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Working towards eradicating pneumococcal disease

Prof Catherine Weil-Olivier

The incidence of acute respiratory diseases, which includes pneumococcal disease, is the number one killer in children under five worldwide. Pneumococcal disease has seen a global precipitous decline since the introduction of pneumococcal conjugate vaccines (PCVs).

Prof Mario Ramirez

Prof Catherine Weil-Olivier, professor of Paediatrics at Paris VII University, was one of the speakers at the recent Africa & Middle East Paediatric Pneumococcal Disease Summit, which took place in Cape Town.

She explained the impact of the PCV programmes around the world to around 175 mostly paediatricians who had gathered to learn of progress in the development of the vaccine and its impact on pneumococcal disease.

Today, pneumococcal disease is the number one vaccine-preventable death, yet countries in the southern hemisphere still experience an incidence three times higher and deaths 50-fold higher than the northern hemisphere, with low-income countries carrying the greatest burden.

The spectrum of pneumococcal disease covers meningitis, pneumococcal septicaemia and pneumococcal pneumonia, which result in hospitalisation and death. Pneumonia and otitis media (OM) are mucosal diseases, where there is a large volume of cases and economic use of antibiotics and resistance are key issues.

Prof Weil-Olivier shared numerous studies from countries around the world demonstrating the pervasive impact of *Streptococcus pneumonia*, not only in children under five but also among the elderly (age ≥65).

Pneumonia is the cause of 20% of deaths in preschool children worldwide, while the global incidence of OM, associated with a loss of hearing or chronic suppurative OM or even mortality, is relatively high in the southern hemisphere.

Global impact of PCV programmes

Pfizer's seven-valent pneumococcal conjugate vaccine, which covers the seven predominant pneumococcal serotypes (4, 6B, 9V, 14, 18C, 19F and 23F) thought to cause up to 90% of all invasive pneumococcal disease (IPD) was introduced in the US in 2001.

Since then, it has been introduced in more than 50 countries worldwide, and numerous studies have shown a significant decline globally. "PCV7 has shown to be highly efficient in preventing IPD and mucosal disease in vaccinated groups," she said. "The consequence was a global decrease of IPD.

"PCV7 is also inducing strong immune responses with immune memory early in life and so is highly efficient in reducing nasopharyngeal carriage of vaccine serotypes."

The US and Europe have shown a precipitous decrease in all PCV7 serotypes, including in children with underlying medical conditions, which would normally predispose them to pneumococcal disease.

"Because of the near-disappearance of the vaccine serotypes in France, we also had a good impact on antibiotic resistance in the country," she added.

Pfizer's 13-valent vaccine was introduced in 2009 (and in May 2011 in SA), and covered the remaining six serotypes (1, 3, 5, 6A, 19A and 7F) thought to cause the majority of remaining pneumococcal disease.

Studies from the US have shown a marked decrease in IPD just one year after its introduction.

"With the six additional serotypes, we halved the incidence of these diseases globally," she said. There is also an acknowledgement that there is a very significant impact on adults aged 50 and older. Although we have seen this very early result among children, this is the first demonstration that we have an indirect impact of PCV13 in populations not vaccinated – in just one year.

"So the impact of PCVs is largely demonstrated."

There has also never been any signal concerning the safety of PCVs, according to Prof Weil-Olivier.

Controlling the disease

The next steps are to increase both the number of serotypes in the PCVs, as well as to expand the number of countries with access to PCVs, in order to control the disease and to decrease the numbers of deaths.

PCVs are cost effective in all the countries including low-income countries and it is a high priority for the World Health Organization, which is promoting PCV worldwide.

"Lessons learned from the introduction of the *Haemophilus influenzae* type B (Hib) vaccine have led them to understand that these vaccines need to be introduced very quickly in order to reach high coverage rate, and therefore a herd effect, in a large number of countries," she said.

Antibiotic resistance

One of the challenges to managing pneumococcal disease is antibiotic resistance to the pneumococcal bacteria.

