Section

I

A Perspective on Pediatric Practice

Chapter 1

Prenatal Screening: Perspective for the Pediatrician

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Births with Down syndrome and other aneuploidies continue to occur with a prevalence of 1 in 925.[1] Prenatal screening for fetal aneuploidies started early with triple test performed in the second trimester (a combination of alfa feto protein, conjugated estriol and beta human chorionic gonadotropin). In the last two decades, the focus of detection has shifted to the first trimester. Two serum markers (pregnancy associated plasma protein A and free beta human chorionic gonadotropin) and one marker assessed by ultrasound (nuchal translucency) are used to predict risk of aneuploidies. Prenatal screening has not been perceived as a health priority in developing countries. Chromosomal and certain common malformations pose additional financial and social constraints in developing countries. In addition, serum screening may also direct attention and resource allocation to high-risk pregnancies complicated by pre-eclampsia/eclampsia and intrauterine growth retardation (IUGR).[2]

DEFINITIONS

Aneuploidies refer to numerical chromosomal aberrations. Common aneuploidies include Trisomy 21 (Down syndrome), Trisomy 18 (Edward syndrome) and Trisomy 13 (Patau syndrome). Sex chromosomal aneupoidy commonly screened for is Turner syndrome (XO). Risk ascertainment refers to the risk of having a child with any of the above mentioned aneuploidies. The likely risk computed in any pregnancy is illustrated in terms of a value for a given population having the same statistical measurements. Thus the risk computation of 1 in 150 means that if all demographic and biochemical parameters have the same statistical correlation, the likely possibility of a woman carrying a fetus with abnormality would be 1 in 150.

A *priori* risk means the baseline risk conferred on the woman either by age alone or as a result of biochemical screening. The risk increases as age increases due to a higher propensity for non-dysfunction. The risk of Trisomy 21 is 1 in 1667 at 20 years of age and increases to 1 in 385 at 35 years of age, and 1 in 30 at 45 years of age.[3] The risk calculation takes into account the gestational age at sampling, the status of the fetus-singleton/twinning, maternal weight, maternal diabetes, maternal smoking, and previous history of baby with Trisomy 21. Incorporation of values of biochemical analytes along with the demographic data into a designated software generates a risk. Individual values of any analyte or factor are less predictive individually compared to the entire risk computed in a statistical manner incorporating all these factors.

Triple test and Quadruple test (addition of inhibin A) are used to compute risk of aneuploidies in the second trimester (16–20 weeks).[4] Screening has now shifted to the first trimester and uses both serum and ultrasound markers. Nuchal translucency (NT) refers to the measurement of skin at the nape of the neck in the fetus in sagittal plane.[5] Integrated screening is the term used for assessing the risk in the first trimester followed by using this generated risk as *a prori* risk for the second trimester. The results of the first trimester are not disclosed before the final risk is generated. Contingent screening indicates that second trimester screening is subject (or contingent to) to risk generated in the first trimester.[6] Table 1.1 presents the performance characteristics of these tests.[7–9]

TABLE 1.1: Performance characteristics of prenatal screening modalities

Test	*Timing (wks)*	*Sensitivity*	*False positive rate*
Triple	15–20	72–74%	5%
Quadruple	15–20	79–81%	5%
Serum integrated	10–13 & 15–19	86–89%	5%
Fully integrated with Nuchal translucency	Same as above 10–12	93–95%	5%

Like any other screening technique, confirmatory testing is required to evaluate the risk generated in the first trimester. Women demonstrating a high risk in the first trimester are offered chorionic villus sampling (CVS) and those demonstrating high risk in the second trimester are offered amniotic fluid sampling. In the integrated screening modality, those demonstrating high risk in the first trimester are offered CVS while those with low risk are asked to report later for screening of neural tube defects.[10] The risk cut-offs are carefully weighed against the risk of fetal loss due to amniocentesis and chorionic villus sampling.[11] Even the best modalities are limited in sensitivity and specificity for a confirmed diagnosis of aneuploidies. Table 1.2 depicts the timing and the procedures as an option for any parent.

A large number of these analytes are also being evaluated as potential tools for adverse pregnancy outcome such as pre-eclampsia, IUGR and intrauterine demise.[12] More recently, noninvasive prenatal diagnosis as a screening test using next generation sequencing technology has been found to be highly accurate with sensitivity and specificity of up to 98–99%.[13] Despite the accuracy, the cost of the test presently is prohibitive as a screening test.

TABLE 1.2: Prenatal screening tests

Test/procedure	*First trimester screening*	*Integrated prenatal screening*	*Serum integrated prenatal screening*
First blood sample	9–13 wks	9–13 wks	11–14 wks
Nuchal translucency ultrasound	11–14 wks	11–14 wks	None
Second blood sample	None	15–18 wks	15–18 wks
Results available	12–19 wks	15–19 wks	15–19 wks
Detection rate (accuracy)	80–85%	85–90%	80–90%
False positive rate	3.9%	2–4%	2–7%
Diagnostic test (if screen positive)	CVS 11–13 wks	Amniocentesis	Amniocentesis

CVS: Chorionic villous sampling

IMPORTANCE FOR THE PEDIATRICIAN

Pediatricians often face the responsibility of revealing the diagnosis to the parents and dealing with the emotional overture. They also have to deal with complications in the neonatal period (IUGR, congenital anomalies) and various comorbidities (hypothyroidism, recurrent otitis media, atlanatoaxial instability, transient myeloproliferative disorders). The problems encountered in a child with Down syndrome are complex and require that the pediatrician liaises with a multidisciplinary team to adequately follow-up every child. Education regarding preventive strategies that reduce the burden of this disorder is of paramount importance.

CURRENT SCENARIO

Prenatal screening is common in developed countries. The biggest challenge in developing countries is late registration of pregnancy missing the opportunity of first trimester screening. Another challenge is the lack of correct recall of maternal age which forms the basis of ascertaining *a priori* risk of screening. With multiple birth orders and large family sizes, mothers tend to forget the date and at times even the year of their birth. A proportion of these women also do not remember the exact date of last menstrual period necessitating a dating scan for correct risk assignment. Since they do not register in the first trimester, this itself is a challenge. Even when women are registered in the first trimester of pregnancy, feasibility and availability of tests are important issues. Inclusion of nuchal translucency and nasal bone parameters improve detection rates and lower false positive rates in first trimester. However, these measurements require expertise and commitment.

The integrated mode of the screening is likely to pose even a bigger challenge because of the attrition between the first and second trimesters. The second trimester is an opportune window for screening not only neural tube defects but also a wider spectrum of malformations.[14] It is very important for the pediatrician to stress upon the availability of the screening modality to fellow obstetricians as it is ultimately the pediatrician who has to deal with a child having disabilities.

The indecisiveness of families to opt for invasive testing after positive screening test is another hurdle delaying the test beyond the permissible time frame of the Prenatal diagnostic techniques (PNDT) act.

THE WAY FORWARD

Mandatory registration of births and deaths may help us overcome certain challenges. However, this is likely to take some time till the current birth cohort registered by workers grows up to become sexually productive. Prenatal involvement of male partner is associated with beneficial outcomes such as higher first trimester antenatal visits, and abstinence from smoking and alcohol consumption.[15,16] This practice must be encouraged at least until female literacy and empowerment improve.

Gynecologists posted at primary and secondary level of care should be trained in methods of correct ascertainment of gestational age. Radiologists should also be roped in for encouraging early scanning and helping the gynecologists to effectively date the pregnancy. In our setting, the strategy should be to encourage early registration, improve availability of an early scan for gestational age assessment, provide serum screening to all who register within the stipulated period, and offer nuchal translucency and nasal bone measurement in screen positive group. A contingent approach in the first trimester is likely to be more feasible, but is unlikely to become universal due to limited care-seeking during this period.

Resource allocation for such a program is justified by the excellent predictability of first trimester markers to predict adverse pregnancy outcomes. Apart from reducing the financial and social burden from the birth of a child with Down syndrome, it would help gynecologists to identify the subset of women

who require closer surveillance and are at a greater risk of developing pre-eclampsia, preterm birth, fetal demise and IUGR. These may also be selected for expert ultrasonic surveillance, both in first and second trimesters. If we take the example of Delhi, approximately 3.6 lakh deliveries take place every year; 63% of these are institutional deliveries.[17] Further, the proportion of women who receive at least one antenatal care visit was 74.4%.[17] Considering this, approximately 75% of pregnant women would be accessible in the second trimester, a time when triple test coupled with a genetic sonogram would pick up more than 70% aneuplodies and a large number of structural defects. Taking Delhi as a model—by implementing screening strategies, approximately 245 births with Trisomy 21 could be prevented every year. We suggest that facilities for collection of samples for triple test should be available at most health facilities. Genetic sonograms currently should be offered in screen positive population, the high risk group and the affordable group. This is probably a trade-off of the limited resources to ensure the best possible yield.

Our second suggestion is implementation of first trimester screening in tertiary-care hospitals. The newer techniques in place can utilize dried blood spots which can be collected at any place and transported across without degradation of biochemical analytes. So the cost of machinery, personnel and expertise need not be duplicated, and the samples collected can be sent to a few centers that are committed and motivated to take up the task of screening. Nuchal translucency and nasal bone parameters can then be used in a contingent manner in the screen positive and high risk group. Preparedness to implement preventive strategies is important today for a better tomorrow.

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Chapter

2

Incorporating Developmental Screening and Surveillance of Young Children in Office Practice

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Development is a continuous process that occurs normally in childhood, wherein skills are acquired in various inter-related developmental domains. It is intricately influenced by a combination of genetic, biological and psycho-social factors.[1] Pediatricians frequently face parental concerns regarding development and/or behavior.[2] Some of these issues may be transient and easily rectifiable but a small but significant proportion may actually be harbingers of neuro-developmental disorders.

The global prevalence of developmental delay in children is reported as 1–3%, while World Health Organization (WHO) estimates that 15% of the world's population lives with some form of disability.[3,4] There is a paucity of community-based data from lower and middle income countries (LMIC), but a similar or higher prevalence is expected.[5] Due to improving maternal and child health care and better neonatal and child survival, there is now a large group of children at high risk for developmental delay in these countries. In addition, the proportion of children experiencing poverty, ill-health, malnutrition and lack of early stimulation–factors that adversely affect attaining optimum developmental potential–are much more in comparison to high income countries.[1]

One of the main reasons for lack of community-based data from India is the absence of routine developmental screening and surveillance. Developmental surveillance is the longitudinal process of identification and monitoring of newborns and children at high risk.[6] This comprises of eliciting parental concerns, acquiring developmental history, identifying risk and protective factors, evaluation, and maintenance of records.[7] Screening is the brief cross-sectional process of evaluating children by screening tools with good psychometric qualities (sensitivity and specificity >70–80%), that have been norm-referenced and standardized on populations representative of the target population.[5–7] In developed countries, both strategies are core components of the health, education and social care systems.[8] The American Academy of Pediatrics (AAP) recommends developmental surveillance of high-risk children at each health visit from birth to 3 years, and routine screening of low-risk children at 9, 18, and 24/30 months or earlier if concerns are elicited.[7] Screening for behavioral disorders and academic/learning disorders is also recommended.[9] Hix-Small, *et al*.[10] reported an increase in screening in USA after these guidelines were framed, though it is still far from ideal. Lack of screening means delay in

detection, initiation of intervention, increased morbidity and parental anguish, more health service utilization and poorer prognosis.[11]

Routine developmental screening in India

In India, there are multiple challenges to practice of universal developmental surveillance and screening. Parents are unaware of the existence and need of these services. Health care seeking is prioritized for acute illnesses which are not appropriate opportunities for screening. A heterogeneous population of doctors with variable proficiency caters to the health needs of Indian children. If parents express concerns, they are often given false assurances without proper appraisal. Well-child visits are primarily for immunization with a few perfunctory questions asked about development, if at all. This was documented in a study of perceptions and practices of 90 pediatricians from Gujarat.[12] Most participants (97.3%) reported parents expressing developmental concerns but only 13.6% used structured tools for evaluation. Reasons cited by those relying on informal assessment were time constraints (72%), non-availability of treatment or referral options (45%), and inability to use screening tools (28%). Contrary to this common misconception, informal evaluation has been proved unreliable in detecting developmental delay. Recognition is difficult in early childhood unless specifically looked for in a structured way, since changes in development are rapid, there is intra-domain overlap, and early indicators are often subtle.

At present, exposure and training in formal developmental screening and assessment is lacking in the post-graduate pediatric curriculum. Pediatricians may be cognitively aware but lack the necessary psycho-motor and communication skills to screen effectively. There is a scarcity of developmental pediatricians. Available assessment tools are mostly of international origin, which are expensive, not easily available, and require training and accreditation. Recommendations for developmental screening by the Indian Academy of Pediatrics (IAP) are yet to be formulated. Although the 'Persons with Disabilities Act, 1995' states that 'children should be screened annually to detect high risk cases', the process is not outlined.[13] In 2013, the '*Rashtriya Bal Swasthya Karyakram (RBSK)*' was launched by the Government of India, which aims at screening for defects at birth, diseases, deficiencies and development delays including disabilities (4 D's) in children between 0 to 18 years.[14] It is envisioned that pre-school children will be screened by *Anganwadi* workers using age-appropriate developmental checklists in the periphery and the positive cases will be re-assessed by trained personnel at the secondary and tertiary care levels. Once this swings into action there will naturally be an upsurge of pediatric consultations by concerned parents, which will need to be tackled responsibly. Reviews of screening tools that may be used in LMICs are available but are hampered by lack of clear guidelines or practice algorithms.[5,15,16]

This article aims at sensitizing pediatricians, reviewing certain general (not domain-specific) developmental screening and monitoring tools validated for use in Indian under-five children, and proposes an office practice paradigm.

