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REVIEW ARTICLE

CHILDREN ARE NOT MINIATURE ADULTS

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ABSTRACT

Biggest challenge that a pediatric dentist has to face is the ever dynamic changes in a newborn and infant through childhood and adolescence. Being a pedodontist, and having to work exclusively on child patients, our foremost requirement is to be able to appreciate fully the massive difference in each and every aspect of biological and behavioural spheres between a child and an adult through adolescence. A thorough knowledge of this significant difference between the two age groups will not only help in better understanding of the patient's present condition and its clinical significance in pediatric dentistry but will also guide a pedodontist to take age appropriate measures in treatment of an individual. The overall management of patients by a pedodontist is not just limited to the care of oral cavity but should also include the consideration of the other body systems like gastrointestinal system, renal system, respiratory system, cardiovascular system, central nervous system, muscular system, immune system, as these systems in themselves effect the treatment protocols.

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INTRODUCTION

The very reason of emergence of a special branch of pediatric dentistry explains the significance of differences, which are present between a child and an adult and a great need to comprehend these differences. A child patient is not just a smaller version of an adult. Instead, with advancing age right from birth through adolescence, an individual passes through different stages of changing physiology, anatomy and behavior, which is particular of that age at any given time. This paper is being written in an attempt to collectively summarize the differences in different body systems other than oral cavity to aid the reader in reviewing the much neglected other body systems in the field of dentistry and also to comprehend how these differences effect our approach in treatment. Before actually beginning with summarizing those, one needs to be clear with the actual age demarcation based on chronology, to define the different stages of development of an individual (Macfarlane Fiona, 2006) - Preterm- born before 37weeks

Neonates- birth to 4 weeks
Infants- upto 12 months of age
Child – 1-12 years
Adolesents-12-18years
(* According to British National Formulary)

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These age defined terms help in better communication not only among the intradisciplinary but also among the interdisciplinary associates. Starting with indivisual body systems,

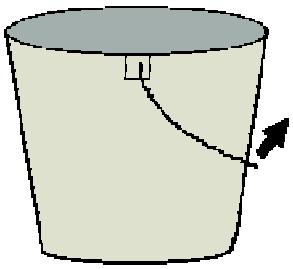
Central nervous system

The physical characteristic of skull in children shows that it is comparatively smaller in size due to obvious smaller size of them. Following the cephalo-caudal growth gradient which shows an increased axis of growth from head to toe, the skull size together with the nervous tissue is the first to complete its growth among the rest of the body systems. Head proportionately larger than their body size makes child susceptible to head injury. Not just that, even the large and uncalcifiedfontanelles effect the ultimate skull shape if proper handling and positioning of the child was not taken care of. But the less rigid skull due to large fontanelles helps in easy estimation of intra cranial pressure by palpation. Together with that it also helps to gauge the degree of brain development depending on the state of its closure. (TandonShobha 2nd edition) The cerebral cortex is less developed including the frontal lobe which is also immature having little influence on the lower parts of brain resulting in not much sustained emotional response of any type. Children present with certain unique reflexes which are not found in adults like rooting reflex and suckling reflex which are developed by 28 weeks of

intrauterine life and are basically the evolved development of their need like breast feeding. The myelination of the nerve fibers is also not complete in children, so many of the test, which rely on the nervous response like pulp sensitivity is also not confirmatory. Children are also known to have lower pain threshold due to more number of nerve endings per unit area and immature development of inhibitory pathways. The thin and fragile vessel walls in children predispose them to increased incidence of intraventricular haemorrhage.

Respiratory system

Anatomically and physiologically, various notable differences are observed which increase airway resistance in children like large head, short neck, prominent occiput, highly and more anteriorly placed larynx at the level of C_2-C_3, long, stiff, U shaped epiglottis which flops posteriorly, funnel shaped airway which is narrowest at the level of cricoid cartilage, short and smaller tracheal diameter, narrow nasal passage, increased nasal secretion, large toungue and enlarged tonsils. Also in children, the increased chest wall compliance due to increased elasticity of ribs and intercoastal muscles, reduced lung compliance (which develops by puberty), less developed alveoli (which equals the number in adult by approx. 8 yrs), increased Functional residual capacity (FRC) is noted. Diaphragmatic ventilation and horizontally positioned ribs in children prevents the normal "***Bucket Handle "***action seen in adults during breathing further limiting an increase in tidal volume in children.