According to Lisbon University Associate Prof Mario Ramirez, two studies from Europe have shown an established, very clear link between the level of consumption of antibiotics (both beta-lactams and macrolides) in various countries and the emergence of pneumococcal resistance.

Another seminal Spanish study also showed for the first time that not only was the consumption of one particular antibiotic influencing resistance to another, but that there could be cross-talk between different antibiotics. "They showed that the consumption of macrolides, in particular the long-acting macrolides, was influencing not only macrolide resistance, as was expected, but it was also the major driver of penicillin resistance," said Prof Ramirez.

There are about 94 different serotypes. He believes antibiotic consumption will drive the expansion of the other antibiotic-resistant serotypes that are not included in the vaccines, which, in due course, will drive the need for further PCVs.

Pneumococcal conjugate vaccines lead to a reduction in antibiotic use, which is also potentially helpful to contain Drug Resistant *Streptococcus pneumoniae.*[1]

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Ref 1. Dagan R, Klugman K.P. Impact of conjugate pneumococcal vaccines on antibiotic resistance. *Lancet Infect Dis.* 2008;8: 785-95

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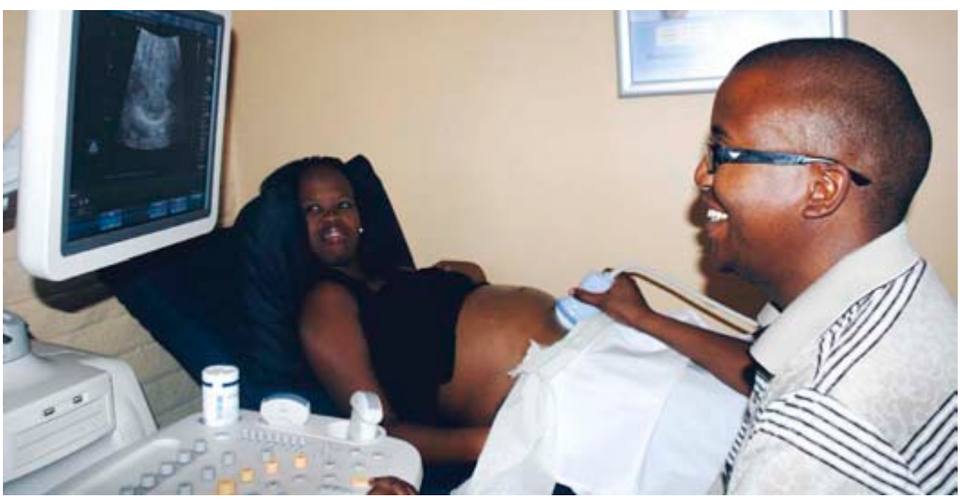
The diabetic pregnancy: A bitter-sweet state

The effects of urbanisation have not only had a profound impact on countries' economies but also on public health, with the emergence of altered dietary patterns (increased consumption of sugar and refined carbohydrates) and more sedentary lifestyles. As a result, low- and middle-income countries, like South Africa, are experiencing rapid increases in overweight and obesity prevalence, as well as, non-communicable diseases, such as diabetes mellitus type 2 (T2D).



Research participant at DPHRU having a foetal ultrasound

According to the South African Department of Health (2007), 30% of men and 56% of women in South Africa are either overweight or obese. Steyn *et al* (2012) assessed the prevalence of obesity among South African women and found that 31% of urban and 21% of rural women were classified as being obese. Recently, the International Diabetes Federation (2012) reported South Africa as having two million cases of diabetes, ranking it second out of the 10 most affected countries in Africa. This combination of over-nutrition, in particular changes in abdominal adiposity and T2D, pose significant public health challenges for South Africa. For example, by being obese while pregnant, a woman is at increased risk for miscarriages and stillbirths, hypertension and preeclampsia, and gestational diabetes mellitus (GDM).