DEVELOPMENTAL SCREENING TOOLS IN USE IN INDIA

Screening tools currently in use in India include those developed and validated in high-income countries, translations of the above in Indian languages, and indigenously developed tools. Each type has its own problems. In addition to the drawbacks outlined earlier, internationally acclaimed tools may not be suitable for our populations due to presence of items that are culturally alien or which lose context after translation. They also require validation on large reference groups comprising of healthy children of the target population without conditions averse to development like iron-deficiency anemia, malnutrition, poverty, and decreased stimulation.[17] Translations may be under-

standable but still face the aforementioned drawbacks, unless validated. Indian tools are language and culturally suitable, have been validated but may not have optimal psychometric properties since most were originally developed largely for community surveys by health workers. Taking these aspects into consideration, a list of screening tools for developmental delay popularly in use or validated in Indian settings was compiled and those that could be administered by pediatricians in any office setting were reviewed. Tools screening for behavior problems or specific domains or overt disability were not included.

Comparing Development Screening Tools

To be able to compare tools qualitatively, it is essential to understand their characteristics. Table 2.1 outlines the definitions and acceptable standards of commonly used psychometric parameters. These are important for making educated decisions regarding quality. If screening tools are not used for their intended purpose (i.e. screening tools being used for diagnosis or in children outside the intended age range), reliability gets compromised. Choice of tools also differs according to level of risk for developmental delay; high-risk children being those with biological and/or environmental risk factors. Constituent items of tools may be historically based (milestones, opportunity-based skills), performance-based or both. In contrast to developed counties, parental interviews are not as reliable in LMICs due to poorer literacy levels, unawareness of milestones and possibility of socially acceptable responses being given due to associated social stigma.[5,15,16] Interpretation of a screening result as pass or fail is done by comparing with scores derived from standardized population norm-references or pre-decided performance criterion.

Tool Best Suited for Indian Children

Hypothetically, an ideal screening tool for Indian children is a brief, inexpensive tool with good psychometric properties, available in Indian languages, comprising of purely developmental/culturally-adapted items, that has been validated on representative healthy Indian children and requiring minimal training.[17] Such a designer tool does not exist in reality; so each pediatrician has to make an educated choice best suited for individual practice. Developmental tools of International origin are compared in Table 2.2. Only two of these have been validated in Indian children.

TABLE 2.1: Definitions and acceptable standards of development tool-related psychometric properties

Term	*Description*	*Acceptable standard*
Standardization	The uniformity of procedure in administering and scoring the test exactly as outlined by the developer of the tool.	On representative population
Validity	The ability of a tool to assess what it is intended to assess in comparison with a gold standard diagnostic tool	70%
Sensitivity	Percentage of children with delay/problem who are correctly identified by the screening test	70–80%
Specificity	Percentage of children without delay/problem who are correctly identified by the screening test	≥80%
Positive predictive value	Percentage of children identified with delay/problem by the screening test who do indeed have the delay/problem	30–50%
Negative predictive value	Percentage of children identified as normally developing by the screening test who are indeed developing normally	+5–7 lines
Reliability Inter-rater Test-retest	How consistently similar results are obtained repeatedly Result variability if test given by different interviewers Result variability when repeated later	High/strong-coefficients >0.60

TABLE 2.2: Comparison of developmental screening tools of International origin

Factors	*Denver developmental screening test II (DDST)*	*Bayley infant neurodevelopmental screen (BINS)*	*Parents evaluation of developmental status (PEDS)*	*Ages and stages questionnaire (ASQ)*	*Developmental* Profile II/ III (DP)*
Age	0–6 years	3–24 month	0–8 years	1–66/3–66 m	0–9 y/12 y 11 m
Format	Directly-administered	Directly-administered	Parent-report	Parent-report	Parent-report
Screens/domains	Expressive and receptive language, gross motor, fine motor, personal, social	Neurological processes, expressive and receptive functions and cognitive	Cognitive, expressive and receptive language fine and gross motor, social-emotional, behavior, self-help and school	Communication, gross motor, fine motor, problem-solving, and personal adaptive skills	Physical, self-help/ adaptive, social/ social-emotional, academic/cognitive and communication
Items	125	11–13	10	22–36	186/180
Scoring/result	Risk category: normal/ abnormal/ questionable	Risk category: high/low moderate	Risk category: low/ medium/high	Pass/fail scores	Total score gives domain wise age equivalents
Time	10–20 min	10 min	2–10 min	10–15 min	10 /20–40 min
Language	English, Spanish	English	English	English, Hindi	English
Psychometric properties	Sensitivity 0.56–0.83 Specificity 0.43–0.80	Sensitivity 0.75–0.86 Specificity 0.75–0.86	Sensitivity 0.74–0.79 Specificity 0.70–0.80	Sensitivity 0.70–0.90 Specificity 0.76–0.91	Validity coefficients* 0.52–0.72
Validated in India	Not validated	Not validated	Sensitivity 62% Specificity 65%	Sensitivity 83.3% Specificity 75.4%	Not validated but used extensively
Cost	$111	$325	$30	$249	$240
Access site	*http://www.denverii.com/*	*www.pearsonassessments.com*	*www.pedstest.com*	*www.brookespublishing.com/asq*	*www.wpspublish.com*

**Internal consistency: 0.89-0.97 and Test-retest reliability: 0.81-0.92*

The Denver Developmental Screening Test (DDST) is a very popular and frequently used International screening test.[18–20] However, its low specificity (43%) leads to over identification of false positives, parental apprehension, and burden on the system for diagnosis and intervention. Hence, it is no longer considered appropriate for the purpose of screening. The Bayley Infant Neuro-developmental Screen (BINS) has been used for monitoring children at moderate to severe high risk.[21,22] Though psychometric properties are acceptable, its drawbacks are lack of validation in Indian children and inability to screen children beyond 2 years of age. The Ages and Stages Questionnaire (ASQ) is a parent-completed questionnaire with acceptable properties.[23] In a study by Juneja, *et al.*,[24] ASQ was validated against the Developmental Scale for Assessment of Indian Infants. After being translated into Hindi and substitution of a few culturally inappropriate items, this version of ASQ was administered to parents by an interviewer to screen children aged 4, 10, 18 and 24 months with both high and low risk. The overall sensitivity in detecting developmental delay was 83.3% (higher for the high-risk children), specificity 75.4% and negative predictive value 84.6%. ASQ has the potential to be used in India after being translated into local languages, if interviewer–administration replaces parent-completion when required.

Studies in the West have shown that asking parents about development concerns is reliable for assessment.[25] Parent Evaluation of Developmental Status (PEDS) considers concerns as either 'not predictive' or 'predictive' of developmental disabilities. The latter categorizes children as having high, moderate or Low risk of developmental disabilities. Each is linked with related management protocols: referral, more screening or continued surveillance, respectively. PEDS has been found reliable in other developing countries; however, there is limited literature from India.[19,26,27] The only available study from India was by Malhi, *et al*.[28] in which it was compared with Developmental Profile II (DP II) and Vineland Social Maturity Scale. Psychometric properties were found to be sub-optimal. The authors suggested that PEDS could be used to identify children requiring in-depth screening in situations involving time constraints. The limitations of this study were use of another screening tool as gold standard and a small sample size. Further research is warranted before its value in the Indian context is clarified.[5,15] Developmental Profile III (DP III) is an updated version of DP II that screens for developmental delay in five key areas.[29,30] Its norms are based on a large representative sample of typically developing American children. Although used in India frequently in numerous research studies, it is yet to be validated in Indian children.

These are some Indian screening tools that were designed for community surveys but can be used for office practice. These are easy to perform and interpret, inexpensive, and have been norm-referenced and standardized in representative populations. The main drawback is less than acceptable psychometric properties. Normative data of both Baroda Developmental Screening Test (BDST) and Trivandrum Developmental Screening Chart (TDSC) are derived from the Bayley Scales of Infant Development (BSID) which has not been re-validated since its inception more than 20 years ago.[31] The same drawback lies in the Indian Council Medical Research Psychosocial Developmental Screening Test (ICMR-PDST).[32,33] In the TDSC validation study, the gold standard that was used was not a diagnostic tool but DDST (no longer considered suitable): so the results may be considered questionable until re-validated against a more robust gold standard.[34] These tools are compared in Table 2.3.

Development Screening Tools of the Future

Two promising screening tools may become available for use in the near future. The first–Guide for Monitoring Child Development

TABLE 2.3: Comparison of Indian developmental screening tools

Factors	*Baroda developmental screening test (BDST)*[24]	*Trivandrum developmental screening chart (TDSC)*[25]	*ICMR psychosocial developmental screening test*[27, 28]
Developed from	Bayley scales of infant development, normative data from Indian children	Bayley scales of infant development (Baroda Norms)	Programme for estimating Age-related gentiles using piece-wise polynomials* normative data from Indian children
Age	0–30 m	0–24 m	0–6 y
Format	Directly-administered 54 items	Directly-administered 17 items	Parent interview 66 items
Domains	Motor and cognitive	Mental and motor	Gross motor, vision and fine motor, hearing, language and concept development, self-help and social skills
Scoring/result	Age equivalent and developmental quotient calculated	Within age range	3rd, 5th, 25th, 50th, 75th, 95th and 97th centiles given significant delay <3rd centile (2 SD)
Training	Minimal training	Minimal training	None
Setting	Community/office	Community/office	Community/office
Time taken	10 min	5 min	Minimal
Psychometric properties	Sensitivity: 65–93%, Specificity: 77.4–94.4% PPV: 6.67–34.37%	Sensitivity: 66.8%, Specificity: 78.8%	Not given
Access site and cost	Promila Phatak, Department of Child Development, University of Baroda, India Inexpensive	MKC Nair, Child Developmental Centre Trivandrum, Kerala, India. Inexpensive	ICMR, free

*ICMR: Indian Council of Medical Research, PPV: Positive Predictive value; * Child Health and Development, Maternal and Child Health and Family Planning, Geneva, 1992.*

(GMCD)—is a parental report-based development monitoring tool for children between 0 to 3.5 years originally developed in Turkey.[8] It comprises of 7 items pertaining to developmental concerns, and takes 5–10 minutes to administer. The sensitivity and specificity are 86% and 93%, respectively. It also has an intervention package that helps in supporting normal development and managing developmental difficulties. A five-year project 'Development of International guide for monitoring child development' is currently underway in India, Turkey, Argentina and South Africa since 2010.[5] The aim of this project is to standardize GMCD for universal use in children irrespective of demographic, cultural or linguistic considerations. The project also aims at examining an approach in which monitoring is done at community health clinics by trained personnel.

The second new kid-on-the-block is the INCLEN Neurodevelopmental Screening Test (NDST) that was developed by the composite efforts of a team of neuro-developmental experts from India and abroad. It screens for 10 neurodevelopmental disorders (NDD): Autism Spectrum Disorders, Learning Disorder, Attention Deficit and Hyperactivity Disorder, Vision Impairment, Hearing Impairment, Intellectual Disability, Speech and Language Disorders, Epilepsy, Cerebral Palsy and other Neuro-Muscular Disorders.

Diagnostic criteria (Consensus Clinical Criteria) have been developed for establishing each diagnosis which are sequentially applied according to an algorithm when the screening test is positive.[35] Application of the NDST in a recently concluded multi-centric validation study in rural, urban, hilly and tribal areas revealed that the prevalence of ≥1 NDD in children aged 2–9 years ranged between 7.5–18.5%.[36]

DEVELOPMENTAL SCREENING IN OFFICE PRACTICE

Setting up routine screening practice involves creating parental awareness and demand, finding the right opportunity, tool selection, acquisition and training in administration, scoring, interpreting results and counseling. This entails planning when, where, and how screenings will be accomplished, devising a method for documenting observations and maintaining records, communicating results to parents, referring to experts for further evaluation when required and scheduling future screenings. Parents can be sensitized by information pamphlets and office displays. Since visits for acute illnesses are not appropriate opportunities; a practical option would be to club screening with pre-existing scheduled visits like immunization and vitamin A prophylaxis. A system needs to be devised to document results, maintain and update records at subsequent visits. Comparison with previous records helps to recognize potential developmental problems or regression, deviancy or dissociation. Experience from other countries has shown that time actually gets saved since it takes the same time that would otherwise have been spent in unstructured questioning and answering other parental queries. Ultimately evaluation time becomes predictable, detection rate increases, parent and provider satisfaction level increases and office attendance increases as parents start appreciating the monitoring process.