Because the thorax expand and contract to allow breathing, the ribs move slightly in a "bucket handle" type of motion with each breath

The muscle of ventilation are easily subjected to fatigue because they have less amount of Type 1fibres in comparison to adults which increases in number by 1 year of age. These fibres are characterized of having increased amount of oxidative enzymes and reduced amount of muscle phosphatase, undergo slow contraction but are fatigue resistant. The epithelium in children is loosely bound to the underlying tissue and with any trauma to airway easily results in edema which further increases the airway resistance to 60% on only 1mm of edema (Resistance $\propto 1/\text{radius}$).

Cardiovascular system

The myocardium of neonate is having fewer contractile elements making the ventricles less compliant and rendering them less ability to provide tension during contraction, which further reduces stroke volume. The cardiac output thus becomes dependent on rate predominantly (*COα stroke volume X rate of contraction*). Increased vagal parasympathetic tone in infants and neonates makes them prone to bradycardias. Sinus arrhythmia is also common in children.

Normal Heart Rates (beats/min) and Systolic Blood Pressure (mmHg)

Age	Average	Range	Mean SBP
Preterm	130	120-170	40-55
New-born	120	100-170	50-90
1-11 months	120	80-160	85-105
2 years	110	80-130	95-105
4 years	100	80-120	95-110
6 years	100	75-115	95-110
8 years	90	70-110	95-110
10 years	90	70-110	100-120
14 years boy	80	60-100	110-130
girl	85	65-105	110-130
16 years boy	75	55-95	110-130
girl	80	60-100	110-130

The fetal circulation needs special description here due to significant difference before and after birth.

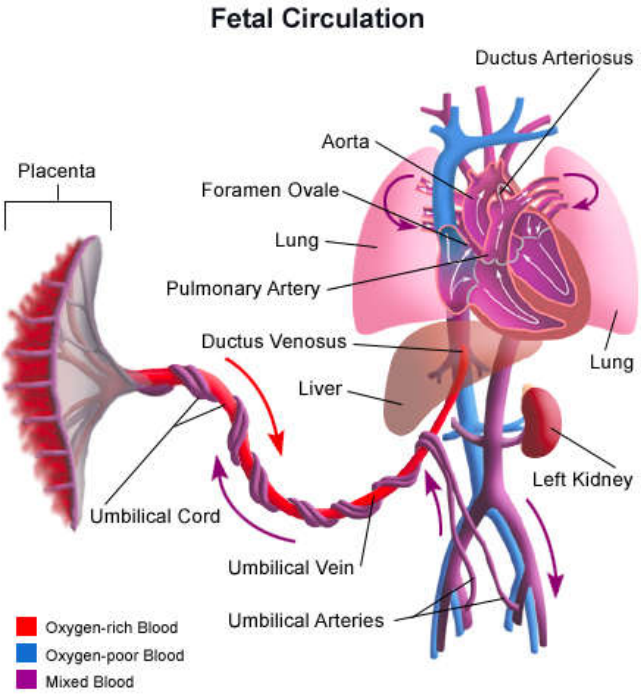
In pregnancy, the fetal circulatory system works differently than after birth:

- The fetus is connected by the umbilical cord to the placenta.
- Through the blood vessels in the umbilical cord, the fetus receives all the necessary nutrition, oxygen, and life support from the mother via placenta.
- Waste products and carbon dioxide from the fetus are sent backto be eliminated through the umbilical cord and placenta to the mother's circulation.
- The fetal circulatory system uses two right to left shunts, to direct blood that needs to be oxygenated. The purpose of these shunts is to bypass certain body parts – particularly, the lungs and liver – that are not fully developed while the fetus is still in the womb. The shunt that bypasses the lungs is called the foramen ovale. It moves blood from the right atrium of the heart to the left atrium. The ductusarteriosus moves blood from the pulmonary artery to the aorta.
- At birth, the umbilical cord is clamped and the baby no longer receives oxygen and nutrients from the mother. With the first breaths of life, the lungs begin to expand, the ductusarteriosis and the foramen ovale both close which is aided by increased oxygen saturation and reduction of prostaglandin from fetal circulation. (2016 University of Rochester Medical Center Rochester)