As pregnancy progresses, so does the demand for insulin production on the mother's pancreas. In most cases, pregnant women are able to naturally meet the increased insulin demand but, in some women, these needs are not met, resulting in poor glycaemic control and, consequently, GDM. The World Health Organization defines GDM as diabetes diagnosed for the first time in a woman during pregnancy and encompasses blood glucose levels within the diabetic range and in the impaired glucose tolerance range. Women with GDM are at risk of delivering macrosomic babies (>4kg), as elevated maternal glucose levels fuel foetal growth. Furthermore, women who are diagnosed with GDM during pregnancy are at increased risk of T2D in their later years. Within 5-16 years of having GDM, 17%-63% of women will have developed T2D.

In addition to maternal risk, there is also a transgenerational effect of risk from mother to baby. The developing foetus is strongly influenced by the *in utero* environment that can alter developmental mechanisms that control physiology and metabolism. Unlike maternal insulin, maternal glucose readily crosses the placenta. Exposure to hyperglycaemia *in utero* affects foetal programming. Much research on this transgenerational effect emanated from the Pima Indians in Arizona; a population with a high prevalence of T2D. The prevalence of T2D in Pima Indian children aged 5-19 years has more than doubled over the past 30 years. Over the same time period, the percentage of children exposed to hyperglycaemia *in utero* has increased from 18% to 35%. Researchers have determined that the exposure of foetuses to GDM *in utero* is almost exclusively accountable for the increase in T2D and

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DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

FACULTY OF HEALTH SCIENCES

obesity in Pima Indian children. Children of mothers with T2D and GDM are, consequently, at risk of developing obesity, insulin resistance and T2D later in life, therefore continuing the vicious cycle.

The Medical Research Council/University of the Witwatersrand's Developmental Pathways for Health Research Unit (DPHRU), nested within the Department of Paediatrics, School of Clinical Medicine in the Faculty of Health Sciences is focused on diseases of lifestyle, including diabetes and obesity, with the aim of conducting research that spans the life course to enhance health and wellbeing from generation to generation.

DPHRU has recently launched a new study that involves following up pregnant women in Soweto from early gestation until the delivery of their babies. The effects of maternal body composition, pregnancy weight gain and glucose metabolism on longitudinal foetal growth and birth outcomes will be investigated. Very little data is reported on GDM in South Africa and we hypothesise that the prevalence of GDM among this cohort of women will be greater or equal to 8%. This pregnancy study will be extended into an infant cohort so as to better understand the impact of maternal pregnancy exposures on infant body composition, growth and development. Such research will provide much-needed data to contribute towards the national health agenda regarding maternal and child health.