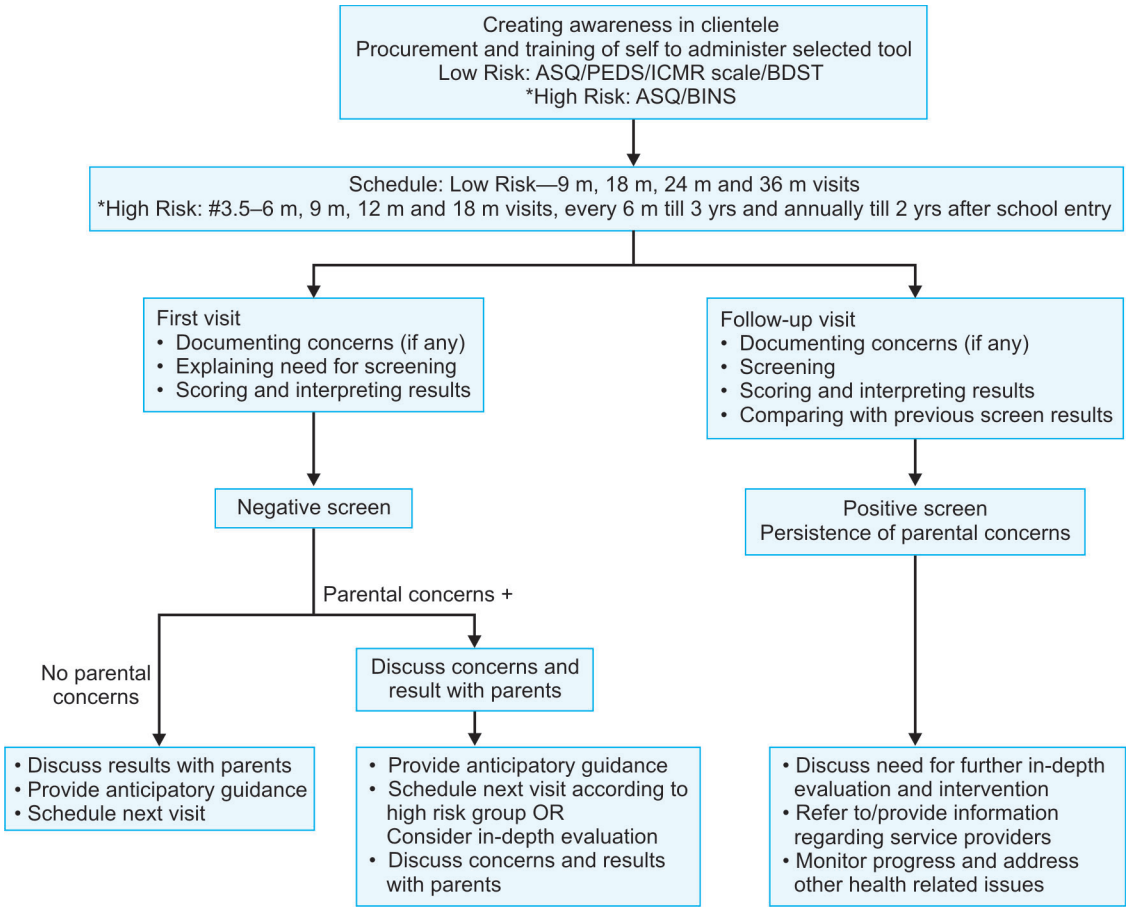
An Algorithmic Approach to Developmental Screening

Based on the advantages and drawbacks of the tabulated tools and until consensus statements are formulated by expert groups, the authors suggest a potential practice paradigm for pediatricians based on degree of risk of developmental delay (Fig. 2.1). Preliminary steps involve creating awareness, procuring tools according to the type of patients encountered (low-risk, high-risk or both), and achieving competency in administration, scoring and interpretation. The schedule of screening and follow up monitoring will differ according to level of risk.

Discussing Parental Concerns and Test Outcomes

Parental concerns should always be asked. In the initial visit, if the parent of a low-risk child expresses developmental concerns, the pediatrician is expected to discuss these with the parents and offer options of more frequent and earlier monitoring (as in the high-risk group) or referral for an in-depth evaluation even if the screen is negative. If the parents opt for the former and the concerns persist at the next visit, immediate referral is warranted. If not, monitoring should continue as for the high-risk group, in this group, the first visit recommended by AAP is 4–6 months (coinciding with the 2nd or 3rd immunization visit). The corresponding immunization visit in India would be at 3.5 months. At this age, a small proportion of infants display transient benign tone abnormalities that may be mistaken as pathological. In these instances, the pediatrician should make a note in the child's records and schedule a repeat visit after a month, without unduly alarming the parents. If it persists, in-depth evaluation would be required.

Once screening is complete, it is important to properly convey the significance of the results. If negative, parents should be reassured that development is currently appropriate, anticipatory guidance should be



**Neonates, infants or children with ≥1 high-risk factors viz., Genetic: positive family history of illness associated with neuro-developmental morbidity; Biological: acute and chronic illnesses, nutritional (macro and micro) deprivation; Environmental: exposure to poverty, violence, neglect, teratogens, arsenic, lead, drugs, etc.; Psycho-social: illiteracy, lack of stimulation, learning opportunities, poor parenting skills, parental illness or substance abuse, maternal depression, etc.; Presence of any parental concerns regarding development. #Abnormality present at 3.5 months: refer to text (discussing parental concerns and test outcomes).*

PEDS: Parent evaluation of developmental status; BDST: Baroda developmental screening test; ASQ: Ages and stages questionnaire; BINS: Bayley infant neuro-developmental scren; ICMR: Indian Council of Medical Research.

Fig. 2.1: Proposed schema of office based developmental screening and surveillance

given about expected milestones and the necessity of returning for the next screening visit should be explained and scheduled. If positive, the implications need to be discussed in depth with the parents, and they should be counseled about the need of diagnostic evaluation and start of stimulation or intervention as indicated post evaluation. Since parents have intrinsic faith in us as health care providers of their children, it is our moral responsibility to be instrumental in arranging referrals (by providing contact details or direct communication) as well as providing continual medical help and moral support. It is good practice to develop a two-way communication system with service providers to instill confidence in parents regarding management issues.

Screening should be considered the initial step of intervention services.[37] Unfortunately,

it is a common practice to falsely reassure or delay referral to alleviate parental anxiety. Actual practice should be 'Refer not defer.' Failing to refer for diagnosis and intervention after detection on screening is considered unethical.[38] In developed countries, a referral rate of 1/6 children screened is considered optimal.[39] It is important to understand that starting multi-disciplinary intervention (speech and language therapy, occupational therapy, physical therapy, special educational services, etc.) should proceed in parallel to diagnosis establishment and not afterwards. In addition to formal intervention, pediatricians must become familiar with home-based intervention strategies that should be shared with the parents. Development oriented packages have been combined with tools like 'Integrated Management of Child Illnesses–Care for Development' (WHO/UNICEF), GMCD, TDSC and Developmental Assessment Tool for Anganwadis (DATA) or are already in practice at the community level via National Rural Health Mission, RBSK, Integrated Child Development Schemes, and other agencies, the details of which are available, can be practiced by parents at home, and have been proven to be beneficial.[8,14,34,40–45]

CONCLUSION

Many parents and children struggle in their daily lives due to problems arising from undetected development delay. Considering the widespread prevalence of developmental problems, the pediatrician must remain vigilant. By adopting developmental screening and surveillance, one can ensure a systematic approach to children with developmental concerns and help improve their future. Both strategies are integral parts of child healthcare, benefit the individual child and society, and also protect the doctor from possible future litigation. In this review, an attempt has been made to sensitize colleagues to the importance of screening and surveillance, compare existing screening tools and propose those suitable for Indian children along with strategies for incorporation into office practice. There is a strongly felt need to develop more culturally appropriate, norm-based, valid and reliable Indian developmental screening instruments. We strongly urge that a consensus be formulated at the National level by experts on appropriate developmental surveillance and screening recommendations. Ultimately, earlier recognition of developmental delay results in better inclusion of affected individuals in society, establishment of prevalence data, educated health policy decisions, and resource allocation at the Government level.

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Chapter

3

Growing Pains: Practitioners' Dilemma

MP Mohanta

Most pediatricians and general practitioners – in their day-to-day office practice–often come across children complaining of pain in their legs. These pains may sometimes point to serious underlying conditions such as malignancies, infections or injuries. However, majority of the cases may be due to 'growing pains', that have a benign and self-limiting course.[1]

Growing pains, though considered benign, can cause considerable anxiety in the parents. Sometimes, the child wakes up in the middle of night with extreme agony, complaining of severe pain in the legs. There are no symptoms in the morning and pediatrician finds no abnormality on physical examination.[2] The pediatrician may be in a dilemma; should parents be simply reassured or the child has to be investigated thoroughly?

This article reviews the current knowledge regarding the diagnosis, etiopathogenesis and management of this fairly common but perturbing condition.

DIAGNOSIS

Growing pains are typically intermittent, nocturnal and poorly localized, usually occurring once or twice per week–though there is never a regular pattern. Children suffering from 'growing pains' are characteristically well without any physical problems, despite severe pain experienced in the night. Night awakenings are common but not an essential feature. The usual age group is 4–14 years with equal gender preponderance.[1–3] The diagnostic criteria given by Naish and Apley[4] are: intermittent lower limb pains for at least 3 months duration, not specifically located in the joints, and of sufficient severity to interrupt sleep. The definition provided by Peterson[5] guides clinicians better, and has several inclusion as well as exclusion criteria (Table 3.1). Growing pains is essentially a clinical diagnosis and laboratory investigations or *X*-rays are unnecessary.[2,6,7]

DIFFERENTIAL DIAGNOSIS

Though diagnosis of growing pain seems easy; there may be a danger of over-diagnosis, if leg pains due to other conditions are not kept in mind.[5,7,8] Entities mimicking growing pains may be grouped under five broad headings (Box 3.1) as follows:

Injury-related leg pains: History is obvious, if there is any trauma, and usually the pain is localized. However, history may not be that obvious in cases of non-accidental trauma or battered child syndrome; presence of injuries of different ages and their inappropriate

TABLE 3.1: Diagnostic criteria for growing pains

Characteristics of pain	*Inclusion criteria*	*Exclusion criteria*
Frequency and duration	Intermittent pains once or twice per week, rarely daily, totally pain free in between the episodes; individual episodes lasting for 30 min to 2 hours	Pain, that is persisting or increasing in severity with time
Site	Usually in the muscles of calf, sometimes anterior thigh muscles, shins and popliteal fossa and affects both limbs	a. Pain involving joints b. Pain occurring only in one limb
Time	In the evening and nights	Daytime pain and nocturnal pain that persists till next morning
Physical examination	Normal	Signs of inflammation

explanation may be the clue. Osgood-Schlatter disease is characterized by pain over the tibial tubercle, usually in athletes and more common in boys between ages 10–15 years. Chondromalacia patella or idiopathic adolescent anterior knee pain syndrome (also known as Runner's knee), on the other hand, commonly affects adolescent girl athletes doing a lots of running.[8]

Box 3.1: Differential diagnosis of growing pains

Injury-related

Inflammation of soft-tissue or bone due to sports injuries or accidental injuries or battered child syndrome, Osgood-Schlatter disease, chondromalacia patella

Infections

Osteomyelitis, septic arthritis, cellulitis and soft tissue abscess

Tumors

Benign: Osteoid osteoma, unicameral cyst, fibrous dysplasia, aneurismal bone cyst, gaint cell tumor, histiocytosis X and osteochondroma

Malignant: Osteosarcoma, Ewing's sarcoma, leukemia and neuroblastoma

Developmental and congenital

Slipped capital femoral epiphysis, hypermobile joints, limb deformities such as genu valgum, flat foot, discoid lateral meniscus, patellar subluxation

Others

Legg-Calve-Perthes disease, osteochondritis dissecans, sickle cell crisis, amplified musculoskeletal pain syndromes, restless leg syndrome, juvenile idiopathic arthritis

Infections: There are usually systemic features such as fever and toxicity. Localized tenderness, swelling and erythema at the site of pain may be found on examination.

Tumors: Benign tumors, which produce pain in leg, are usually associated with swelling and are well localized. Pain in Osteoid osteoma can cause night awakening, but it is persistent and gradually increasing in severity as opposed to intermittent painful nights in growing pains.[9]

Malignant tumors that can cause leg pain are associated with systemic features such as fever and weight loss. Osteosarcoma can present with deep bone pain with night awakening, but there is usually a palpable mass.[8]

Slipped capital femoral epiphysis may present as knee pain due to referred pain along the course of obturator nerve. Usually, patients with this disorder have some limp and have externally rotated lower limb and restriction of movements at hip.[9]

Hypermobile joints can produce knee pain, that is worse after activity and relieved by rest. Hypermobile joints have abnormally increased range of motions and may be assessed with the Beighton scale.[8]

Legg-Calve-Perthes disease may present as referred pain in knee, but there is usually associated limp and restriction of movements in hip. Osteochondritis dissecans often presents with vague knee pain. However, localized tenderness over medial femoral

condyle may be elicited on careful examination. The leg pain in sickle cell anemia is persistent in nature. Other characteristic features of sickle cell anemia will be difficult to miss by careful history and physical examination.

There are two major forms of amplified musculoskeletal pain syndromes (AMPS); diffuse AMPS and localized AMPS.[8] Diffuse AMPS, also known as juvenile primary fibromyalgia syndrome (JPFS), reveals well defined tender points, and usually affects older child or adolescent with a female preponderance. These children look debilitated; have disturbed personality and daytime symptoms.[8] Localized AMPS, also known as complex regional pain syndrome (CRPS), is characterized by ongoing burning pain in leg subsequent to an injury or other noxious event. Other characteristic features include allodynia, hyperalgesia and autonomic dysfunction.[8]

Restless leg syndrome (RLL) may sometimes be confused with growing pains as both these conditions tend to manifest during the evening hours and are related to discomfort in the legs. However, the uncomfortable feeling in the legs in RLL is associated with an irresistible urge to move the legs, worsened by rest and relieved by movements such as walking or stretching (only as long as motion continues).[10,11] Juvenile idiopathic arthritis may present as leg pains initially, where minimal joint involvement may be missed. The key here is the persistent nature of pain and morning symptoms.[9]

Presence of red flag signs in a child with leg pain should alert a clinician for further investigations (Box 3.2).[8,9]

Box 3.2: Red flag signs in a child with leg pain

i. Involvement of joints,
ii. Systemic involvement,
iii. Persistent pain or daytime pain or pain that is localized, and
iv. Limping.

PREVALENCE AND NATURAL HISTORY

It is believed that growing pains affect about 10–20% of children.[1] Estimated prevalence ranges from 2.6% to 36.9%. This is mainly due to different and unspecified sample sizes, different age ranges in the literature, and lack of objective diagnostic criteria adopted in different studies.[4,12,13]

Abu-Arafeh and Russell determined the prevalence rate to be 2.6%, among school children aged 5–15 years.[14] Evans, *et al*.[12] estimated the prevalence of growing pains among children aged 4–6 years to be 36.9%, in a well-designed sample using a validated questionnaire. A relatively recent study by Kaspiris and Zafiropoulou[15] reported a prevalence of 24.5% among 532 children of age 4–12 years.