Haematology

Blood– volume is 80ml/kg in the full term infant (20% higher in preterm infant). 70-90% of Hb present at birth is of the fetal type, which has a leftward shift on the oxy-hemoglobin dissociation curve, which enables it to "hold on" to oxygen better while circulating through the placenta. HbF combines more readily with oxygen but less readily releases oxygen, as there is less 2,3-Diphospho glycerate (DPG). HbF is seen to have protective action against red cell sickling and provides

infants with natural immunity to sickle cell anemia. But within almost three months, HbF levels drop to 5% and HbA predominates. Consequently, the 0_2/Hbdissociation curve shifts to right as levels of HbA and 2,3-DPG rise. The haemoglobin level in infant is also high, around 18-20gm/dl then drops over 3-6 months to 9-12 g/dl as the increase in circulating volume increases more rapidly than bone marrow function. Transfusion is generally recommended only when 15% of the circulating blood volume has been lost. The vitamin K dependent clotting factors (II, VII, IX, X) and platelet function are deficient in the first few months and so, vitamin K is given at birth to prevent hemorrhagic diseases of newborn.



Normal Blood Volumes

Age Blood Volume
New-born 85 –90 ml/kg
6 weeks to 2 yrs85 ml/kg
2 yrs to puberty 80 ml/kg

Thermo-Regulation

Babies and infants have minimal subcutaneous fat and a larger surface area in relation to body mass. When performing exercise, the temperature of the body increases. In children, roughly 20% of the energy is converted into work and rest of the energy, which is approximately four times that of the work done, is converted into heat energy and is dissipated throughout the body. This is in contrast to adults in which, a larger proportion of energy is converted into work done and less is dissipated into heat. The body has produced ways to deal with the temperature rise by sweating primarily, in adults but not in children. The low sweat production is related to the immaturity of sweat glands. In humans, the number of sweat glands varies between 1.6 and 4 million, that is distributed throughout the body surface and showing a positive correlation between the number of sweat glands and sweating capacity. (Shibasaki *et al*., 1997; Inoue *et al*., 2004) By 2-3 years of age, there is no further formation of new glands after this phase. But contributes to increased sweating with age as in adults by increased sweating rate by the sweating glands. (Shibasaki *et al*., 2006) Though heat dissipation by means of sweating is not developed in children but the larger surface area in them aid in heat loss as larger surface area means larger proportion of heat can be released in to the environment through skin. To help give off more heat, kids divert more heat and therefore warmth by increasing the blood supply to skin from tissues that are not working currently. The large surface area to body mass ratio makes children far less tolerant to temperature extremes than adults. As in summers, the larger surface area not only helps in larger area of heat loss but also of heat gain and in winters, cause children to lose heat too fast. But normal mild temperatures are suitable for children, infact advantageous as less developed sweating causes less fluid loss and likewise less dehydration. The optimal ambient temperature to prevent heat loss is 34ºC for the premature infant (born before 37 weeks), 32ºC for neonates and 28ºC in adolescents and adults.

Renal system

The renal system is developmentally and anatomically closely related to the reproductive systems especially in males and is therefore called as urogenital system. The kidney in fetus begins to function by around 10 weeks, though the urine formed then is not to carry out waste out of the body but to add to the volume of amniotic fluid reaching 200ml/day in production. The kidney and bladder continue to develop after birth with their development not completed until end of first year and bladder development not completed until puberty. The structural components of kidney and a full complement of nephrons have been established at birth. Further development of kidneys involve growth and development of renal tissues and maturation of nephrons which further increase their ability to filter and absorb. Adult values of glomerular filtration is not complete until 1-2 years of age and so newborn is unable to excrete excess water or solutes as efficiently as adults. Also the short loop of henle in newborn posess reduced ability to reabsorb sodium and water producing very dilute urine. As the tubules grow and mature, their concentrating ability increases reaching adult levels of maturation by 8 months of life. Another notable difference of renal physiology in children are that, reduced capacity of hydrogen ion excretion and low plasma bicarbonate levels make the infant more liable to develop severe metabolic acidosis. (Carlson, 1999; Larsen, 1998; Mac Gregor, 2000)

Urinary Output in Paediatric Patients

- Normal: 1 – 2ml/kg/hr
- Oliguria: <1.0ml/kg/hr
- Polyuria: > 3ml/kg/hr
- Older children: 30 ml/hr is the minimum normal output.