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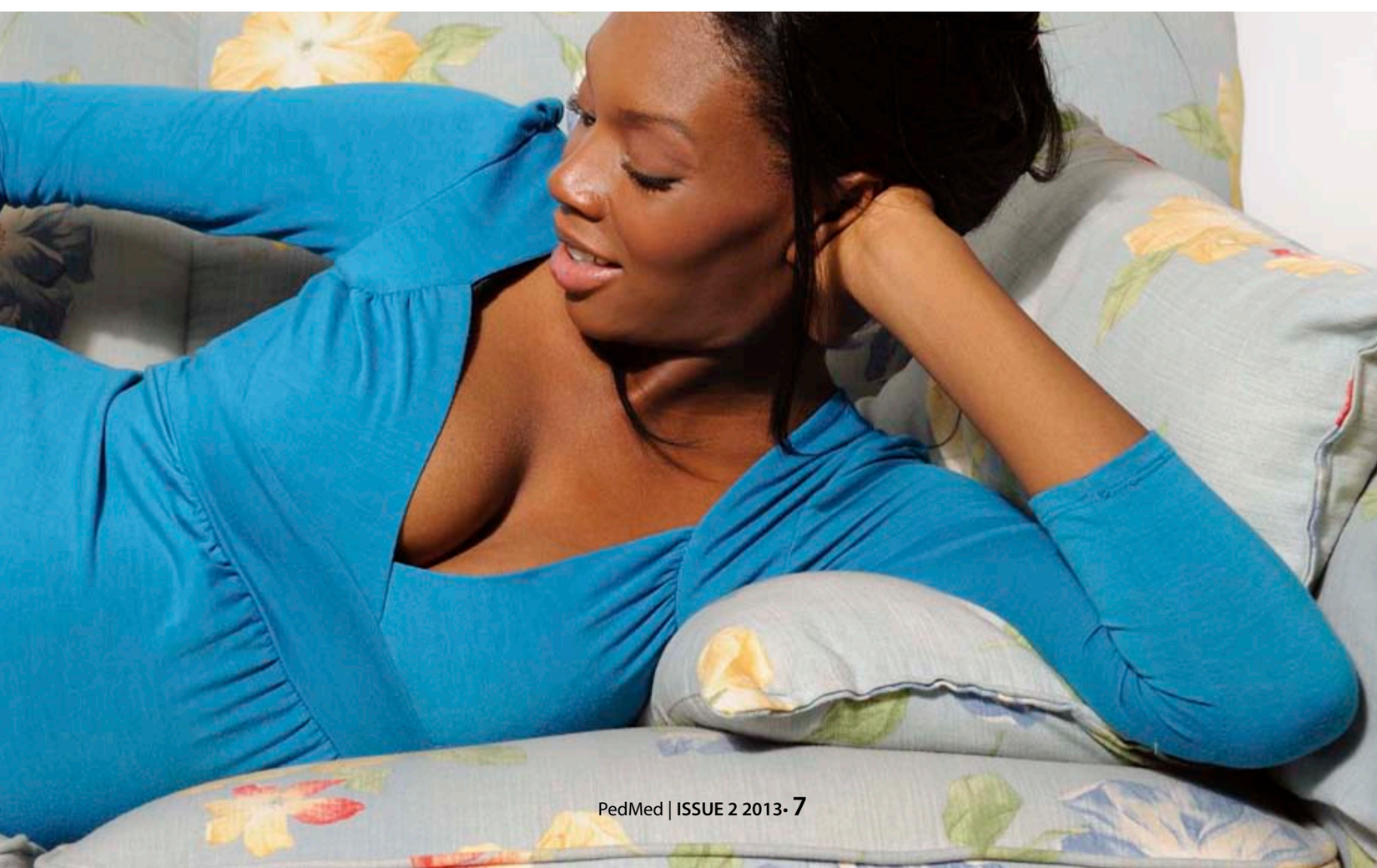

The diagnostic approach to coeliac disease

Sylvia van den Berg | Clinical Pathologist | Immunology/Serology | National Reference Laboratory, Ampath

Coeliac disease (CD) is an immune-mediated inflammatory disease triggered by an environmental agent (the gliadin component of gluten) in genetically predisposed individuals. It can be difficult to diagnose because it can present in a variety of different ways. Left untreated, further complications can develop, such as other autoimmune diseases, osteoporosis, thyroid disease and cancer.

The pathogenesis is a complex interplay between genetic factors (remarkably close association with the human leukocyte antigen (HLA)-DQ2 and/or HLA-DQ8 gene loci), serum autoantibodies (tissue transglutaminase IgA and endomysium IgA), the innate immune system and gliadin reactive T-cells. Tissue transglutaminase is released in response to mechanical irritation or inflammation and subsequently cross-links and deamidates glutamine proteins found in wheat. Deamidation produces a negative charge in gluten peptides and increases their affinity for HLA-DQ2 and/or DQ8, which, in turn, stimulates T helper cells. An immune reaction is triggered, causing villous atrophy and hypertrophic crypts.

Gluten is found in various cereals (such as wheat, barley and rye). If patients with CD consume food containing gluten, this will eventually lead to damage to the mucous membranes of the small intestine.