Growing pains is the most common cause of recurrent musculoskeletal pain in children.[1] Two recent studies reported that most of cases of unexplained recurrent limb pains in children could be classified as growing pains.[16,17]

Usually, there is a gradual decline in the frequency of pain episodes over a period of 1 to 2 years and most cases of growing pains resolve by adolescence.[18] Uziel, *et al*.[19] reported persistence of growing pains in 18 out of 35 cases in 5-year follow up, though the episodes became less frequent and milder. However, more recently, Pavone, *et al*.[20] reported resolution of all pain episodes of growing pains after 1 year, in all 30 cases.

TERMINOLOGY

The terminology growing pains is being used since 1823, since the condition was first described in medical literature by French physician Marcel Duchamp as *Maladies de la Croissance* (pains of growth).[21] Many authors have raised objections and questioned the validity and rationale of the term.[5] Clearly, these pains cannot be attributed to growth. Peak age for growing pains (4–8 years)

corresponds to the relatively slower growth period of childhood. Moreover, the sites of pain (diaphyses) do not match the site of maximal growth (epiphyses).[4] Besides, no difference of rate is seen between the children with and without growing pains.[13] Thus the term growing pains appears to be a misnomer; there is no evidence that growth *per se* can cause pain. Alternate terms such as 'paroxysmal nocturnal pains'[4] and 'recurrent limb pains in childhood'[14] have been suggested. However, these terms are non-specific and describe the disorder incompletely. The terminology benign idiopathic paroxysmal nocturnal limb pains of childhood[9] perhaps describes the condition properly, but sounds too long and inconvenient for general use. On the other hand, the term growing pains has the advantage of emphasizing the benign nature of the disease and indicates that the pain occurs in the growing children, and not after growth is complete.[5] Thus, despite the controversy, the term growing pains enjoys wide acceptance and popularity.[22]

ETIOPATHOGENESIS

In the 19th century, at the time when the term growing pain was coined, growth was considered to be the causative agent of nearly all pains during the childhood.[7] By early 20th century, medical community believed that growing pains were actually a sub-acute form of rheumatic fever.[7,23] Studies of Sheldon in 1936 and thereafter Hawksley in 1939 proved that growing pains are not associated with rheumatic fever.[24,25]

The exact mechanisms, by which these pains occur, are still poorly understood. Some of the theories, put forward to explain the etiology of 'growing pains', are summarized below.[2,3]

Anatomical/mechanical theory: Hawksley observed that growing pains were often associated with postural or orthopedic defects such as flat foot, knock-knee, scoliosis or bad stance.[25] Mechanical instability such as flexible flat feet with hind foot valgus had been suggested as a cause of growing pains.[20] A small controlled study reported that shoe inserts were effective in reducing the frequency and severity of growing pains.[26] However, subsequent study by the same author did not found any association between foot posture and growing pains.[27] A cross sectional study[28] reported a statistically significant association between joint hypermobility and growing pains. Some cases of growing pains occurring after increased activity may be explained by hypermobile joints. However, due to absence of universally reliable and valid assessment tool for hypermobility in children, the notion of hypermobility causing growing pains remains largely unproved.[3]

Fatigue theory: It was observed that bone strength (based on speed of ultrasound in tibia), in children with growing pains, was significantly lesser than in controls.[2] Often episodes of growing pains are reported on days of increased activity and during the latter part of a day. These observations probably signify that growing pains represent, a *local overuse syndrome* leading to bone fatigue.[7]

Psychological theory: John Apley (1951) found emotional disturbance and family stress to be associated with 'growing pains'.[4] His famous saying *"physical growth is not painful, but emotional growth can hurt like hell"* often gets quoted.[29] Oster (1972) also showed that psychogenic abdominal pains and nervous headaches are more often found in children with growing pains than in other healthy children.[13]

Lower pain threshold: Haskes, *et al*.[30] have recently shown that children with growing pain have decreased pain threshold when compared with the age- and sex-matched controls. They suggested that 'growing pains' may represent a form of non-inflammatory

pain amplification syndrome. This was further supported by the findings of Uziel, *et al*.[19] in a 5-year follow-up study of growing pains. They found a correlation between persistence of symptoms and lower pain threshold. Pathirana, *et al*.[31] also demonstrated a lower threshold of pain response to cold, vibration and deep pressure in cases of growing pains than in controls.

Other associations: A positive family history associated in some cases of growing pains suggests that there may be a genetic component playing role in the pathogenesis.[3] Some cases of growing pain may be actually having childhood onset, e.g. restless leg syndrome.[11] Children with growing pains may also represent a parasomnia such as sleep walking and sleep terrors.[32] A study found hair of children with growing pain contained increased levels of lead and zinc and decreased levels of copper and magnesium.[33] However, the usefulness of the analysis in the pathogenesis is not validated.[3] In a recent study–Golding, *et al*.[34] could not find any role of dietary omega-3 fatty acids in the development of growing pains.[34]

Thus growing pains may be caused by lower extremity overuse, in children having lower pain threshold or decreased bone strength.[2,20] The negative psychosocial environment may also be a contributing factor.

MANAGEMENT

The most important component of management is proper explanation regarding the benign nature of growing pains. The family may be reassured that these pains will be resolved in time and will not progress to any serious organic disease.[35] The parents may be advised to use analgesics as well as non-pharmacologic measures to relieve pain such as leg massages, rubbing, and hot fomentation. But it remains unclear whether these interventions actually help to resolve the attack, as the pain episodes are self-limiting. Considering the intermittent nature of pain, use of analgesics on regular or long-term basis can be harmful, and should not be advised.[8]

In this era of evidence-based medicine, treatment modalities proven with randomized controlled trials are the gold standards for management. A randomized controlled trial[36] involving treatment of growing pains described efficacy of a muscle stretching program (involving the quadriceps, hamstrings, and gastrosoleus muscle groups) in faster decline of pain episodes. These exercises may be taught to the parents and done at home twice-a-day for 10 minutes in the morning and at night. This treatment modality has further advantage of providing an extra attention of the parent, fulfilling the psychological needs of the children.[22]

Evans[26] reported use of in-shoe devices such as tri-plane wedges and orthoses was effective in children with pronated foot posture. However, the study involved single-case experimental design, which is much lower in evidence hierarchy.[26] These in-shoe devices may be helpful in selected cases with postural defect.

Widespread vitamin D deficiency is being reported among population at large, and vitamin D may affect body's endocrine system, immune system, cardiovascular system, neuro-psychological functioning and neuromuscular performance.[37] Thus, it is interesting to know whether vitamin D has any role in management of growing pains. A recent study reported insufficient vitamin D levels in majority of cases with growing pains.[38] However, the study does not mention, if the children without growing pains had different vitamin D levels. Efficacy of vitamin D supplementation in growing pains has not been studied. Currently, there is insufficient evidence to use vitamin D for the management of growing pains. Use of vitamin C, calcium or magnesium etc. have no scientific basis and should not be advocated.

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Chapter

4

Approach to Constipation in Children

Ujjal Poddar

Constipation is a common problem in children and it accounts for 3% of visits to general pediatric clinics and as many as 30% of visits to pediatric gastroenterologists in developed countries.[1] There is very little information about its prevalence from developing countries. However, some recent reports from South Asia have suggested that it is not uncommon in Asia.[2–4] The common perception in South Asia is that functional constipation is uncommon as diet here is rich in fiber. Hence, many children with constipation are subjected to detailed investigations to rule out Hirschsprung disease. However, whatever limited information we have from Asia shows that functional constipation is the commonest type of constipation in Asia as well.[2–4] The prevalence, etiology, pathogenesis, assessment and management of constipation in children is discussed in this review.

STOOL PATTERN OF NORMAL INFANTS

Normal variation in stool frequency and consistency often leads to over-diagnosis of constipation especially in infants. Two recent studies from the Europe (12,984 healthy children, 1–42 months from UK[5] and 600 healthy infants from Netherlands[2]) have shown that the median stool frequency at 1 month of age was 3 (0–9) per day and it decreased significantly at 3 months of age to 2 (0–6) per day. Moreover, there was a significant difference in stool frequency between breastfed and formula-fed babies at 1 month of age [4 (0–9) *vs.* 1 (0–5) per day, respectively, $P<0.01$] but there was no difference at 3 months of age [2 (0–6) *vs.* 1 (0–5) per day].[5,6] Another study from Turkey in 911 children aged 0 to 24 months has shown that the median defecation frequency at 1 month of age was 6 per day and by 4–6 months of age it became 1 per day. The most interesting observation of this study is that the stool frequency was <1 per day (once in 2–3 days but soft stool) in 39.3% babies in 2–6 months of age.[7] Hence, while considering constipation we should remember the normal variations of stool frequency and consistency in healthy infants and variations as per their feeding pattern (breastfed *versus* bottlefed).

DEFINITION OF CONSTIPATION

In view of wide variations in stool frequency and consistency in normal healthy children, ROME III criteria[8,9] have included other variables besides frequency of stool to define constipation in children. As per ROME III criteria, functional constipation is defined as presence of two or more of the following in absence of any organic pathology and the

duration should be at least 1 month in <4 years of age, and at least once per week for at least 2 months in ≥4 years of age; (i) two or less defecations per week, (ii) at least one episode of fecal incontinence per week, (iii) history of retentive posture or stool withholding maneuver, (iv) history of painful or hard bowel movement, (v) presence of large fecal mass in the rectum, (vi) history of large-diameter stools that may obstruct the toilet. In children <4 years of age, the history of retentive posture or stool withholding maneuver is being replaced by history of excessive stool retention as retentive posture is difficult to assess in younger children.

PREVALENCE

Constipation is a common problem in children and an estimated prevalence of functional constipation is 3% worldwide.[1,10,11] Though, we do not have any prevalence data from Asia, in a study from our center we reported 138 cases of constipation diagnosed over a period of 6 years and 85% of them were functional.[2] In next 8 years (2007 to 2014), we managed another set of 330 children with constipation and the proportion of functional constipation was 82% (270 of 330) (unpublished data). Hence, constipation is not uncommon in the Indian subcontinent. It is commonly seen among toddlers and preschool children, and in 17% to 40% of cases, constipation starts in first year of life.[12,13]

ETIOLOGY

The common perception in South Asia is that functional constipation is uncommon as diet in South Asia is rich in fiber. In our study,[2] we have shown that this perception is incorrect. Constipation is quite common in India and functional constipation is the commonest cause. Common causes of constipation in children are given in Box 4.1. In fact 95% cases are due to functional and only 5% are due to some organic causes.[14] Among the organic causes, Hirschsprung disease is the most common and important cause.[2]

Box 4.1: Causes of constipation in children

- Functional constipation of childhood
- Motility related: Hirschsprung disease, myopathy
- Congenital anomalies: Anal stenosis, anteriorly located anus, spinal cord anomalies (meningomyelocele, myelomalacia, spina bifida)
- Neurological: Cerebral palsy, mental retardation
- Endocrine/metabolic: Hypothyroidism, renal tubular acidosis, diabetes insipidus, hypercalcemia
- Drugs: Anticonvulsants, antipsychotic, codein containing anti-diarrheal

Pathogenesis of Functional Constipation (Fig. 4.1)

The initiating event in functional constipation is a painful bowel movement which leads to voluntary withholding of stools by the child who wants to avoid unpleasant defecation.[15] Events that lead to initial painful defecation are change in routine like timing of defecation or diet, stressful events, inter-current illness, non-availability of toilets (travel etc.), child's postponing defecation because he or she is too busy (morning school), and forceful toilet training (too early). All these events give rise to large, hard stool and passage of such stool leads to stretching of the pain sensitive anal canal, and that frightens the child. As a result of which the child fearfully determines to avoid defecation by all of means. Such children respond to the urge to defecate by contracting their external anal sphincter and gluteal muscles, in an attempt to withhold stool. Withholding of feces leads to prolonged fecal stasis in the rectum, with resultant absorption of fluids and harder stools. Successive retention of stools in rectum make them larger. As the cycle is repeated, successively greater amounts of larger and harder stools are built up in the rectum and passed with even greater pain accompanied by severe "stool withholding maneuvers". Thus a vicious cycle sets-in (Fig. 4.1). These children develop a "stool-withholding maneuver" or retentive posture

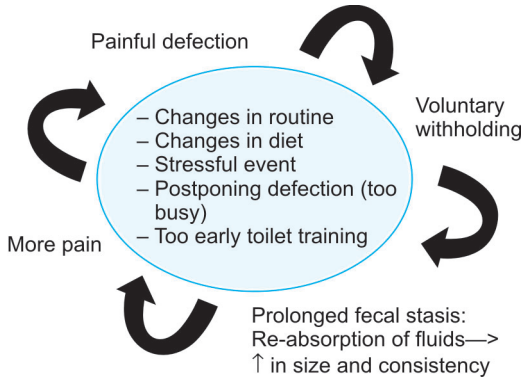

Fig. 4.1: Pathogenesis of functional constipation

which parents erroneously think it as an attempt to defecate. They feel that the child is trying hard (straining) in an attempt to pass stool when the child is actually trying his best to stop it. In response to the urge, they refuse to sit on the toilet, rather rise on their toes, hold their legs and buttocks stiffly and often rock back and forth, holding on to a furniture, scream, turn red until a bowel movement finally takes place. With time, such retentive behavior becomes an automatic reaction. They often perform this while hiding in a corner. Eventually, liquid stool from the proximal colon may percolate around hard retained stool and pass per rectum involuntarily (fecal incontinence). Sometimes, this fecal incontinence is mistaken as diarrhea. In fact almost 30% children with functional constipation develop fecal incontinence.[12] Eventually, with more and more stasis, the rectum becomes dilated and redundant, and the sensitivity of the defecation reflex and the effectiveness of peristaltic contractions of rectal muscles decrease. This is the stage when it becomes more difficult to have a normal defecation due to fecal impaction.