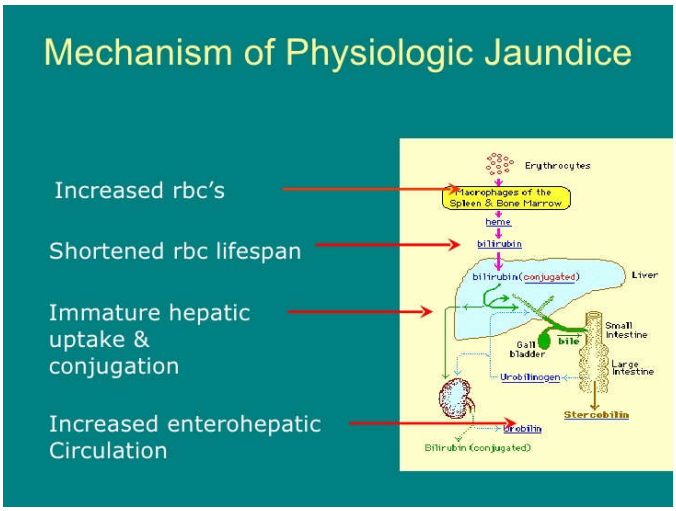
Digestive system

The gastro-intestinal tract starting from mouth through esophagus, stomach, small intestine, large intestine and including liver and pancreas has significant anatomical and physiological differences which are worth discussing and have

a pivotal role in explaining the child physiology. The sudden separation of a newborn from the secure maternal environment in womb and separation of nutrients from maternal circulation causes the infant to lose 5-10 % of body weight due to shock at birth. The well known infantile swallow characterized by forward tongue placement and increased circumoral muscle activity with anterior open bite is also differentiated from adult swallow by "sucking blisters" or "pars villosa" which helps to seal when the baby sucks. Sucking usually follows a rhythm of one breath to one or two swallows and increases in efficiency after birth. Saliva with little amylase enzyme secretion and function is not achieved as equal to that of adults by 2 years of age. Pharynx is poorly designed to allow simultaneous passage of food and air. Until the striated muscles in throat show cerebral connections, swallowing is an autonomic reflex till 3 months of life but by 6 months of the baby is able to swallow, hold or spit out the food. Prior to birth, gastrointestinal tract of fetus is completely filled of gas. By 5 months of intrauterine life, the fetus is swallowing amniotic cavity, dead hair, skin cells and bile excreted from liver. All of it together forms meconium, which passes through rectum as infant's first stool and proof of normal anal function. After birth, at the first few breaths, the git is filled with gas by swallowing air and by 3 hours entire gut is filled with gas and it continues to happen till the baby continues to be fed orally. A 3.5 kg baby usually takes in 100ml of food in fifteen minutes and approximately the same volume of air. This fact in children makes it desirable to always make them burp after meal by laying them straight and back and neck supported to help gas bubble up the straight esophagus. Position of the stomach is transverse in children than vertical in adults and the emptying capacity is 2 and ½ to 3 hours of a newborn reaching 3-6 hours by 5 years of age. The immature lower esophageal sphincter and short length of esophagus are the main cause of frequent regurgitation seen in infants. Less developed gastric mucosal barrier makes infants vulnerable to orally transmitted gut infection. The pH is neutral at birth due to swallowing of amniotic cavity but the gastric acid (hydrochloric acid) secretion does commence by 8 hours of life though still low. Acid secretion reaches adult level by 10 years of age and this also makes them less likely to develop gastroenteritis as the acid will kill orally taken bacteria completely.

food and the incompletely digested food passes onto the colon, where rise in osmotic pressure draws more water from interstitial spaces and lead to increased peristalsis and loose stools. However, the true colic pain is self-limiting.

The neonatal liver is also functionally immature by having reduced enzyme needed for production of conjugated bilirubin (which is water soluble and added with albumin and a sugar molecule and is excreted in bile via gut) from 'haem' of hemoglobin for an increased destruction of red blood corpuscles in neonates due to reduced life span of only 70 days of erythrocytes in comparison to 120 days in adults. This enzyme takes 2 weeks to reach a normal functioning level. So by then high chances of development of physiologic jaundice occurs due to increased deposition of unconjugated bilirubin (fat soluble) in adipose tissues of the body. Normal bilirubin levels are less than 1.5mg/ml and is detected when rises above 3mg/ml, most easily detected in sclera, soft palate and skin of infant which appears yellow. This physiological jaundice worsens with dehydration due to inappropriate feeding due to relative rise in proportion of bilirubin to the circulating blood volume.