Clinical presentation

Coeliac disease used to be a disease of infancy, with children presenting with life-threatening malabsorbtion. Currently, the disease often presents between the ages of 10 and 40 with milder manifestations.

Gastrointestinal manifestations

- Steatorrhoea and flatulance
- Consequences of malabsorbtion including growth failure, weight loss, severe anaemia, neurologic manifestations due to vitamin B deficiencies and osteopenia due to vitamin D and calcium malabsorbtion.

Subclinical disease

Symptoms include fatigue, unexplained elevation of serum aminotransferase and borderline iron deficiency. It is important to detect subclinical disease - as these patients have an increased risk to develop malignancies, they may have nutritional deficiencies. Affected mothers may have low birth-weight infants and the disease is associated with other autoimmune disorders.

Who should be tested?

- Patients with unexplained symptoms and signs of chronic or intermittent diarrhoea, weight loss, iron-deficiency anaemia, nausea or vomiting, chronic abdominal pain, cramping or distension, chronic constipation, chronic fatigue, recurrent aphthous stomatitis, dermatitis herpetiformis-like rash, fracture with inadequate traumas, osteopenia, osteoporosis, abnormal liver biochemistry and failure to thrive, stunted growth, delayed puberty, amenorrhoea.
- Asymptomatic patients with increased risk for CD such as T1DM, Down syndrome, autoimmune thyroid disease, Turner syndrome, Williams syndrome, selective IgA deficiency, autoimmune liver disease.
- Asymptomatic patients with first-degree relatives with CD.

Diagnostic tests

1. CD-specific antibodies

These include autoantibodies against tissue transglutaminase (TTG), endomysial antibodies (EMA) and antibodies against deamidated forms of gliadin peptide (DGP).

Positive anti-TTG and/or EMA is associated with a high probability for CD, although low levels of anti-TTG have been noted in other conditions, including other autoimmune disorders, tumours, infections, myocardial damage, liver disorders and psoriasis. Endomysial antibodies have not been associated with the above and are, therefore, considered to be more reliable.

Several studies suggested that high anti-TTG antibodies levels, defined as exceeding 10 × upper limit of normal (ULN), correlate better with villous atrophy and should be used in the initial approach to diagnose CD.

Features of CD but negative serological tests:

- Selective IgA deficiency (total serum IgA <0.2g/ℓ).
- Immunosuppressive drugs.
- If gluten exposure was short or the individual was on a low-gluten diet (several weeks to years).
- The serologic test could be falsely negative, in which case, a small bowel biopsy is needed.
- Other causes of symptoms or villous atrophy should be considered.

2. HLA testing for HLA-DQ2 and HLA-DQ8

HLA DQ2/DQ8 typing is a useful tool to determine if the patient is genetically susceptible to CD. If HLA DQ2/DQ8 testing is negative, CD is excluded or highly unlikely. The HLA-DQ2 allele is found in 90%-95% of individuals with CD and the remaining 5%-10% possesses the HLA-DQ8 allele. However, CD is a multigenetic disorder, so the expression of HLA-DQ2 or HLA-DQ8 molecules is necessary but not sufficient to cause disease and approximately 30%-40% of the European population holds the HLA-DQ2 haplotype, but only 1% develops CD.

Recommendations for HLA-DQ2 and HLA-DQ8 typing:

- HLA typing may be offered as a first-line test to select individuals for further antibody testing, especially in asymptomatic people.
- If CD is strongly suspected in a child with high specific antibodies present and a small bowel biopsy is not going to be performed, it is then recommended to perform HLA DQ2/DQ8 typing in order to add strength to the diagnosis.
- Offer HLA-DQ2/HLA-DQ8 typing in patients with uncertain diagnosis, such as in patients with negative antibody levels and mild infiltrative changes in small bowel biopsy.
- If HLA-DQ2/HLA-DQ8 typing is negative, offer investigations for other causes of symptoms.

