alzheimer Disease. JAMA 2002; 287: 235-2338
4. Gao S, Hendric HC, Hall KS, Hui S. The relationship between age, sex and the incidence of dementia and Alzheimer's disease. Arch Gen Psychiat 1998: 55; 809-815
5. Seshadri S, Frachman DA, Lipps CF. Apolipoprotein E4 allele and the life time risk of Alzheimer's disease. Arch Neurol. 1995: 52; 1074-79
6. Scheelenberg GD, Bird TD, Weijsman EM, et al Genetic linkage evidence for a familial Alzheimer's disease locus on chromosome 14. Science 1992: 258; 668-71
7. Levy-Lahad E, Weijsman EM, Namens E, et al. Familial Alzheimer's disease locus on chromosome-1. Science. 1995: 269; 970-2
8. Selkos DJ. Presenilins, Beta-amyloid precursor protein and the molecular basis of Alzheimer's disease. Clin Neurol Res. 2001: 1; 91-103
9. Hardy J, Selkos DJ. The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics. Science. 2002: 297; 353-6
10. Cummings R, Vinters HV, Cole GM, Khachaturian ZS. Alzheimer's disease. Neurology 1998: 51; 53-57

11. Palmer AM, Stratmann GC, Proctor AW, Bowen DM. Possible neurotransmitter basis of behavioral change in Alzheimer's disease. Ann Neurol 1988: 23; 616-20

12. Diagnostic and Statistical Manual of Mental Disorders. 4th edn. Washington DC, American Psychiatric Association. 1994

13. Ownby RI, Crocco E, Acevedo A, John V, Lowenstein D. Depression and risk for Alzheimer disease: systemic review, meta-analysis, and metaregression analysis. Arch Gen Psychiatry 2006: 63; 530-8

14. Silverman DH, Small GW, Chang CT, et al Positron emission tomography to evaluation of dementia regional brain metabolism and long term outcome. J A M A 2001: 286; 2120-7

15. Hansson O, Zetterberg H, Buchhave P, London E, Blonnow K, Minthon I. Association between CSF biomarkers and incipient Alzheimer's disease in patients with mild cognitive impairment: a follow-up study. Lancet Neurol 2006: 5; 228034

16. Smach MA, Charfeddine B, ben Othman L, et al. Evaluation of cerebrospinal fluid tau/beta amyloid (42) ratio as diagnostic markers for Alzheimer Disease. Eur neurol 2009: 62; 349-55

17. Wiley CA, Lopresti BJ, Venneti S, et al. Carbon 11-labeled Pittsburgh compound B and carbon 11-labeled ®-PK 11195 positron emission tomographic imaging in Alzheimer disease. Arch Neurol 2009: 66; 60-7

18. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlian EM. Clinical diagnosis of Alzheimer's disease: report of NINCDS-ADRDA Work Group. Task Force on Alzheimer's disease. Neurology 1984: 34; 939-44

19. Folstein MF, Folstein SE, McHugh PR. Mini-Mental State. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975: 12; 186-198

20. Farlow MR, Evans RM. Pharmacologic treatment of cognition in Alzheimer's dementia. Neurology 1998: 51; S36-44, S65-7

21. Chandra V, Barucha NE, Schoenberg BS. Conditions associated with Alzheimer's disease at death: case-control study. Neurology 1986: 36; 209-11

22. Doody RS, Stevens JC, Buck C, *et al.* Practice parameter: Management of dementia (an evidence-based review): report of the quality standards subcommittee of the American Academy of Neurology. Neurology. 2001; 293: 1446-1447

23. Giacobini E. Do cholinersterase inhibitors have disease-modifying effects in Alzheimer's disease? CNS Drugs 2001: 15; 85-91

24. Cummings R. Cholinesterase inhibitors: a new class of psychotropic agents. Am J Psychiatr 2000; 157: 6-15

25. Cummings JL. Use of cholinesterase inhibitors in clinical practice. Evidence-based recommendations. Am J Geriat Psychiatry. 2003: 11; 131-45

26. Cummings JL. Alzheimer's disease. N Engl J Med. 2004: 351; 56-67

27. Rogers SL, Doody RS, Prati RD, Ieni JR. Long-term efficacy and safety of donepezil in the treatment of Alzheimer's disease: final analysis of a US multicentre open-label study. Eur Neuropsychopharmacol 2000: 10; 195-203

28. Tariot PN, Farlow MR, Grossberg GT, Graham SM, McDonald S, Gergel J. Memantine treatment in patients with moderate to severe Alzheimer's disease already receiving donepezil: a randomized controlled trial J A M A 2004: 291; 317-24.