Stomach capacities by age (ml)

New-born	1 week	2–3 weeks	1 month	3 months	1 year	2 years	10 years	16	Adult
10-20	30-90	75-100	90-150	150–200	210–360	500	750-900	1,500	2000-3000

Till first 3 months, pancreatic juice contain only little lipase enzyme which limits the capacity of baby to convert fat into fatty acid and glycerol. But nature has also matched according to the demand of the physiology of infants, by producing breast milk rich in long chain polyunsaturated fatty acids to feed the large developing brain and are also easily digestible. The amylase enzyme activity unlike the lipase is high in small intestine at birth to be able to digest the milk diet but then declines during infancy and almost disappears in some adults. Children also suffer from frequent colic pain on start of intake of complex food within 6 months. This is because, the less developed gastric enzymes do not cause complete digestion of

Peristaltic waves are experienced usually 15 minutes after breakfast all through the gut and large intestine originating from stomach after it is filled after meal. The stimulates the defecation reflex of internal rectal sphincter and it persists for only few minutes. This is commonly used by carers/mothers to 'potty train' or 'toilet train' the child. Babies on average pass stools 3-5 times a day or may occasionally pass no stool at all for 3 days. Constipation is usually defined for stool frequency of less than 3 times per week and can be cured by appropriate vegetables and dietary fibers. (Catto-Smith, 2005; Cole, 2007; Baker, 2005; Geissler and Powers, 2005; Bailey and Martin, 1994; Levine *et al*., 2007; Marieb and Hoehn, 2007; Goyal and Mashimo, 2006)

Skeletal system

Growth of any system including skeletal system is a continuous process. The building and destruction as part of moulding process of the skeleton occurs throughout life. Likewise body proportion also change over period of childhood, with increase in relative length of legs in relation to height as the child moves to puberty. Overall reduction of basal metabolic rate BMR over the childhood years is reflected by the decreasing body mass in relation to surface area. However periods of rapid growth and periods of little change is also reported, oftenly described as ***"Christmas tree"*** pattern. Finally the adolescent growth spurt is adorned with peak height velocity and maximum growth rate. At birth, vertebral spines present with two primary curves (thoracic and sacral) but by adolescence four vertebral spines are developed namely cervical, thoracic, lumbar and sacral. Different head and neck anatomy with difference in position of larynx and trachea demands a difference in techniques of resuscitation in children of less than 7 years of age. Small children have small sinuses, which does not complete its growth till 10-12 years of age. This makes it difficult to distinguish the similar high-pitched voice of these small children. With increase in size of sinus, chances of lodgment of infection, running nose and not being able to differentiate between voices all become history. Ear and throat infections are also reduced. Fact that bones of children are being built and are not in their full strength as adults make them respond differently to mechanical stress and also have some weak zones that adults don't have. Increased flexibility of bones in children oftenly results in ***"green stick fracture"*** having fracture at only one side of bone, i.e including only one cortical plate. Exercise is also seen to have a remarkable effect on bones. It was found by Rodriguez in 2006, that intensity of load was more important than duration in children. Repeated vigorous weight bearing physical activities like football leads to gain in bone formation. This increase in bone mass thereby causes reduction in load over larger bone eventually creating a balance between bone loss and bone gain. 90% of bone mass has been laid down by puberty, while 25 % of the adult bone mass is attained within two-year period of growth spurt (11-13 years for girls and 12-14 years for boys. Early skeletal maturation offers children with an observable advantage of being stronger, faster and increased oxygen uptake in comparison to their younger peers. Many of such children with early skeletal maturity are also accompanied with advanced sexual development, as the hormones (testosterone) that stimulate growth in bone and muscles, also effect sexual organs). (Quiros-Tejeira, 2007; Branca, 1999; Geissler and Powers, 2005; Jenkins *et al*., 2007; Kahn *et al*., 1994; Mallan *et al*., 2003; Pellegrini and Smith, 1998; Morris *et al*., 1997; Neilland Knowles, 2004; Patel *et al*., 2006; May *et al*., 2006; Rodriguez, 2006; Siranda and Pate, 2001; Tanner, 1989; Thibodeau and Patton, 2007; Voss *et al*., 1998; Wood and Attfield, 2006; Watts *et al*., 2005)