3. Duodenal biopsies

Histological features may be patchy, may only appear in the duodenal bulb and may be of variable severity. The pathology report usually grades the pathology according to the Marsh-Oberhuber classification.

Follow up

If a diagnosis of CD has been made, a gluten-free diet (GFD) should be instituted. Follow up regularly for symptom improvement and normalisation of CD-specific antibodies (within 12 months of starting a GFD).

Conclusion

A diagnosis of CD can be made when gluten-dependant symptoms, CD-specific antibodies, HLA-DQ2 and/or DQ8 and characteristic histological changes (villous atrophy and crypt hyperplasia) are present. High anti-TG2 levels (>10 × ULN) show high diagnostic accuracy and with the presence of these together with suspicious symptoms, positive EMA and HLA; biopsy may be omitted. The diagnosis is confirmed with a decline in antibody levels and symptom improvement on GFD.

References available on request.

"Only those who regard

healing

as the

ultimate

goal

of their efforts can,

therefore,

be designated as physicians."

- Rudolf Virchow

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Meeting the challenge: **Adolescents and adherence to ART – Part 6**

Dr Leon Levin, Right to Care

In previous editions, we have dealt with ensuring adherence in adolescents, disclosure and pill fatigue. All of this has the purpose of preventing treatment failure. Treatment failure is something that you should try and avoid at all costs in adolescents, since it's not easy to remedy.

If our adolescent patients fail their treatment, we need to have an approach. If teenagers are left to their own devices, it is almost inevitable that they will fail in their treatment adherence at some stage. We know that it is pretty normal that adolescents will rebel against the status quo and, unfortunately, this will include not taking their medication. Therefore, it is far preferable to prevent treatment failure by watching them swallow their medication, as we have discussed previously. If it does happen, however, it is important to recognise that the child is not being naughty. Don't blame the child and certainly don't shout at the child. Rather, say something like, "I was expecting this. Don't worry; it happens to many people your age." Your chances of success are much higher if you have an intact relationship with the child and by shouting at the child, you are likely to destroy your relationship. You are also more likely to get truthful answers if your questions are non-threatening and the child knows that you won't get angry.

After many years of experience, I have come to the conclusion that dealing with an adolescent who has failed a regimen is different from dealing with any other age group with treatment failure. What follows is my own personal approach. I must stress that this differs from standard guidelines.

Changing to a new regimen (second or third line)

Most teens who fail one regimen will fail the next regimen fairly quickly, as it's virtually impossible to resolve the adherence issues and second- or third-line regimens are invariably more complex than previous regimen. Therefore, I would only change to a new regimen as a last resort if the CD4 is extremely low (<150 cells/µl) and then I would attempt to first resolve the adherence issues (easier said than done) and preferably do directly observed therapy (DOTS).

Delaying the new regimen

A patient who remains on a failing regimen will continue to accumulate resistance mutations, which may even affect drugs that the patient has never been exposed to (cross-resistance). The motivation behind delaying the regimen is to keep the CD4 count relatively stable while reducing the amount of resistance that develops. There are three techniques employed for this purpose:

- Treatment interruption
- 3TC monotherapy
- Holding regimen.

Treatment interruption

This is out of favour for adult patients because the SMART study showed an increase in HIV- and non-HIV-related events. Some people do still stop ART if a teen is failing his/her regimen and the CD4 count is ok but there are other safer alternatives. Consult with an expert in this case.

3TC monotherapy and holding regimens

The motivation behind these is putting the child onto one or more drugs to which their virus is resistant in order to maintain the resistance mutations. Resistant virus is weaker than wild-type virus (has reduced viral fitness, i.e. it replicates at a reduced rate). As long as the patient remains on the drug to which the virus is resistant, the wild-type virus remains suppressed and the weaker resistant virus predominates in the body, thus causing less damage to the immune system. So, keeping the patient on this drug keeps the weakened mutated virus predominating in the body so that the immune system remains relatively intact. These strategies can only be used if the CD4 count is reasonable (>200 cells/µl in teens) and the patient has failed or has resistance to the drugs that will be used. 3TC monotherapy utilises 3TC only, whereas holding regimens utilise three or four NRTIs (usually AZT/3TC/ABC±TDF) for the same purpose. Generally, 3TC monotherapy is used after first-line failure, whereas a holding regimen is used after second-line failure where there is extensive NRTI resistance.