29. Parssons CG, Danysa W, Quack G. Memantine is a clinically well tolerated N-methyl-D-aspartate (NMDA) receptor antagonist: a review of preclinical data. Neuropharmacology 1999: 38; 735-67

30. Hartmann S, Mobius HJ. Tolerability of memantine in combination with cholinesterase inhibitors in dementia therapy. Int Clin Psychopharmacol 2003:18; 81-85

31. Sano M, Ernesto G, Thomas RG, et al. A controlled trial of selegiline, alpha-tocopherol, or both as treatment of Alzheimer's disease N Engl J Med. 1997: 336; 1216-1222

32. Schachter AS. Alzheimer's disease. Dialogues in Clinical Neurosciences. 2000: 2; 81-100

33. Goutte C, Tsunozaki M, Hale VA, et al. APH-1 is a multipass membrane protein essential for the notch signaling pathway in Caenorhabditis elegans embryos. Proc Natl Acad Sci USA 2002: 99: 775-9

34. Farlow MR, Cummings H. Effectiv pharmacologic management of Alzheimer's disease. Am J Med. 2007: 120; 388-97

35. Rich JB, Rasmusson DX, Folstein MF, et al. Nonsteroidal anti-inflammatory drugs in Alzheimer's disease. Neurology 1995: 45; 51-5

36. Street J, Clark WS, Gannon KS, et al. Olanzapine treatment of psychotic and behavioural symptoms in patients with Alzheimer's disease in nursing care facilities. Arch Gen Psychiatr 2000: 57; 968-76

37. Tariot PN, Erb R, Podgorski CA, et al. Efficacy and tolerability of carbamazepine for agitation and aggression in dementia. Am J Psychiatr 1998: 155; 54-61

38. Lyketson CG, Sheppard J-ME, Steele CD, et al. Randomized, placebo-controlled, double-blind, clinical trial of sertraline in the treatment of depression complicating Alzheimer's disease: initial results from the depression in Alzheimer's disease study. Am J Psychiatr 2000: 157; 1686-89

39. Wolfe MS. Therapeutic strategies for Alzheimer's disease. Nature Reviews Drug Discovery. 2002; 1: 859-866

40. Selkos DJ. Presenilins, B-amyloid precursor protein and the molecular basis of Alzheimer's disease. Clin Neurol Res. 2001; 1: 91-103

41. Cummings R, Vinters HV, Cole GM, Khachaturian ZS. Alzheimer's disease. Neurology. 1998; 51: 53-57

42. Palmer AM, Stratmann GC, Proctor AW, Bowen DM. Possible neurotransmitter basis of behavioral changes in Alzheimer's disease. Ann Neurol 1988; 23: 61020

43. Wolfe MS. Shutting down Alzheimer's. Sci Amer India 2006; 1: 60-67

44. Parikh A, Shan Z, Song Y, et al A novel formulation of curcumin for Alzheimer's disease (AD): in vitro and in vivo evaluation Alzheimers Dementia 2016; 12(7) Suppl: P 1024

45. Tang M, Taghibiglou C The Mechanisms of Action of Curcumin in Alzheimer's Disease J Alzheimers Dis 2017; 58(4): 1003-1006

46. Akhondzadeh S, Sabet MS, Harirchian MH Saffron in the treatment of patients with mild to moderate Alzheimer's disease: a 16-week, randomized and placebo-controlled trial J Clin Pharm Ther 2010; 35(5): 581-8