Immune system

The less developed immune system in children makes infants and children susceptible to attack of microorganisms. Before birth, protection to infants, is largely offered by mother's defence. Following birth, a three line of defence mechanism provides protection to child. First line of defence is ***"the skin".*** Intact skin and mucosa surface provides non immunological host defence in a very effective and efficient manner. Also, lysozyme (an antimicrobial enzyme) body secretions like saliva, sweat, tear, acidic pH of the gastric juice and ciliary movement of the upper respiratory tract all together aid the first line of defence in sweeping off the body from micro-organisms. The second line of defence is offered by ***"white blood cells"***. The white blood cells together with platelets and mast cells initiate a complex reaction called as inflammation, which provides a normal protective barrier to harmful organisms entering the body. The third line of defence is acquired by ***"acquisition of immunity"***. Immunity is acquired in an active or passive manner. Active immunity is developed following exposure to any infection and stimulation of the immune system to that particular infection or after immunization. Passive immunity on the other hand is short lived immunity and is gained on direct transfer of antibodies to the individual, either through mother or through immunization. The immunoglobulins (Igs) produced by B cells are- IgA, IgM, IgE and IgG. IgG is the major immunoglobulin found in lymphoid tissue and is 75% of all the Igs. It is secreted in breast milk and colostrum in high concentration and is capable of passing easily through placenta offering mother's immunity (passive immunity) to the child for first three months after birth. IgA comprises of 5-10% of Igs, secreted in high concentration in respiratory and gastrointestinal secretions including saliva and tears and provides protection to breastfed infants from intestinal infections in early life. IgM comprises of 10% of Igs and is the major Ig produced in infancy. IgE is Ig involved in allergic, anaphylactic and other atopic reactions and is raised in sensitized children. The levels of IgM, G and A are all low in fetus till the unborn baby is exposed to any infection, when B cells are seen to synthesize IgM first at as early as 28 weeks of gestation. After birth, these levels of Igs begins to fall, as the newborn begins to form its own Igs. Premature baby is seen to have low amounts of IgG as major portion of this Ig is transferred in the third trimester. All these Igs reach adult levels by 4 years of age and this explains the increased vulnerability of children under 4-5 years of age to infection. Another point worth discussing here is the Rhesus immunization that occurs when a fetus is with rhesus positive antigen on its red blood cells and mother is rhesus negative. In such cases, mother produces IgM and IgG of which IgG passes placenta and clumps fetal red cells to destroy them. This reaction is sensitized by first pregnancy but turns highly fatal in subsequent pregnancies as the now the mother antibodies quickly recognize this antigen.

Having mentioned this, now coming on to the different aspects of patient management, which are to be considered while attending a young patient. These includes, (Mcbrien Dianne 5th edtion)-

1. Rate and route of drug administration
2. Dosage
3. Onset and duration of action
4. Possibility of toxicity.

1. Rate and route of drug administration

Several routes of drug administration are available which have their own limitations and advantages which will be enlisted here one by one.

a) Oral route-Most universally accepted and easiest method of drug administration is the oral route. This is certainly true, especially in young patients who will not object oral route instead of injections. The unpalatable taste of the drug can be compensated with certain flavoring agent but one should keep an extra care on oral hygiene as these can be a contributing factor in caries. But the ease of intake of this route comes in hand with certain limitations too like-

- The variability of this route of drug administration. The variability arises because of its dependence on absorption through the gastrointestinal mucosa. That is, it depends on the condition of the stomach and intestines, the absorption characteristics of the drug and also the bioavailability of the drug.
- The drug given by this route varies in their peak and consistency of effect.
- Reversal of any unwanted effect is difficult.
- Titration of drug is not possible to achieve optimal effect from moment to moment as is possible with other methods like intravascular injection.
- Recovery time from the effects of drug if used in sedation by oral route may be delayed, if the drug is slowly metabolized. (Granoff *et al*., 1971)
- Flavoured syrup based oral medications when used (eg. In patients of iga immunoglobulin deficiency) raise the suceptibilty of teeth for dental caries.

b) Intramuscular route-For obvious reasons, the acceptability of this route by younger patients is less when compared to oral route. However, situations may arise in which use of this route may be advantageous over oral route that is when patient for any reason does not want to take drug orally or is not able to do so. Alike oral route, route of intramuscular drug administration shares similar limitations

- Need of prolonged time for peak effect of drug though less when compared to oral route.
- Variability seen with its onset and effect of drug.
- Total lack of reversibility except in certain drugs.
- More chances of idiosyncratic reactions.
- Increased chances of tissue necrosis.
- Increased incidences of persisting pain at the injection site.