ASSESSMENT OF A CHILD WITH CONSTIPATION

A careful history and thorough physical examination (including digital rectal examination) are all that is required to diagnose functional constipation provided, there are no "red flags" like fever, vomiting, bloody diarrhea, failure to thrive, anal stenosis, and tight empty rectum.[16] Abnormal physical findings, which help to distinguish organic causes of constipation from functional, are failure to thrive, lack of lumbo-sacral curve, sacral agenesis, flat buttock, anteriorly displaced anus, tight and empty rectum, gush of liquid stool and air on withdrawal of finger, absent anal wink and cremasteric reflex. Features which differentiate Hirschsprung disease from functional constipation are given in Table 4.1. The most important features in the history, which help to distinguish Hirschsprung disease from functional constipation, are onset in first month of life and delayed passage of meconium beyond 48 hours and the most important examination finding is empty rectum on digital rectal examination. It has been shown that 99% healthy, term neonates and 50% babies with Hirschsprung disease pass meconium in first 48 hours of life.[17,18] In fact, in a classical case of functional constipation, no investigation is required to make the diagnosis. There is no need to do barium enema in all cases of constipation to rule out Hirschsprung disease. If the clinical suspicion of Hirschsprung disease is strong (based on history of delayed passage of meconium and empty rectum on digital rectal examination) then only one may consider getting barium enema done.

TABLE 4.1: Differences between functional constipation and Hirschsprung disease

Features	*Functional constipation*	*Hirschsprung disease*
Delayed passage of meconium	None	Common
Onset	After 2 years	At birth
Fecal incontinence	Common	Very rare
History of fissure	Common	Rare
Failure to thrive	Uncommon	Possible
Enterocolitis	None	Possible
Abdominal distension	Rare	Common
Rectal examination	Stool	Empty
Malnutrition	None	Possible

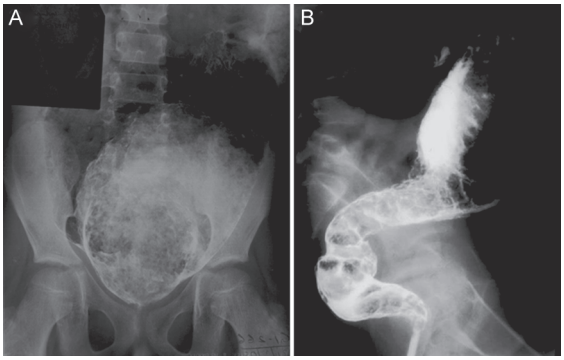

Fig. 4.2: (A) Barium enema (delayed film) of functional constipation; (B) Barium enema of a patient with Hirschsprung disease

However, to diagnose Hirschsprung disease, rectal biopsy is a must. The common mistake that leads to further confusion is delayed film (24 hours) showing retention of barium which is a common finding in functional constipation as well. The interpretation of barium enema should be on the basis of reversal of recto-sigmoid ratio (sigmoid becomes more dilated than rectum) and documentation of transition zone and not on mere presence of barium in rectum after 24 hours (Fig. 4.2).

MANAGEMENT

Most children with functional constipation get benefited from a precise, well-organized treatment plan, which includes cleaning of fecal retention, prevention of further retention and promotion of regular bowel habits. The general approach includes the following steps: (a) determine whether fecal impaction is present, and treat the impaction if present, (b) initiate maintenance treatment with oral laxative, dietary modification, toilet training, and (c) close follow-up and medication adjustment as necessary.[16] Suggested approach to constipation is given in Fig. 4.3.

Disimpaction

First step in the management of constipation is to decide whether the child has fecal impaction or not. This can be accomplished by abdominal examination (in half of the cases hard fecal mass or fecalith is palpable in the lower abdomen),[19] by digital rectal examination (rectum is usually loaded with hard stools), or rarely by abdominal X-ray. Routinely abdominal X-ray is not required to detect fecal

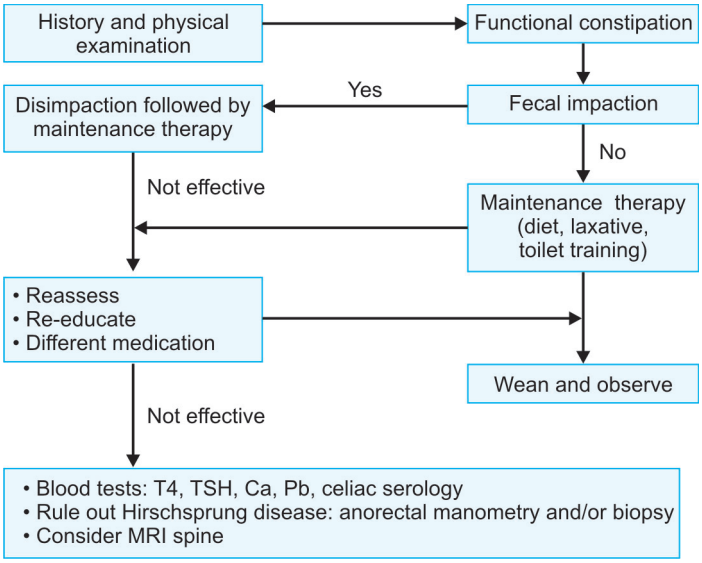

Fig. 4.3: Suggested approach to functional constipation. Modified from ESPGHAN recommendations

impaction. However, if the child refuses rectal examination, if he/she is obese, or if there is a doubt about the diagnosis of constipation then only an abdominal X-ray is required to document excess fecal matter in the colon.

If there is fecal impaction (most of the children with functional constipation do have), then the first step in the management is disimpaction, means clearing or removal of retention from the rectum. This can be achieved by oral or by rectal route. Oral route is non-invasive, gives a sense of power to the child but compliance is a problem. Polyethylene glycol (PEG) lavage solution is given orally (1–1.5 g/kg/day for 3–6 days) or by nasogastric tube (25 mL/kg/h, reconstituted PEG solution) until clear fluid is excreted through anus. Adequate disimpaction means both output (stool) and input (lavage solution) should be of same color in case of nasogastric tube disimpaction.[16] Successful disimpaction for home-based regimen (3–6 days) is defined as either empty or a small amount of soft stool on rectal examination and resolution of the left lower quadrant mass if it was there.[20, 21]

Rectal approach (enema) is faster but invasive, likely to add fear and discomfort that the child already has in relation to defecation. This may aggravate defecation avoidance or retention behavior and usually not preferred. However, if PEG is not available then enema can be used for disimpaction [sodium phosphate enema (proctoclysis): 2.5 mL/kg, maximum 133 ml/dose for 3–6 days].[16] In a retrospective chart review of 223 children, Guest, *et al*.[22] have shown that 97% children treated with PEG were successfully disimpacted compared to 73% of those who received enemas and suppositories (P <0.001). In a randomized-controlled trial, Bekkali, *et al*.[20] have compared 6 days enemas with dioctyl sodium sulfosuccinate (60 mL in <6 years and 120 mL in ≥6 years) in 46 children with PEG in 44 children and showed that both were equally effective for disimpaction. However, two retrospective studies have shown that the reimpaction rate after initial disimpaction with enemas was much more than that with PEG.[22,23] For infants, glycerine suppositories are to be used for disimpaction as enemas and lavage solution are not indicated in them.[16]

Maintenance Therapy

To prevent re-accumulation after removing impaction maintenance therapy in the form of dietary modification, toilet training and laxatives needs to be started immediately after disimpaction or if there is no impaction, then as a first step.

Dietary modification: The diet of most children with functional constipation lacks fiber. Many of them are predominantly on milk with very little complementary food. The children with functional constipation should be encouraged to take more fluids, absorbable and non-absorbable carbohydrate as a method to soften stools. Non-absorbable carbohydrate (sorbitol) is found in some fruit juices like apple, pear and prune juices. A balanced diet that includes whole grains, fruits and vegetables is advised. The recommended daily fiber intake is age (in years) + 5 in g/day. In our practice, where most children are predominantly on milk diet, we counsel the parents to restrict milk so that the child starts eating solid foods. Though cow milk protein allergy (CMPA) was proposed as one the common causes of constipation,[24] subsequent studies[16,25] and our experience did not substantiate that claim.

***Toilet training*:** It should be imparted after 2 to 3 years of age. Too early and vigorous toilet training may be detrimental for the child. The child is encouraged to sit on the toilet for 5 to 10 minutes, 3 to 4 times a day immediately after major meals for initial months.[26] The gastro-colic reflex, which goes into effect shortly after a meal, should be used to advantage.[27] Children are encouraged to maintain a daily record *(stool diary)* of bowel movements, fecal soiling, pain or discomfort, consistency of stool and the laxative dose. This helps to monitor compliance and to make

appropriate adjustment in the treatment program. Parents are instructed to follow a reward system. Children should be rewarded for not soiling and for regular sitting on the toilet. This acts as a positive reinforcement for the child.

***Laxatives*:** Doses and side effects of various laxatives are presented in Table 4.2.[28] It has been shown that lactulose, sorbitol, milk of magnesia (magnesium hydroxide), and mineral oil (castor oil), all are equally effective in children. Milk of magnesia and mineral oil are unpalatable and due to the risk of lipoid pneumonia mineral oil is contraindicated in infants. The commonly used laxative in children so far was lactulose, until the introduction of PEG. The study by Loening-Baucke[26] has shown that low volume (0.5 to 1 g/kg/day) polyethylene glycol (PEG) without electrolytes is as effective as milk of magnesia in the long-term treatment of constipation in children. Low volume PEG has been compared with lactulose in the treatment of childhood functional constipation and a meta-analysis of five RCTs comprising of 519 children has shown that PEG was more effective than lactulose with equal tolerability and fewer side effects.[29] Side effects, especially bloating and pain are less with PEG. With long term use, lactulose loses its efficacy due to change in gut flora but PEG does not.[30] The dose of laxative should be adjusted to have one or two soft stools/day without any pain or soiling. Once this target is achieved, the same dose should be continued for at least 3 months to help the distended bowel to regain its function. Point to be remembered here is that laxative needs to be continued for several months and sometimes years at the right dose. Early and rapid withdrawal is the commonest cause for recurrence. Stimulant laxatives (senna, bisacodyl) are not used routinely and are contraindicated in infants. They may be used for a short course in refractory cases as a rescue therapy.[16]

Follow-up Schedule

A close and regular follow-up is a key to the success of treatment of functional constipation. Initial follow-up should be monthly till a regular bowel movement is achieved. After that it should be 3 monthly for 2 years and then yearly.[26] On each visit, by reviewing stool records and repeating abdominal and (if

TABLE 4.2: Laxatives–dosage and side effects (modified from NASPGHAN position statement)[28]

Drugs	*Dose*	*Side effects*
Lactulose	1–2 g/kg, 1–2 doses	Bloating, abdominal cramps
Sorbitol	1–3 mL/kg/d, 1–2 doses	Same as lactulose
Milk of Magnesia	1–3 mL/kg/d, 1–2 doses	Excess use leads to hypocalcemia, hypermagnesemia, hypophosphatemia
PEG		
for disimpaction	25 mL/kg/hr (R/T) or 1–1.5 g/kg for 3–6 d	Nausea, bloating, cramps, vomiting
for maintenance	5–10 mL/kg/d or 0.4 to 0.8 g/kg/d	
Mineral oil		
for disimpaction	15–30 mL/y of age (max. 240 mL)	Lipoid pneumonia, interference with absorption of fat soluble vitamins
for maintenance	1–3 mL/kg/d	
Senna	2–6 y: 2.5–7.5 mL/d (8.8 mg/5 mL) 6–12 y: 5–15 mL/d	Melanosis coli, hepatitis, hypertrophic osteoarthropathy, neuropathy
Bisacodyl	0.5–1 suppository (10 mg)1–3 tabs/ dose (5 mg)	Abdominal pain, diarrhea, hypokalemia

PEG: Polyethylene glycol; R/T: Ryle's tube

required) rectal examination, progress should be assessed. If necessary, dosage adjustment is to be made. Once a regular bowel habit is established, the laxative dosage is to be decreased gradually before stopping.