47. Schultz R, O'Brien A, Bookwala J, et al. Psychiatric and physical morbidity effects of dementia care giving, prevalence, correlates, and causes. Gerontologist 1995: 35; 771-91

48. Vas CJ, Rajkumar S, Tanyakitpissal P, Chandra V. Alzheimer's disease: The brain killer. New Delhi, Regional Office for South East Asia, World Health Organization. 2001

49. Berchtold NC,Cotman CW. Evolution in the conceptualization of dementia and Alzheimer's disease. Grecp-Roman period to the 1960s. Neurobiol Aging 1998: 19;172-89

50. McKhann G, Drachman D, Foistein M, *et al*. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services. Task Force on Alzheimer's Disease. Neurology 1984: 34(7); 939-944

51. Clifford TR, Albert MS, Knopman DS, *et al.* Introduction to the recommendations from the National Institute of aging-Alzheimer's Association Workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011: 7(3); 257-262

52. McKhann GM, Knopman DS, Chertknow H, *et al*. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute of Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011: 7(3); 263-269

53. Albert MS, DeKosky ST, Dickson D, *et al.* The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute of Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011: 7(3); 270-279

54. Sperling RA. Aisen PS, Beckett LA, *et al*. Towards defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute of Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011: 7(3); 280-292

TELEMEDICINE - THE FUTURE OF HEALTH CARE : AN OVERVIEW

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TELEMEDICINE - THE FUTURE OF HEALTH CARE : AN OVERVIEW

Introduction

India is a 'land of opportunity' where the need for health care initiatives is concerned.

The term 'hard to reach', in medical and health research, relates to the ability of health services to reach out to certain difficult to contact groups. It could also be equated with the 'underserved' i.e. either no services are available for these groups or they are not accessing the available services.

Given the diversity in the country, despite the progress made since Independence, the disease burden has doubled. The prevalence of risk factors for chronic diseases such as diabetes, heart diseases and cancers are on the increase while the struggle to reduce maternal and child deaths, malnutrition related and infectious diseases continue. With all the challenges, the supply of healthcare services especially to the 'hard to reach' population, falls significantly short of the demand.

Over time the innovations in technology; have made it possible to consider reversing the scenario of both accessibility and manpower shortage. The innovations encompass diagnostic, monitoring and supportive tools like MRI scanners, pregnancy tests, wheelchairs, implants, pacemakers, orthopedic shoes, insulin pens, spectacles and contact lenses among others, which we take for granted today.

The focus of the healthcare industry today is on delivering 'economical quality health care, to maximum numbers irrespective of geographical barriers'. To ensure the delivery of healthcare to the 'hard to reach' calls for connecting more treatment centres to the broader medical community with a network that can efficiently tie them together.

Telemedicine is the bridge technology that brings medical resources to the 'hard to reach' population. "*Tele*" means "distance" in Greek while "mederi" is Latin for "to heal". Telemedicine together essentially means, "delivering medicine at a distance". It is a way of providing healthcare services at a distance using telecommunications technology, medical expertise and computer science.

History of Telemedicine

While the explosion of interest in telemedicine over the past decade or so makes it appear as a relatively new use of telecommunications technology, the truth is that the idea of performing medical examinations and evaluations through the telecommunication network is not new. Shortly after the invention of the telephone, attempts were made to transmit heart and lung sounds to a trained expert who could assess the state of the organs.

1906:ECGTransmission

Einthoven, the father of electrocardiography, first investigated on ECG transmission over telephone lines in 1906! He wrote an article 'Le telecardiogramme at the Archives Internationales Physiologie' 4:132, 1906

1920s:Helpforships

During this time, radios were used to link physicians standing watch at shore stations to assist ships at sea that had medical emergencies.

1924: The first exposition of Telecare

The "Radio News" magazine from April 1924 includes an article with a spoof electronic circuit diagram which combined all the gadgets of the day into this latest marvel!

1955:Telepsychiatry

The Nebraska Psychiatric Institute, USA, was one of the first facilities in the country to have closed-circuit television in 1955. In 1971 the Nebraska Medical Center was linked with the Omaha Veterans Administration Hospital and VA facilities in two other towns.