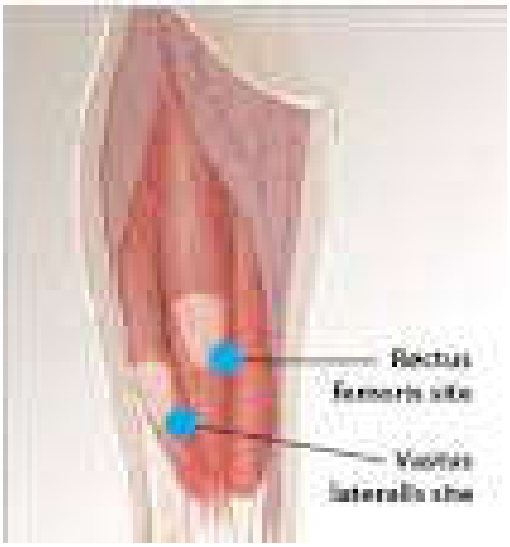
One must also take care of certain cautions with intramuscular route of drug administration like

- Because of better peripheral perfusion in children, onset of drugs administered by this route may be more rapid.
- Anatomical difference in the site of injections for IM route. The primary consideration of which is presence of adequate tissue mass and reduced risk of injury due to needle penetration. These sites are namely-

I. Vastuslateralis muscle- on the anterior thigh, which is the safest site specially for young children

II. Gluteus maximus muscle- outer and upper quadrant of this muscle.

III. Deltoid muscle- middle and posterior lateral aspect of this muscle.



Vastus lateralis

Gluteus maximus

Deltoid

c) **Intravenous route-** this route requires hands of properly trained professionals for easy, efficient and safe drug administration. It offers the biggest advantage of fastest onset of drug action among rest of the routes, that is within 20-25 seconds. Total reversibility of drug effects and titration of drug effect is also possible by this route. But poses with disadvantages like-

- Difficulty in venipuncture in very small children due to small vein size and availability with added difficulty of restraining the child movement.
- Increased possibility of phlebitis, especially in drugs which are water insoluble.
- Hematoma at the site of injection is also very common.
- Increased need of close monitor of the patient.

d) **Sublingual/Buccal route-** Drug in the form of pellet or tablet can be applied under the tongue or can be crushed and spread to be applied in the buccal mucosa. Possibility of administration of only lipid soluble and non irritating drugs limits this route being routinely used. (Tripathi, 2008) Yet it provides some advantages in children-

- Use of injection is evaded.
- Bypassing of liver which is already deficient in many vital hepatic enzymes in children especially upto 2yrs.
- Can spit the drug after onset of desired effect.

e) **Rectal route-** Certain drugs which are unpleasent can be administered by rectal route as suppositories and retention enema for obtaining systemic effect. This can be used in patients who are having recurrent vomiting or are unconscious. However,

- Its inconvenient and embarrassing
- Absorption is slow
- Effect is irregular and unpredictable
- Rectal inflammation can occur from irritating drug

f) **Cutaneous route-**Drug in the form of ointment is applied directly over intact skin for slow and prolonged absorption and offers advantage of liver bypass like sublingual and rectal route. *Dentipatch*, a transorallidocaine delivery system is based on this concept of transdermal therapeutic system of cutaneous route of drug administration. It's used in conditions requiring longer durations of surface anesthesia (eg. excision of small papillary growth or mucocele or small vestibular swelling in oral region) unlike other local anesthetics which provide only shorter duration of surface anesthesia. (Dean, McDonald, 19th edition)

g) **Inhalation-** gases and liquids which are volatile can be given by this route for systemic action eg- general anaesthetics. But the increased respiratory rate in children of up to approximately 12 years to compensate for the reduced functional capacity will increase the amount of gas intake. So need to be taken with extra care with drugs which are CNS depressants. Also,

- Irritant vapors such that of ether can cause respiratory tract inflammation.
- Increased respiratory tract secretion.

2) Dosage- Pediatric doses when given should be calculated properly from authenticate pediatric dosage reference text and should never be simply extrapolated from adult dose. Dosage in children can be calculated by many means like age, body weight, body surface area or a combination of these. Of all the different methods, body surface area (specifically that given by Boyd & Mosteller formula) is the most accurate since many physiological phenomenon likebasal metabolic rate, glomerular filtration rate, cardiac index, oxygen consumptionetc relate most closely with an individual's body surface area. Anticancer chemotherapeutic drugs are especially given according to body surface area owing to their low therapeutic index. 8