Outcome

In a long-term follow up study [mean (SD), 6.9 2.7 years] on 90 children, who were <4 years at diagnosis, Loening-Baucke[31] showed that 63% had recovery but symptoms of chronic constipation persisted in one-third of cases 3 to 12 years after initial evaluation and treatment. In another study, it has been shown that 50% of patients were off laxative at 1 year, another 20% at 2 years and the remaining 30% were on laxative for many years.[14] von Ginkel, *et al*.[32] in a long-term follow-up (mean 5 years) study on 418 cases have also shown that 60% were successfully treated at 1 year but 30% of cases in the 16 years or older age group continued to have constipation. They found that age at onset of constipation (<4 years) and associated fecal incontinence were poor prognostic factors. In a large study on 300 children, Clayden[33] has shown that 22% required laxative for <6 months, 44% for <12 months and 56% for >12 months. By summarizing all these studies it can be said that half to two-thirds of children with functional constipation had successful outcome with laxative therapy for 6 to 12 months but the remaining one-thirds require long-term therapy and they may continue to have constipation as an adult. Recurrence of constipation after initial recovery is common (50% may have relapse within a year of stopping therapy) but they respond well to retreatment.[12] Poor prognostic factors are; early onset (<4 years), associated with fecal incontinence, and longer duration of symptoms (>6 months).[16]

REFRACTORY CONSTIPATION

A case of constipation is labeled as refractory when there is no response to optimal conventional treatment for at least 3 months.[6] The prevalence of refractory constipation is said to be 20–30%[16, 34] but the prevalence is much higher in India at primary care pediatrician level due to lack of awareness about optimal conventional treatment. At primary care level, disimpaction is hardly practiced and as a result of which the response of laxative therapy is not optimal. The second important reason is early discontinuation of therapy which leads to refractoriness of constipation. The true refractory constipation is extremely uncommon in primary care set up. Even at tertiary care centers, refractory constipation is uncommon.[2]

Besides organic causes of constipation, motility disorders (like slow transit constipation), disorders of stool expulsion like dyssynergic defecation, internal anal sphincter achalasia and sphincter dysfunction in children with Hirschsprung disease which persist after surgery are important causes of refractory constipation.[34] While approaching refractory constipation common organic causes like Hirschsprung disease, hypothyroidism, celiac disease, hypercalcemia, spinal cord abnormalities should be ruled out first and then motility studies [like colon transit time (CTT), anorectal manometry with balloon expulsion test, colonic manometry] to be done to find out motility disorders.[34,35] The simplest and the most informative of all these tests is colon transit time (CTT) study which can be done by radio-opaque markers and by radionuclide scintigraphy (NTS or nuclear transit studies).[34] In radiographic CTT study, a capsule containing 20 radio-opaque markers (different shape in different days) are given daily for 3 days and plain X-ray abdomen is taken on day 4 and if required on day 7 (when all markers are retained on day 4). From X-ray, markers are counted in right colon, left colon and recto-sigmoid regions and the mean segmental time is calculated. Slow transit constipation is defined as retention of markers for 62 hours or more.[36,37] As per the CTT study, constipation can be divided into three categories; (i) normal transit constipation,

(ii) functional outlet obstruction or dyssynergic defecation (retention of markers in rectosigmoid region) and (iii) slow transit constipation (retained markers are distributed all over) (Figs 4A and B). In a study of 225 children (135 pediatric constipation, 56 non-retentive fecal incontinence and 24 recurrent abdominal pain) Benninga, *et al*.[36,37] have shown that 56% of constipated children had normal CTT, 24% had functional outlet obstruction and just 20% had slow transit constipation. In another study on 85 children with functional constipation with rectal fecal impaction by Bekkali, *et al*.[20] have shown that 93% had delayed CTT and as expected majority (83.5%) of them had delayed rectosigmoid segment CTT. As the basic pathophysiology of functional constipation is voluntary withholding of feces, it is expected that most children with functional constipation will have either functional outlet obstruction/dyssynergic defecation or normal transit constipation.

In normal defecation there is synchronized relaxation of puborectalis muscle (makes anorectal angle straight) and external anal sphincter along with generation of propulsive force through contraction of colon and increased in intra-abdominal pressure, which propels stools out of rectum. In dyssynergic defecation, there is paradoxical contraction or failure of relaxation of external anal sphincter and puborectalis muscle with or without increased rectal pressure (propulsive force).[38] These features are detected on anorectal manometry. Therapeutic option of refractory constipation due to dyssynergic defecation is biofeedback (to restore the normal pattern of defecation) and for slow transit constipation is to enhance colonic transit with newer drugs like colon-specific prokinetics like prucalopride (5HT4 agonist)[39] and intestinal secretagogue (lubiprostone),[40] which increases intestinal chloride secretion and accelerates small intestinal and colonic transit. Antegrade continence enema helps in refractory slow transit constipation cases.[41]

Most reports of slow transit constipation in children are from Australia and the clinical presentations of this subset of patients are different from functional constipation (Box 4.2). In a study of 100 children with slow transit

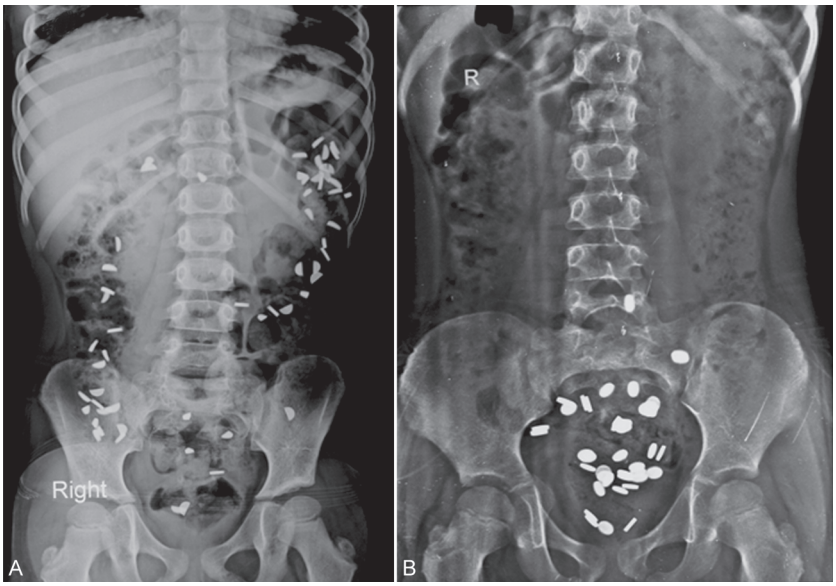

Fig. 4.4: (A) Colon transit time (CTT) study by radio-opaque markers showing slow transit constipation; (B) Functional outlet obstruction

Box 4.2: Clinical features of slow transit constipation in children[42]

- High frequency of delayed passage of meconium
- Onset of symptoms early in first year and/or failure to toilet training
- Feces soft rather than rock hard
- Failure of high fiber diets (they tend to make symptoms worse)
- Global delay in colonic transit on transit study.

constipation, Hutson, *et al*.[42,43] have shown that a history of delayed passage of meconium was seen in 30% of cases, onset of severe constipation in infancy in 63% and half (52%) of those presenting after 2 years of age had history of soiling (fecal incontinence) and failure of toilet training, and the majority (90%) had no hard fecal mass in rectosigmoid area. The management of slow transit constipation is quite difficult as they do not respond to conventional laxative therapy and the main concern is soiling. Fiber therapy is contraindicated (as the motility is slow), the newer drugs like colon-specific prokinetics like prucalopride[39] and chloride channel activator (lubiprostone)[40] are still investigational drugs in children. The only effective therapy for this subset of patients is antegrade continence enema. Here, appendix is used as conduit to insert cecostomy button (Chait trapdoor button) to give enema.[44,45] It has minimal scar and just a button at right iliac fossa which is used in the morning to give antegrade enema and the whole day patient remains dry (no soiling). In a recent study on 203 cases (median age 10 years, follow-up 5.5 years, 62% due to refractory chronic idiopathic constipation) of this modality, Randall, *et al*.[41] showed good result in 93%, soiling prevented in 75% and symptoms resolved (no longer on antegrade continence enema) in 26% (81% of them were chronic idiopathic constipation).

Colonic manometry plays an important role in guiding both medical and surgical treatment in refractory constipation. In fact, it has been shown that the success of antegrade continence enema procedure depends on colonic manometry results.[46] If there is generalized colonic dysmotility [absence of high-amplitude propagating contraction [HAPC] in the entire colon] then there is no point in putting cecostomy catheter. Similarly, colonic manometry results can dictate the type of surgery following colonic diversion; subtotal colectomy if small bowel motility is normal but whole colonic motility is abnormal, left hemicolectomy if only left colonic motility is abnormal and reanastomosis if colonic motility is normal.[47]

A relatively less common but important cause of refractory constipation is internal anal sphincter achalasia. In a study of 332 patients with severe constipation, De Caluwe, *et al*.[48] have reported this as a cause in just 4.5% of cases. This subset of patients usually present with severe constipation (99.7%) which often associated with fecal incontinence (46%) and are diagnosed by absence of anorectal inhibitory reflex (ARIR) on anorectal manometry along with presence of ganglion cell on rectal biopsy.[49] The treatment options for internal anal sphincter achalasia are posterior anal sphincter myectomy and intrasphincteric botulinum toxin injection. In a recent meta-analysis, it has been shown that former is better.[49]

CONCLUSION

Constipation is quite common in Asia, and most often of functional origin. Detailed history and proper physical examination, including digital rectal examination, can easily differentiate functional from organic constipation. There is no need to do any investigation before starting treatment in functional constipation. Disimpaction with oral polyethylene glycol is the main step in the management and skipping this step leads to refractoriness of constipation. Polyethylene glycol is shown to be superior to lactulose in the management of constipation. In most cases, prolonged (months to years) laxative therapy is required and early withdrawal leads to recurrence.

Radiological colon transit time study plays an important role in the management of refractory constipation. Slow transit constipation is altogether a different entity and antegrade continence enema helps in this subset of patients.

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Chapter

5

Organic Foods for Children: Health or Hype?

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Concerns regarding quality of food are on the rise. A surge in diseases like cancers and atopic disorders has motivated health professionals, consumers, and policymakers to look for safe and healthy lifestyle measures. Organically grown foods are being promoted as a promising alternative by their manufacturers and certain activists and lobbies concerned with human health, environment and animal welfare.[1] As a result, the market is flooded with a variety of organic foods, including fruits, vegetables, cereals, dairy products and baby foods. Nutrition and safety are two important aspects that prompt the consumers to prefer organic over conventional foods. We intend to probe the status of organic foods, regulations governing their production, marketing and advertising, and whether these foods really hold an edge over the conventional foods, especially for the children in India.

PRODUCTION (ORGANIC FARMING AND REARING)

National Organic Program (NOP) was implemented in 2000—by United States Department of Agriculture (USDA) to enforce regulations for certifying a food product as organic. National Program for Organic Production (NPOP) under the aegis of Ministry of Commerce and Industry, India released its recommendations in 2000, to provide standards for organic production to farmers, producers and traders. The certification scheme was initiated in 2002, with its logo of 'India Organic'. It defines organic farming as the process of developing a viable and sustainable agro-ecosystem where the foods are grown without application of synthetic fertilizers, pesticides, fumigants (containing nitrogen or other heavy metals), human excreta, growth hormones or genetically engineered techniques.[2,3] The land has to be free of any of these substances for at least 3 years, before organic crop is grown. Organic production increases with suitable crop rotations, green manure, early and pre-drilling seed bed preparation, mulching, physical or mechanical control of pest and weeds, and disturbing the developmental cycles of the pest.[2]

Organic animal products (milk, egg, chicken, meat, etc.) are produced from animals fed on 100% organic food for at least 12 months.[2] For organic animal rearing, biological needs (food, shelter, reproduction) of these animals should be met naturally, and in time. Diseased animals should be promptly and adequately treated. Antibiotics, synthetic growth promoters, hormones for heat induction, and genetically engineered vaccines to increase the yield are prohibited.[2, 3]

Natural food is often confused with organic food. Natural food refers to minimally processed foods free of synthetic preservatives, artificial sweetener, colors, flavors, additives, and stabilizers. Natural foods can be prepared through conventional means but are preserved with minimal artificial techniques. On the other hand, organic foods are prepared, processed, and preserved in natural environment.[4]

THE GROWING MARKET FOR ORGANIC FOOD

Global organic food market has shown a boom over the last two decades; United States, Germany, France, and Australia are the major consumers. The domestic market for organic foods in India was estimated to be of one billion rupees (2007–2008), and export market approximately 100 million USD.[5]

According to the status report of National Program on Organic Production, 5.2 million hectares of land in India is currently undergoing organic farming, of which 0.5 million hectares is certified. More than 6,00,000 farmers are involved in organic farming. India's primary organic produce include cereals, pulses, oil seeds, spices, fruits and vegetables, nuts and dry fruits, sugar, honey, milk and milk products, poultry, and other animal products.[5] The major buyers are supermarkets, embassies, five-star hotels, hospitals, and Ayurveda clinics. The availability and consumption of organic products is primarily urban. Advertising and marketing strategies are evolving.

ORGANIC FOOD PRODUCTS FOR CHILDREN IN INDIA

There is a scope for a large market for organic food products meant specifically for infants and toddlers. These products include baby cereals, smoothie fruits, yogurts, toddler meals, biscuits, nibbles, cereal flakes, which are specially produced, flavored and packaged keeping in view the needs of children of different ages. A few of these products are available in the Indian market, mostly through online purchase. Most manufacturers are international. No Indian company, to the best of our market survey, is producing and marketing organic baby foods for the local consumer. India, due to its largest birth cohort in the world, is a luring proposition for the corporate world dealing in organic products. The need of the hour is therefore to be prepared for the onslaught, and have a clear-cut policy or guideline on the utility and consumption of organic foods by children in India. Parental education programs will also need to be developed accordingly.

Due to rigorous procedures required for organic farming and rearing, the price of organic foods is much higher than the conventional foods. Production cost is high because of requirements of farmer training, post-harvest handling, pesticide-free storage, segregated marketing and high retailer margin.[6] Additionally, organic foods have a shorter shelf-life. High cost of organic food is visualized as a major barrier for its widespread use. On the flip side, the higher cost is also perceived to be a marker of higher quality (in terms of nutritive value); but is it really true?

NUTRITIVE VALUE

Organic food is considered to be of higher nutritional value despite lack of high-quality scientific evidence. Most of the research is observational; there is a lack of controlled trials on their health benefits. Organic foods are said to be rich in antioxidants, phenolics, vitamins A, C and E, potassium, phosphorus, and nitrates. Omega-3 fatty acids, and alpha linoleic acid (ALA) are also claimed to be in higher amount in the organic foods.[7] Worthington reported higher levels of vitamin C, iron, magnesium and phosphorus, lower quantities of proteins (though of better quality), lesser nitrates and lesser amount of heavy metals in crops produced by organic farming system.[8] A recent meta-analysis documented higher

concentrations of protein, ALA, total omega-3 fatty acid, cis-9, trans-11 conjugated linoleic acid, trans-11 vaccenic acid, eicosapentanoic acid, and docosapentanoic acid in organic dairy products.[9] Rist, *et al.*[10] compared the levels of conjugated linolenic acid isomers (CLA) and trans-vaccenic acid (TVA) between breastmilk of mothers consuming organic or conventional foods. CLA is suggested to have anti-carcinogenic, anti-atherosclerotic, anti-diabetic and immune-modulating properties in animal models. It is also known to modify bone mass composition.[11] Rumenic acid–the most common isomer of CLA–and TVA were significantly higher in mothers on organic diet.[10] In a recent observational study, Vrèek, *et al.*[12] demonstrated lower levels of protein, calcium, manganese, and iron in organically grown wheat flour, in comparison to conventional one. The protein digestibility and levels of potassium, zinc, and molybdenum were significantly higher. Lombardi-Boccia, *et al.*[13] compared the composition of organic yellow plums with conventional plums. The authors found only marginal differences in levels of macronutrients, whereas antioxidant vitamins like vitamin C, vitamin E, β-carotene, and phenolic compounds showed significant differences. Interestingly, the levels also differed with the type of organic cultivation used.