1967: Massachusetts General Hospital, USA

This station was established in 1967 to provide occupational health services to airport employees and to deliver emergency care and medical attention to travellers.

1970s: Satellite telemedicine

Via ATS-6 satellites. In these projects, paramedics in remote Alaskan and Canadian villages were linked with hospitals in distant towns or cities.

Since the 1970s, NASA has been in the forefront of research and demonstration in the field of telemedicine.

Definitions and Concepts: Telemedicine & Telehealth

The World Health Organization (WHO) defines 'Telemedicine' as, "The delivery of healthcare services, where distance is a critical factor, by all healthcare professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation and for the continuing education of healthcare providers, all in the interests of advancing the health of individuals and their communities."

Tele- health can be used for **epidemiological surveillance** as also i**nteractive health communication and disease prevention.**

An Epidemiological Surveillance

Telemedicine applications for epidemiological surveillance are gradually reaching new heights with the development of technology such as geographic information systems (GISs).

- It can help in health assessment of the population while giving new insights into the geographical distribution and gradients in disease prevalence and incidence.
- It can provide valuable information of the differential at risk populations based on the risk factor profiles.
- The risk factors in the population can be differentiated and delineated.
- Interventional planning, assessment of the strategies and their effectiveness can be studied.
- It can help in anticipating epidemics.
- It can help in in real-time monitoring of diseases, both local and global.
- It helps give an understanding of the spread of vector-borne diseases. Remote sensing techniques have been recently used in this regard.

- It uses a different methodology to help aggregate and integrate disparate data from diverse sources which in turn can guide the formulation of public health programs and policy decisions.

Interactive Health Communication and Disease Prevention

Information technology and telemedicine can be used to inform, influence and motivate individuals and population organizations on health, health-related issues and adoption of healthy lifestyles. It has the potential to advance and support primary, secondary and tertiary health promotion and disease prevention agendas.

- Being interactive it can relay information to individuals as well as to the population as a whole. It can provide an easy access to those living in remote areas.
- It enables informed decision-making while simplifying the health decision-making process / or communication between healthcare providers and individuals regarding prevention, diagnosis or management of a health condition.
- The technology can be used to promote behavioural changes and their maintenance in the community.
- It can also help in peer information exchange and emotional support. Examples include online Internet applications that enable individuals with specific health conditions, needs or issues to communicate with each other, share information and provide / receive emotional support.
- The technology promotes self-care and domiciliary care practices. As a result, those living in the remote areas can benefit by self-management of health problems which will supplement existing health care services.
- It can be a very important tool for the evaluation and monitoring of healthcare services.

The Need of the Day

A hospital is recognized by the social connect it establishes. This comes from quality care both out and inpatient, 'humanness', availability of facilities especially expert care particularly in emergency situations and care that continues even after the patient goes home. The hospital patient connect is responsible for patient loyalty and the reputation enjoyed by the hospital.

Telemedicine is suggested as the way forward to overcome the challenges in the country's health sector. Telemedicine allows patients to be examined, monitored and treated, even when the patient and doctor are located in different places. Text, voice, images or even video can be used to transfer the patient's records to the medical consultant and expert medical advice offered from a remote location. It offers reach, expansion of patient care, better utilization of existing expertise and strengthens the bond.

- There is an effort by many organizations to build 'peripheral' medical centers to increase their outreach. Using telemedicine, the expertise available at the main centers can be used, to diagnose, treat and if required call the patients to the mother hospital for further treatment.
- Even interpretation of specialized medical investigations, like X-rays, CT scans and ECGs, can be done by experts from wherever they are located. This allows wider coverage and those identified with potential problems could be referred to higher centers.
- In emergency situations such as transportation of a patient with a heart attack, the telemedicine equipment used to capture, store and transmit critical patient data and an ECG allows an expert to offer a diagnosis and advise emergency measures from wherever located.
- In cases of public hospitals where resources are limited, telemedicine services can help identify the patients who really need to be referred to higher centers while advice from experts can be used to manage all other cases at the primary centers.
- The use of telemedicine technology and SMS based health surveillance reporting can help speed up disease detection, treatment and help to monitor communities in remote locations. The same could be utilized to spread awareness among remote communities about what can be done to prevent communicable diseases from turning into epidemics.
- Early detection of problems would also reduce the incidence of complications, reducing morbidity rates and subsequent need for healthcare facilities and long term medication.