Few to enumerate are

a) **Clark's rule-** child dose = (Weight (in pounds)/ 150) x Adult dose.
b) **Young's rule-** child dose = (Age of child/ Age +12) x Adult dose.
c) **Cowling's rule-** child dose = (Age at next birthday/24) x Adult dose.
d) **Dilling's rule-** child dose = (Age of child/20) x Adult dose.
e) **Gabius rule-** fractions of adult dose which were to be used at different ages, **1yr-** $1/12^{th}$ of adult dose, **2yrs-**$1/8^{th}$ of adult dose, **3yrs-** $1/6^{th}$ of adult dose, **4yrs-** $1/4^{th}$ of adult dose, **7yrs-** $1/3^{rd}$ of adult dose, **14yrs-** 1/2 of adult dose, **20 yrs-** $2/3^{rd}$ of adult dose, **21 yrs-** adult dose
f) **Bastedo's rule-** child dose = (Age of child+3/30) of the fraction of adult dose
g) **Fried's rule-** child dose = (age of infant (in months)/150) of the fraction of adult dose. *This is recommended for use in infants less than 1 year.*
h) **Catzel's rule-**based on surface area and expressed as percentage of adult dose. **1yr-** 25% of adult dose, **3yrs-** 35% of adult dose, **7yrs-** 50% of adult dose, **12yrs-** 75% of adult dose.
i) **Body surface area rule-**many formulae are proposed by different contributors of which the Du Bois formulae in 1916 was the first to be contributed. BSA [m^2] = Weight [kg]$^{0.425}$ × height (cm)$^{0.725}$ × 0.007184 Child dose = (child's BSA/ 1.7) x Adult dose

Boyd formula- in 1935
BSA [m^2] = Weight [kg]$^{0.4838}$ × Height [cm]$^{0.3}$ × 0.017827)
Mosteller formula- 1987
Height [cm] × Weight [kg]/3600)^{½}

3) Onset and duration of action

- The poorlyformed blood brain barrier in neonate which is completed only by almost 2-3 years post nataly results in a prolonged and variable duration of action of drugs such as barbiturates, opioids, antibiotics and bilirubin which cross it easily.
- Increased functional residual capacity in children can cause increased intake of inhalational drugs resulting in increased concentration of it in blood and may again increase the duration of action of the drug and can delay the reversal time.
- Low body temperatures in children causes' respiratory

depression, acidosis, decreased cardiac output, decreases platelet function. The duration of action of drugs is also increased within creased the risk of infection.

- Any medication delivered to child rectally must be introduced gently through rectum which is always in state of contraction at the external rectal sphincter and becomes tensed more so in state of anxiety.
- School aged children taking cow milk protein of tenly develop constipation because of their habit of not wanting to visit school toilets out of embarrassment. Stool softeners such as lactulose as the first choice of medicine in case of such constipation provides great help by drawing more water into the gut so the stool swells and softens making its passage easier.
- Infants having longer emptying times and irregular peristalsis result in slower gastric drug absorption.
- Diazepam, phenobarbitone and phenytoin are associated with slow oxidation owing to low levels of cytochrome P-450 in first two months of life in infants.
- Drugs like morphine, acetaminophen, sulpha antibiotics and steroids require glucoronyltransferase for conjugation and should be given with caution in neonates as it does not reach the adult levels till first month of life.
- Deficient levels of pseudocholinesterase in infants till 2 years of life make them vulnerable to succinylcholine administration in cases of undiagnosed myopathies and thus should be avoided.

4) Possibility of toxicity

- Increased alveolar ventilation to functional residual capacity ratio, increased blood gas partition coefficient and increased tissue blood partition coefficient causes increased amount of drug in cerebral blood flow, so any drugs which cause central nervous depression whose level if not monitored can cause central nervous system and respirator center depression at much lower levels.
- Because 40% of a child's cardiac output is perfused to brain, any sudden decrease in heart rate results in decreased cardiac output which in turn increases the rate of inhaled anesthetic uptake will cause significant depression of the central nervous system. (Hillier *et al*., 2004)
- Drugs like penicillin, short-acting barbiturates and phenobarbital with renal route as primary route of excretion should be used with caution and after proper drug dosage calculation in children to prevent chances of drug toxicity due to low GFR values in children.
- Morphine, atropine, sulpha antibiotics and many other drugs in which renal tubular transport plays an excretory role carry a narrow margin of safety due to reduced development of renal tubular transport mechanism in them. (Fernandez *et al*., 2011; Kearns *et al*., 2001)
- Any water soluble drug must be administered at higher levels per unit of body weight in children to attain therapeutic concentration, as 80% of the total body weight is water in them and only 50-60% in adults.
- Warfarin and digoxin and similar drugs which are highly protein bound should be given at low levels per unit of body weight due to low levels of serum albumin and globulin in newborn and young infant.

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