An important nutritional advantage of organically produced foods is their antioxidant effect. It is hypothesized that organically grown foods develop the capability to produce more antioxidants than conventionally grown foods, as an adaptive response to fight insect and fungal attacks. However, Caris-Veyrat, *et al.*[14] failed to demonstrate significant difference in two major antioxidants, namely, vitamin C and lycopene, *in vivo*, in organically grown tomatoes.

Table 5.1 presents a comparison of macronutrient contents of commonly consumed foods (organic *vs.* conventional) as available in the Indian market. There is hardly any difference between the calorie and protein content of organic and conventional foods. However, the fat content of baby food and egg appear to be somewhat lower than their conventional counterparts.

TABLE 5.1: Macronutrient content and cost (per 100 g) of organic and conventional food items

Food item (per 100 grams)	*Calories (kcal)*	*Protein (grams)*	*Fat (grams)*	*Cost* (INR)*
Chicken				
Organic	134	29.1	17	35
Conventional	119	21.4	3.1	23
Corn flakes				
Organic	383	8	1	66
Conventional	357	7.1	0	30
Mixed whole grain baby food				
Organic	393	14.3	5.4	156
Conventional	393	14.3	10.7	43
Mustard oil#				
Organic	884	0	100	28
Conventional	884	0	100	11
Poultry egg				
Organic	123	10.6	7.0	15
Conventional	135	11.4	9.0	10
Regular basmati rice				
Organic	345	6.8	0.5	18
Conventional	333	6.7	0	5
Toor dal				
Organic	335	22.3	1.7	16.5
Conventional	365	21.9	1.7	10
Wheat flour				
Organic	347	20.1	1.5	6
Conventional	380	20	0	3
Whole wheat bread				
Organic	225	10	2.5	16
Conventional	224	7.6	1.6	7
Ghee (cow's)#				
Organic	900	0	100	74
Conventional	900	0	100	30

**Costs are approximate costs in Indian market, and may vary with brands. Nutritive content is based on a market survey by the authors that recorded the display on packaged foods by the manufacturer; this may again vary with different brands. #per 100 mL.*

HEALTH BENEFITS

A large number of studies have compared organic and conventional produces with respect to macro- and micro-nutrient composition, and their potentially harmful effects, but not many studies have evaluated the direct health benefits of organic foods on humans. Chabbra, *et al*.[15] used fruitfly (*Drosophila melanogaster*) model to assess the overall health benefits of organic fruits, and demonstrated improved fertility and longevity of the fly on organic diet.

We could identify only one study evaluating organic *vs* conventional food in children. This questionnaire-based study from Netherlands conducted on a birth cohort of 2764 infants concluded that the risk of eczema was lowered (OR 0.64, 95% CI 0.44–0.93) in infants less than 2 years of age consuming organic dairy products.[16] However, the study could not demonstrate any association between consumption of organic meat, fruits and vegetables, eggs, or proportion of organic products within the total diet, with developing eczema, wheeze or atopic sensitization. Authors were uncertain whether their findings represented a true association and recommended further studies for confirmation.

Most of the International health authorities are silent on issues regarding benefits of organic food. American Academy of Pediatrics reviewed the scientific evidence available on the merits and demerits of organic produces with the aim to provide a recommendation for pediatricians and parents. In the absence of well-planned human studies showing any direct health benefit of organic foods, the report[17] supports incorporation of a wide variety of foods to provide a balanced nutrition to the children, which need not necessarily be organic. Facts about composition, pesticide residues, health benefits, and cost of organic foods should be widely available to parents.[17]

ORGANIC FOODS: ARE THEY REALLY PESTICIDE-FREE?

Pesticide exposure and use of synthetic chemicals are a major concern with conventional farming. However, Gonzalez, *et al*.[18] reported contamination of organically grown crops of tomatoes with organochlorine pesticide (OCP) residues which were never used in these farms. Similar results were also reported by Baker, *et al*.[19], though less (one-third) often than conventional foods. The possible causes include previously contaminated fields, wind dispersion, surface run-off and volatilization. Interestingly, the levels in the crops grown by both conventional and organic methods are well below the safe limit of pesticide residues.[20] Recently, 61 commercially available brands of cheese were evaluated for OCPs and polychlorinated biphenyls (PCB) in Spain. The authors reported OCP levels to be lower than recommended total dietary intake (TDI) in both types of products, though the levels of PCBs were in the higher centile range of TDI.[21] Lu, *et al*.[22] in an interventional study, reported that urinary excretion of metabolites of commonly used organophosphorus pesticides (malathion and chloropyrifos) were immediately and greatly reduced when the child switched from conventional to organic diets.[22]

POTENTIAL RISKS OF ORGANIC FOODS

Microbiological safety of the organic animal foods is a questionable domain, the reason being prohibited use of antimicrobials. Cui, *et al*.[23] analyzed organic and conventional chicken samples for prevalence and antimicrobial resistance of *Campylobacter* and *Salmonella*. They found organic chicken to be more contaminated with these organisms, although the pathogen isolated from organic chicken were more susceptible to some antimicrobials. In a contradictory study, foods from conventional farms isolated *Salmonella* more frequently with higher level of resistance to streptomycin and sulphamethoxazole.[24] Contamination by

mycotoxins has also been reported with organic farming.[25,26]

CERTIFICATION

United States Department of Agriculture (USDA) certifies any food as '100% Organic', if it has 100% organically-produced ingredients and processing aids, and 'Organic', if it fulfills 95% of the above criteria. Remaining 5% should be non-agricultural substances approved in their national list. Another category with 70% organic components can use the label reading 'Made with organic ingredients', but cannot use USDA logo.[27] EU Oganic is the certification given to products with more than 95% organic ingredients by European countries. 'India Organic' certification is provided to the organic products complying with the USDA standards by INDOCERT, the nationally and internationally operating certification body by NPOP. The certificate is valid for 3 years and needs to be renewed every 3 years.[2] Guidelines are available for ingredients, additives, processing, packaging, labeling, storage and transport to ensure the quality of products. The certification is liable to suspension or termination in the event of violation.

THE ROAD AHEAD

With the dramatic increase in the growth of organic food market globally, issues regarding nutritive value and safety need to be answered. The consumer is willing to pay a higher price for a healthier option. The literature shows that there are few qualitative differences between organic and conventional foods, but whether they actually produce a beneficial effect on human health is currently not known. Evidence available till date is insufficient to promote or refute the use of organic foods over conventional foods, with particular consideration of high cost involved. There is a need for controlled trials to study the actual health benefits with organic foods, and efforts to reduce the cost by working on organic farming techniques.

American Academy of Pediatrics issued its report on health and environmental advantages and disadvantages of organic foods. The report gives the guidelines to pediatricians for the purpose of guiding the parents. Despite the increasing market of organic produces in India, Indian Academy of Pediatrics (IAP) has not formulated any guidelines for their use in children. The brands available in India should provide exact details of the composition of the product, to enable the consumers to compare and chose the option best suited to their pocket. Manufacturers should abide by the guidelines for factual display of contents in advertising, and not just use it merely to lure the consumers; IAP can play an important role in this regard.

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Chapter
6

Energy Drinks: Potions of Illusion

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In a competitive world–where achieving targets rules the roost–more energy is a desirable virtue. Some adolescents are naturally energetic, while others look for commercially available stamina boosters to provide instant energy. Energy drinks seem to be just the solution this group is looking for.

Energy drinks are non-alcoholic beverages containing stimulants like caffeine, herbal extracts (*guarana, ginseng, yerba mate, ginkgobiloba*), glucuronolactone, taurine, inositol, L-carnitine and B-vitamins as the main ingredients to enhance physical and mental endurance.[1] In addition, these drinks may contain carbonated water. Energy shots are a specialized form of energy drinks which contain the same amount of caffeine in a small amount of liquid, typically 60–90 mL small bottles or cans. These may be considered as concentrated energy drinks with lesser calories and lower sugar content.[2] Energy drinks/energy shots are consumed to improve the stamina and energy levels before and during exercise, to rehydrate the body, to keep awake in demanding situations, to compensate for loss of sleep especially during examinations, or to get a kick as a mood elevator by mixing it with alcohol. Natural caffeinated beverages including coffee, cocoa, tea, and cola drinks are not regarded as energy drinks. Energy drinks should not be confused with sports drinks that contain carbohydrates, minerals, electrolytes, and flavoring agents. These are intended to replenish water and electrolytes lost through sweating during exercise. Unlike energy drinks, sports drinks do not contain any stimulants.[3]

GROWING DEMAND

Energy drinks were introduced to the world in 1949 by the name of 'Dr Enuf' in US; these were fortified with vitamins and projected as a better alternative to sugar sodas. Subsequently, these became available in Europe and Asia in 1960s.[4] Lipovate D, an energy drink that still dominates the Japanese market, was launched in 1962. Later, several companies introduced similar drinks but none could make a mark till 1997, when 'Red Bull' was introduced by an Austrian entrepreneur.[4] This brought a boom to the industry and ever since the market for energy drinks is growing exponentially. More than 300 variants of energy drinks are available in the US market alone. India, China, and Brazil are considered as the growing markets. Red Bull was launched in India in 2003. With a 75% market share, it is presently leading the Indian market of energy drinks. The energy drink market in

India was pegged at ₹ 700 crore in 2013; comprising of 5% of the total soft drinks market dominated by colas, fruit juices, and flavored milk (5), compared to 8–9% in global market.

Manufacturers have now shifted their focus from athletes–the primary target for energy drinks–to teenagers and young adults. According to an estimate, about 71% of adolescents in urban centers of India consume energy drinks.[6] Despite the cost factor, youth do not mind spending money on energy drinks due to their much advertised perceived benefits on endurance, attention, and stamina.

CONSTITUENTS OF ENERGY DRINKS

The main constituent of energy drinks is caffeine. In non-alcoholic energy drinks, caffeine content varies between 75 mg and 150 mg per can[1] compared to 80–120 mg and 60 mg in a cup (250 mL) of coffee and tea, respectively.[7] Maximum recommended intake of caffeine per day, varies from 2.5 mg/kg/day to 6 mg /kg/day in children, 100 mg/day in adolescents and up to 400 mg/day in adults.[8]

Caffeine attaches to the adenosine receptor due to its similar chemical structure as that of adenosine. Due to this, the adenosine effect to promote sleep is stopped by competitive inhibition resulting in speeding up of neurons. Caffeine also improves the physical and mental performance by increasing epinephrine secretion. Once ingested, caffeine is rapidly absorbed from the gastrointestinal tract where it is demethylated to form paraxanthine (84%), theobromine (12%), and theophylline (4%). Caffeine intake leads to increased energy utilization and thereby better performance. It has also been found to enhance mood and alertness. In addition, it has been found to decrease food intake and promote lipolysis [9].

Guarana (also called guaranine, *Paullinia-cupana*, and *Sapindaceae*)–another ingredient of energy drinks–is a plant extract containing large amounts of caffeine with small amounts of theobromine, theophylline, saponins, flavonoids, and tannins. The seeds contain about twice the concentration of caffeine found in coffee beans. One gram of guarana is equal to approximately 40 mg of caffeine.[9] Consumption of guarana increases energy, enhances physical performance, and promotes weight loss. These effects are largely contributed to the high caffeine content of guarana.

Ginseng (*Panax ginseng*) is a herbal supplement; root being its most important part. Athletes use ginseng for its alleged performance-enhancing attributes; however, no scientific evidence is there till date to support its performance-enhancing claims.[9]

Yerba mate, obtained from *Ilex paraguariensis* is known for its anti-inflammatory, anti-diabetic, and anti-oxidative properties. It is a central nervous system stimulant due to its high caffeine concentration (78 mg in 1 cup of yerba mate tea).[9]

L-carnitine, D-glucuronolactone, taurine, and inositol are other ingredients of energy drinks. Data remain insufficient regarding their safe use and claims to increase endurance.[6,9,10] Certain other ingredients like milk thistle, ginkgo, acai berry, L-theanine and creatine have bioactive properties for which they are sometimes added to energy drinks.[9]

POTENTIAL ADVERSE EFFECTS

When consumed in moderation, most energy drinks are considered safe. Over-consumption is fraught with potential adverse effects attributed to the high caffeine content.