- Encouraging the use of telemedicine homecare products makes patients more proactive and allows the patients to monitor and transmit critical health data to the expert care center.
- The medical tourism business in India is estimated at $333 million (Rs 1,450 crore). Telemedicine as a way to stay connected with patients and their healthcare professionals across the globe both before and after treatment procedures if needed makes business sense.
- Reduction in the unnecessary doctor consultations will enable the medical consultant to efficiently utilize his consulting services to attend to those who really need to visit him.
- Using telemedicine follow up monitoring of both chronic medical and post-surgical patients can be done effectively from across geographical locations.

The initiative to implement telemedicine rests in the hand of the clinician. The doctors must understand and realize the true potential by 'innovating' the application of telemedicine in their clinical practice irrespective of their specialty, to make their expertise available to more irrespective of geographical boundaries.

Current Efforts

In spite of well-planned public health care system in place, access to healthcare in rural areas is far from satisfactory. Several case studies in the country and abroad have proved the technical capabilities of telemedicine in satisfactory transfer of knowledge and information pertaining to patient care, professional and skill development of healthcare providers and administrators from tertiary level through secondary to primary level. This will not only educate the doctors but also improve the quality of patient care at these levels.

Tele-health Care

Both government and private agencies are venturing into Tele-healthcare by providing communication link, hardware and software solutions for tele-health care.

- The Indian Space Research Organization (ISRO)in collaboration with state governments has established a Telemedicine Network consisting of 225 Hospitals-185Remote/Rural. District Hospital / Health Centers connected to 40 super specialty hospitals located in the major states.
- The Ministry of Health and Family Welfare (MoH & FW) has set up a National Task Force on Telemedicine in the year 2005 which is addressing various issues in telemedicine in the national context. Various sub-committees are working to develop a national policy document. The initiatives include:
  - Implementation of integrated Disease Surveillance Programme network with the help of ISRO.
  - Under the National Cancer Control Program, MoH&FW establishing OncoNET India, a network connecting 25 Regional Cancer Centers and 100 peripheral centers to provide comprehensive cancer treatment facilities and carry out cancer prevention and research activities
  - Approved tele-ophthalmology project to provide eye care specialty services to the patients of rural and remote areas of Punjab, Uttar Pradesh, West Bengal states of India through tele-ophthalmology mobile van.
  - Draft proposal for National Telemedicine Grid has also been prepared by ISRO and submitted to MoH &FW.
  - Apart from this some telemedicine programs are also supported by some super specialty hospitals in government and corporate sectors and state governments.

Distant Medical Education

Imparting quality medical education in all the medical colleges and maintaining a uniform standard across the country is not only dependent on adopting a uniform curriculum prescribed by a regulatory body but also requires availability of excellent infrastructure such as qualified teachers, knowledge resources, learning materials and teaching technology. Though all these measures are ensured and followed in developed countries it is not so in developing countries due to financial and logistic constraints.

Capacity Building

Both the Government and the private sector are helping in capacity building. The Apollo telemedicine network foundation in collaboration with Anna University, Chennai has started a 15 days certificate course in Tele-health Technology which is a blend of technical, medical and managerial skills. SGPGIMS, Lucknow in collaboration with the State and Central Governments and Ministry of Information Technology has taken up the initiative and set up a School of Telemedicine and Biomedical Informatics in its campus.

Tele-health Industry operating in India

In the past two years, the pilot project on Telemedicine in Karnataka has already provided more than 10,000 tele-consultations. In the operational phase, the Karnataka Telemedicine Project is expected to bring multi-specialty healthcare to a significant section of the rural population of Karnataka. This network would serve as a model for the utilization of 'HEALTHSAT,' which is proposed for launch in the future.