Caffeine tolerance varies between individuals, though most people would develop toxic symptoms in doses of 200 mg (1 mg = 4 ppm). Some of the energy drinks may contain caffeine as high as 300–500 mg per can.[1] Table 6.1 shows the caffeine content of commonly available energy drinks in the Indian market. Symptoms of caffeine intoxication include palpitations, anxiety, insomnia, nausea, vomiting, restlessness, and tremors.[1] The risk increases if multiple drinks are

TABLE 6.1: Caffeine content of commercially available energy drinks in the Indian market

Brand	*Amount (mL)*	*Cost (₹)*	*Caffeine content declared by manufacturer (ppm)*	*Caffeine content as tested by CSE (ppm)*
Red Bull	250	95	320 (80 mg/250 mL)	310.08
Tzinga	250	25	300 (75 mg/250 mL)	258.37
Triple X	250	75	100	117.14
Cloud 9	250	85	Not given	142.25
Burn	300	75	320	291.73

Source: *CSE (Centre for Science and Environment)*

consumed in a short period of time. A cocktail of energy drinks when mixed with alcohol decreases the awareness of the amount of intoxication, leading to a higher risk of alcohol-related injuries.[11] The combination might also increase the risk of arrhythmia if there is an underlying heart disease. Teens are shown to mix their energy drinks with alcohol.[12] This can be potentially dangerous cocktail as the drinkers will be unaware of the amount of alcohol they have actually consumed. Caffeine content of beverages consumed by adolescents has also been linked to high blood pressure.[13]

Caffeine, taken in large amounts over an extended period of time, leads to caffeinism characterized by nervousness, increased risk of addiction, irritability, anxiety, tremulousness, muscle twitching, insomnia, headache, respiratory alkalosis, and palpitations.[1] The Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) recognizes four caffeine-induced psychiatric disorders: caffeine intoxication, caffeine-induced anxiety disorder, caffeine-induced sleep disorder, and caffeine-related disorder. Studies in adult twins have shown a significant positive association between major depression, generalized anxiety disorder, panic disorder, antisocial personality disorder, alcohol dependence, and cannabis and cocaine abuse/dependence; with lifetime caffeine intake, caffeine toxicity, and caffeine dependence.[14]

Another demerit of caffeine is its ability to foster dependence. Genetic factors have also been found to play some role in caffeine intoxication, dependence, and withdrawal.[14].

Ginseng has been associated with adverse effects like hypotension, edema, palpitations, tachycardia, cerebral arteritis, insomnia, mania, and cholestatic hepatitis but they are not noted at levels found in energy drinks. Studies are insufficient to prove its safety.[15]

Most energy drinks contain a lot of sugar or artificial sweeteners to mask the bitterness of caffeine. The sugar content in energy drinks ranges from 21 g to 34 g per 8 oz. Sugars in energy drinks may be in the form of sucrose, glucose, or high fructose corn syrup. Their intake poses a risk for obesity and diabetes in children.

Most sports and energy drinks have citric acid, which lowers their pH in the acidic range (pH 3–4). A pH this low is associated with enamel demineralization and dental problems.

ENERGY DRINKS AND MEDICAL CONDITIONS

- Energy drinks if taken by children being treated for attention deficit hyperactivity disorder, can be very harmful as they are already taking stimulant medications.[16]
- Patients of ion channelopathies and hypertrophic cardiomyopathy should not take energy drinks because of the risk of hypertension, syncope, arrhythmias, and sudden death due to unwanted stimulant effect of caffeine.[17] In August 2008, a study conducted by the Cardiovascular Research Centre at the Royal Adelaide Hospital in Australia assessed the cardiovascular status of 30 young adults one hour before and after the intake of a popular energy drink and found that it could increase the risk of stroke and heart attack.[1]
- High amounts of caffeine help to counter caloric-restriction–associated fatigue, and suppress appetite, and thus have often been taken by patients of anorexia nervosa. But as these patients have a propensity for

cardiac morbidity/mortality and electrolyte disorders, intake of high-caffeine energy drinks can trigger cardiac dysrhythmias and intracardiac conduction abnormalities.[18.]

- Other high-risk groups include adolescents with obesity, hemodynamic compromise, diabetics and individuals with pre-existing cardiovascular, meta-bolic, hepatorenal, and neurologic disease, those who are taking medications that may be affected by high glycemic load foods, caffeine, and/or other stimulants, and adolescents in rapid growth phase.[12]
- Caffeine also acts as a diuretic; therefore, energy drinks should be avoided during exercise as fluid losses from sweating coupled with diuresis can lead to dehydration.

WHERE WE STAND?

Considering the potential adverse effects, energy drinks have been banned in some countries like Denmark, Uruguay and Turkey. Energy drinks with caffeine more than 320 ppm are banned in Australia.[19] European countries have stipulated that energy drinks with caffeine more than 150 ppm should be labeled as having 'high caffeine content'.

In the first year of the launch of a leading energy drink, there was a tussle between the manufacturers and government agencies on labeling of the product. The central food laboratory continued to label it as carbonated beverage (maximum allowable caffeine content–200 ppm, now lowered to 145 ppm). The manufacturers maintained it as proprietary product (caffeine content–320 ppm), and claimed it to be safe. The maximum limit of caffeine of 200 ppm in carbonated beverages was reduced to maximum level of 145 ppm on recommendations by Central Committee on Food Standards (India) and notified vide notification GSR 431(E) dated 19.06.2009. Food Safety and Standards Authority of India (FSSAI) then constituted an expert group on energy drinks and made certain observations (Box 6.1).[1]

Center for Science and Environment (CSE), a Delhi-based NGO, tested eight brands of energy drinks and showed that caffeine levels were exceeding 145 ppm in 6 of them.[20] FSSAI constituted an expert group, followed by a risk assessment study commissioned by National Institute of Nutrition (NIN), Hyderabad. On the basis of NIN report, FSSAI has now recommended a limit of 320 ppm of caffeine in energy drinks. In June 2012, FSSAI announced the mandatory use of statutory safety warnings and that all energy drinks should be renamed as "caffeinated beverages."

Box 6.1: Food safety and standards authority of India observations on energy drinks

- Caffeine is not an additive but a chemical with addictive property. Caffeine up to 200 ppm is added as a flavoring agent but above 200 ppm it is a functional ingredient. The functionality of caffeine at 320 ppm needs to be ascertained along with justification for fixing a cut-off limit at 320 ppm.
- Energy drink is a beverage which is fortified with vitamins and there is no case for encouraging its consumption. The name 'energy drinks' is a misnomer as it gives the impression that this should be taken to get energy.
- The vegetarian and non-vegetarian symbol should also be given on the label of energy drinks as per the source of ingredients added.
- Standards for energy drinks, both carbonated and non-carbonated need to be laid down to enable better regulation of the product. These may be termed as 'caffeinated drinks'.
- There is a need to limit consumption of energy drinks by a person per day taking into account total caffeine content from all ingredients and items in the diet.
- Alternatively, instead of laying down separate standards for carbonated energy drinks, standards for carbonated beverages per se can be amended to include other ingredients like taurine, glucurono-lactone, etc. which are found in energy drinks.
- There is also a need to get the market data of availability of energy drinks in India and analyze samples as a basis for fixation of standards according to Indian requirements.

TABLE 6.2: Caffeine content of common fast moving consumer goods

Products	*Caffeine content/250 mL*
Tea	60 mg
Coffee	80–120 mg
Carbonated beverages	25–40 mg
Dark chocolate (100 g)	43 mg
Hershey's syrup (2 tbsp/ 39 g)	5 mg

Following this, the energy drinks now boldly write "contains caffeine". Further, they mention clearly "Not recommended for children, pregnant or lactating women and persons sensitive to caffeine. Use not more than 2 cans a day." FSSAI has also proposed that such products be packed in only 250 mL containers. However, consumers need to keep in mind that there are other sources of caffeine intake like coffee, tea, chocolate products, and carbonated drinks. Table 6.2 depicts the caffeine content of commonly consumed beverages. As of now, this caffeine cap of 320 ppm for energy drinks does not take into account the total caffeine content from other beverages. There is no sample study in India to determine the caffeine intake of the population as such. Also the justification for propagating the use of energy drinks for a source of vitamins, minerals, and amino acids is not acceptable as these can be easily obtained from a normal healthy diet.

CONCLUSION

Intake of energy drinks prior to physical activities may be undertaken while keeping their possible deleterious effects in mind. Their use during physical activity is not recommended. Sports drinks (non-caffeinated) are designed to be taken during physical activity and should be preferred. Energy drinks claim to have stimulant effects; these may be pleasant at times. However, intake of these drinks can be harmful. Considering this fact and the growing popularity of these drinks, one should be cautious before and during intake of energy drinks. More awareness needs to be created in the younger generation regarding their appropriate intake. Further research should be done to assess the benefits and ill-effects of various ingredients present in these drinks. Indian Academy of Pediatrics should lead a campaign to educate parents and pediatricians about the risk of caffeinated drinks.

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Chapter

7

Undesirable Effects of Media on Children: Why Limitation is Necessary?

Aysu Turkmen Karaagac

Teachers, pediatricians and pediatric psychiatrists agree on the fact that sustained intellectual exercise contributes to the brain growth and more sophisticated thinking, and thus brain must be challenged regularly. Communication and analytical thinking abilities of children develop if they regularly converse with their families and/or develop good reading habits. Families may unintentionally contribute to the mental deprivation and limited brain growth of their children by allowing unlimited use of media devices.[1–3]

The social media network sites which have provided children with easy ways of establishing friendships, and satisfy their feelings of belonging and acceptance by others, have become more and more popular especially in developing countries.[4] However, there is no sufficient research/guideline on protecting children's safety in use of media devices in developing countries.[5] The results of the national school violence study in South Africa showed that 80.2% of secondary school learners have a mobile phone, while 54.3% have access to a computer or a tablet computer. About 70% of these children were reported to use social network sites and talk with strangers at least once a week.[5] Research findings in Vietnam have revealed that up to 25% of children in the urban areas and 20% of children in the rural areas had shared personal information such as their phone number or name of their school with strangers online. It was also reported that 49% of the urban children and 20% of the rural children in Vietnam were subjected to cyberbullying, or were threatened or embarrassed online. Unfortunately, only 1 in 10 of these victims informed a parent or an adult about this abuse.[4,5] Several studies have reported that victims of bullying are 2 to 9 times more likely to consider committing suicide.[3–5] Families should help their children realize the danger of cyberbullying by controlling their computer/tablet computer use.

Watching television (TV) is the first-choice lesiure time activity of the families, especially in the urban areas of developing countries.[6] Burdette, *et al.*[7] reported that children in urban areas spent an avarage of 2.2 hours per day watching TV. Children's exposure to media violence plays an important role in the etiology of violent behaviors.[7,8] TV programs in US show 812 violent acts per hour, a typical American child would have followed 200,000 acts of violence, containing more than 16,000 murders, until the age of 18 years.[8] Furthermore, 15–20% of music videos and many of video games include violence.[8] Children tend to imitate the characters they watch on TV

programs or on video games because they can not distinguish between fact and fantasy until 5 years of age. They may accept the violence as an ordinary means to solve problems over the time.[8,9] Therefore, physicians, especially pediatricians, should make parents and teachers media-literate meaning that they should comprehend the risks of exposure to violence, and teach their children how to interpret what they see on TV, in the movies, or in the cartoons.

How does media affect weight in children? Watching television or playing with computer over 2 hours/day might result in obesity in children due to the lack of activity. Studies also suggest that 80% of obese children might become obese in adult life.[9,10] The incidence of childhood obesity–which may lead to hypertension, diabetes mellitus, coronary artery disease, cholecystitis, dyslipidemia, osteoarthritis or sleep apnea in adulthood–has doubled in the last two decades in America in proportion to the increase in children's media use.[11]

Moreover, American Academy of Pediatrics has declared that an average child watches 20,000 or more commercials every year, more than 60% of which promote junk foods related with obesity.[12,13] Costa, *et al*.[14] reported that 13.8% of 1369 commercials screened during 176 hours of TV programming in Brazil were related with foods as sugars, sweets (48.1%) and fats (29.1%). It has been suggested that the content and the timing of commercials should be carefully controlled because children under the age of 8 years are unable to differentiate the advertisements from the regular programs, and commercials have considerable influence on them.[13]

Yousef, *et al*. reported a positive correlation between excessive TV watching (>2 h/d) and aggressive behaviors, attention problems, low self-esteem and internalizing and externalizing problems of children.[15] The use of electronic media devices beginning from the preschool age has been associated with 1.2–2 folds higher rate of emotional disorders like major depression, bipolar disorder or anxiety attacks. In addition, poorer family functioning has been reported with excessive TV watching or computer use.[16]

Obesity and impaired glycemic control due to lack of exercise is one of the major risk factors for cardiovascular diseases.[17] If children's media use is not limited, they neglect regular activities as hiking, running, swimming and riding bicycle.[14] Therefore, it is important to encourage families to monitor their children's media use and to spend more time doing physical activities with their children to improve cardiovascular health in their adulthood.

Children usually sit in unsuitable body postures for a long time in front of TV or computers. Drzal, *et al*.[18] demonstrated that prolonged sitting position resulted in decreased angle of inclination of the thoracolumbar spine, reduced thoracic kyphosis and lumbar lordosis, and pelvic asymmetry in children aged 11 years to 13 years in Poland. Posture education programs should be advocated for school children to avoid such advanced spine abnormalities.

Melatonin is a very important antioxidant that protects nuclear DNA and cell membrane lipids from oxidative damage. It has been strongly suggested that prolonged exposure to magnetic fields might cause hematopoetic system cancers, especially in children, due to melatonin supression.[19]

The most effective way of protecting children from the undesired effects of media is to provide the family control via media literacy education programs. The success of media literacy education of families depends on the power of communication between parents and children. One of the most important steps of this education is to set some rules about limiting the time their children spend watching TV or playing video games. Children's media use should be limited to 1–2 hours/day after they finish their homework and/or sport activities.[20] Parents should watch TV with their children to teach them how to

interpret the media messages or content of commercials. Parental supervision during watching cartoons and movies enables the children to distinguish between reality and fantasy. Families should talk with their children about how violent scenes create false excitement, and how problems can be solved non-violently.[19,20] Besides family relationships and willingness, several demographic factors such as age, educational status or income of the parents may affect the results of media literacy applications. Studies have shown that the educated parents can have a better control of children's media use and its content. On the other hand, two-thirds of 8- to 18-year-old children of the families with higher socio-economic status have their own TV sets, computers or video game consoles, which makes family control difficult.[20,21]

In conclusion, harmful effects of uncontrolled media use by children is a common problem shared by most of the countries throughout the world. It is impossible to forbid children's media use; however, physicians can promote healthy use through public education. Media organizations should also be trained to be more sensitive about the determination of program contents and timing. Pediatricians should play a key role in raising awareness of media literacy of families as well as encouraging politicians to create effective media-literacy education policies.

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