The Government Initiative: The Eleventh Five Year Plan (2007-2012)

The Eleventh Five Year Plan envisages appropriate use of IT for an enhanced role in health care and governance. It is feasible to set up a National Grid given the advantage of a strong fibre backbone and indigenous satellite communication technology with trained human resources which the country already has. The Grid could be shared by health care providers, trainers, beneficiaries, and civil society. Pilot projects that have been running at various levels would be evaluated and scaled up.

Health Management Information System (HMIS)

The Health Management Information System will allow the establishment of a computerized web enabled data capturing and analytical system which would provide valid and reliable data and reports for use at all levels. The data will flow directly from the periphery.

The wastage of drugs due to date expiry needs to be curtailed by demand-driven management and redistribution of medicines nearing date of expiry. The HMIS when fully developed and implemented will track demand and supply and continuously monitor the drug situation.

So far about 3 lakh people have benefited from this programme. Facility of telemedicine will be provided in district hospitals and government medical colleges.

The Cost Consideration

While the initial investments appear to be large, the realisation is over time by virtue of the quality care delivered to the doorstep of number of individuals. The realisation is from the saving that accrues when the individual does not travel for every ailment, the early diagnosis which avoids complications and further costs and the prevention of overload on the clinics and hospitals with patients who can be treated at peripheral centres.

Challenges to the Implementation of Telemedicine

One would ask 'If telemedicine is the answer and has been around for so long why has it not been implemented yet?'

While there are a lot of government and private efforts being initiated to adapt telemedicine to reach the hard to reach population, the efforts are not attaining the results they should.

Tele-health services is an amalgam of an intelligent user- in terms of its implementation, the telemetry equipment, development of the technicians who understand the use of the equipment, the telecommunication department to ensure good connectivity and the willingness of the medical practitioner to leverage the technology to benefit the hard to reach groups. To support all these needs good financial backing. And of course, the acceptance of the deliverer and the population for whom it is meant.

Despite the advantages that are offered by telemedicine the number of those advantaged remains low.

The probable reasons that the programs that have been implemented are not having the impact could be:

- Doctors are not fully convinced and familiar with e-medicine.
- Virtually no exposure to the applications of IT and technology in the curriculum of medical colleges.

- Lack of training facilities and enough trained personnel to take the initiative forward. Terms like HIS, RIS, PACS etc. are unheard of by the medical/healthcare community.
- The lack of awareness about availability of such technology among the individuals that should benefit from it.
- Probable lack of trust among the population about the technology being offered. There is a lack of confidence in patients about the outcome of e-Medicine..
- The efforts are more 'local' in nature. Local both in terms of geographical locations and in terms of groups being serviced. The area of work is being decided by the interest and capability of the local provider rather than as a 'whole'.
- The various programs that are being run are independent of each other. For e.g. One maybe a diabetic but only the teleopthalmology initiative is underway only offering an eye check-up and not total diabetic care.
- The lack of availability of working implementation models that can be duplicated.
- Issues of connectivity in the remote hard to reach areas.
- The technology and communication costs being too high, it sometimes makes Telemedicine financially unfeasible.

The Way Forward

The amazing thing about telemedicine is that it can be customized to suit the local need and program for which it is meant. The uses of *Telemedicine* are limited only by the imagination.

The blueprint of the Eleventh Five Year **(2007-2012)** Plan includes:

- Training, education, and capacity building for e-Health
- Monitoring by e-enabled HMIS to ensure timely flow of data and collation to be used at various levels
- Optimization of utilization using Geographical Information System (GIS) Resource Mapping of various health facilities (Allopathic and AYUSH), Laboratories, Training Centres, Health Manpower among others

- Providing of service delivery and other e-enabled activities like, disease surveillance, tele-consultations, health helpline, district hospital referral net, and e-enabled mobile medical units

While today we have separate health related laws and technology related laws, unlike other countries there are no separate laws pertaining to Telemedicine. Given the present medico-legal climate in the country, to allow acceptance and optimal utilisation of technology in medicine there is a need to:

- Clearly define separate telemedicine and electronic media-related health laws
- Legalize tele-consultation
- Enlist the requirements for tele-consultation
- Introduce the concept of tele-consultation to the insurance sector
- Provide the necessary infrastructure
- Work out the remuneration and reimbursement issues
- Define the area of jurisdiction

From the standpoint of the users, the areas of concern that would need to be addressed include:

- For the patient: issues of privacy, confidentiality, right to avail expert treatment and informed consent
- For the doctor: the responsibility of treatment, usage of data for both treatment and research, maintenance of patient privacy and confidentiality, the commitment to meet the patient if needed and adaptation to the local needs
- For the administrators and those providing the services: issues of cultural and language cross border differences, definition of responsibility of conferencing and safe data storage as also the doctor's willingness, availability and more importantly the level of expertise being offered.

Conclusion

Telemedicine is an innovative need-based cost-effective point of care technology offering comprehensive telemedicine solutions. Its aim is to reach the 'hard to reach' and 'under-serviced' populations through virtual physical examination modules such as tele-ENT, tele-dermatology, tele-medical and surgical consult, tele-cardiology, tele-ophthalmology, rapid diagnosis of diabetes, etc.

Healthcare providers across the country are now familiarising themselves with Telemedicine technology which can be used for delivering healthcare and distance education. Although adoption has started in some states, most of the applications are in project modes. It will take time and conscious will for diffusion of this technology into health delivery system. Governmental support and appropriate regulatory measures will further help implementation and acceptance.

References

1. 'Adapting evaluation measures for hard to reach audiences';:Earthman, E, LS Richmond, DJ Peterson, MS Marczak & SC Betts (1999);*Children, Youth and Families Education and Research Network*, University of Arizona. <http://ag.arizona.edu/fcs/cyfernet/evaluation/adapeval.pdf>
2. Asystematicre view of the benefits of home telecare for frailelderly people and those with long-termconditions; James Barlow, Debbie Singh, Steffen Bayer and Richard Curry; Journal of Telemedicine and Telecare 2007; 13: 172–179
3. The use of an electronic audience response system for data collection; Eduard J. Gamito, Linda Burhansstipanov, Linda U. Krebs, Lynne Bemis, Alice Bradley; Journal of Cancer Education. 2005; 80-86
4. Capitol Hill Steering Committee Discuss the Current Status of TeleHomecare,*Federal Telemedicine News* (November 5, 2007)
5. Telemedicine: A New Horizon in Public Health in India; Aparajita Dasgupta and Soumya Deb; Indian J Community Med. 2008 January; 33(1): 3–8

6. Telemedicine in India: Initiatives and Perspective; B.S.Bedi; Senior Director Department of Information Technology Ministry of Communications & IT Government of India eHealth 2003: Addressing the Digital Divide-17th Oct. 2003

7. http://www.sti.nasa.gov/tto/spinoff1996/27.html; Health and Medicine

8. Allen A, Allen D. Telemedicine programs: 2nd annual review reveals doubling of programs in a year. Telemedicine Today. 1995;3(1):10–4.

9. Kopp S, Schuchman R, Stretcher V, Gueye M, Ledlow J, Philip T, et al. Telemedicine. Telemedicine J E-health. 2002; 8:18

10. www.isro.org

11. www.mit.gov.in

12. Report of the Technical Working Group on Telemedicine Standardization, Technical working group for Telemedicine Standardization Department of Information Technology (DIT), Ministry of Communications and Information Technology (MCIT), May 2003; Saxena G, Singh JP. E-medicine in India: Hurdles and future prospects, paper presentation at an International seminar organized at The International Institute of Professional Studies. Devi Ahilya University

13. http://planningcommission.nic.in/plans/planrel/fiveyr/11th/11_v2/11th_vol2.pdf

14. Cost Effectiveness of Telemedicine for the Delivery of Outpatient Pulmonary Care to a Rural Population: Zia Agha, Ralph M. Schapira and Azmaira H. Maker. Telemedicine Journal and e-Health. September 2002, 8(3): 281-291.