Since the aim is not to suppress the viral load (VL), VL measurements are unnecessary, just do CD4 counts 3-6 monthly. When the CD4 drops below 150-200 or the child develops symptoms, then you can put the child onto a definitive suppressive regimen. Because these holding strategies are simple, they are usually very well tolerated by non-adherent teenagers. Consult with an expert.

DOTS

Where the CD4 count is low and it is not possible to implement a holding strategy, then it is very helpful if DOTS can be instituted. It is preferable to place the child on a once-daily (or virtually once-daily) regimen. Several ARVs can be dosed once daily, even if they are not routinely used in this fashion. Examples include 3TC, FTC, ABC, EFV, LPV/r, ATV/RTV, TDV, ddI. Then try to find a suitable person to supervise the treatment, either from the family, the community or the healthcare facility. With a bit of ingenuity, it is often possible to find someone suitable.

Conclusion

Changing regimens for treatment failure is seldom successful in adolescents. Helpful alternatives include treatment interruptions or preferably delaying tactics like 3TC monotherapy or holding regimens where the CD4 count is not too low. Where the CD4 count is low and it is necessary to change to the next-line regimen, DOTS can be useful. It is always useful to consult with an expert in these difficult cases.

References available on request.

The fact that 'breast is best' remains undisputed. However, there are times when breastfeeding is not possible. It is here that infant formulas are crucial in early nutrition. We explore the impact of early nutrition on health and the role of formulas.

Focus on **infant formula**

The period immediately following the birth of an infant is recognised as being an important time for bacterial colonisation of the infant's gut. During this period the infant needs to be exposed to the best possible environment that will encourage colonisation with large amounts of bifidobacteria and some lactobacilli. This combination is known to promote the growth of indigenous lactic-acid producing bacteria,[9] which reduces faecal pH and prevents the growth of putrefactive bacteria, thereby enhancing immunity.[2] Breastfeeding, which provides this ideal environment and all the immunonutrients an infant needs,[5] should be encouraged and promoted.

Does the mode of delivery make any difference?

There is a clear difference between the gut flora of an infant born via caesarean section and one born vaginally. The latter is exposed to the mother's vaginal and faecal flora during delivery and therefore gut colonisation is almost immediate, whereas infants born via caesarean section will have delayed colonisation.[4,10]

Another important difference is that vaginally-delivered infants have a greater number of bifidobacteria in their gut flora.[4]

How can probiotics help in such cases?

By definition, 'probiotics' should exert a health benefit on the person consuming them. The probiotic strain, *Bifidobacterium lactis*, is a well-researched strain with proven safety with respect to the growth, metabolism, stool habits, and behaviour of the infants consuming it.[11-13]

The benefits of *Bifido-bacterium lactis* include:

- Increased bifidobacteria colonisation in the gut, which enhances the epithelial barrier function[14]
- Increased production of IgA in the gut, which enhances mucosal immunity and decreases the incidence and duration of infectious diarrhoea[5,8]

Administering Bifidobacterium lactis is an effective way of enhancing the neonate's immune function, including those born via caesarean section.

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Creating a healthy bifidobacteria–rich environment in neonates.

Science has confirmed that breastmilk is uniquely formulated to provide and promote colonisation of the infant's gut with immune-enhancing bifidobacteria immediately after birth.[1-3] At the same time, some women cannot, or choose not to breastfeed. In some cases this is preceded by birth via caesarean section, which also limits opportunities for the infant to be exposed to bifidobacteria.[4] It is for these reasons that Nestlé has added the probiotic *Bifidobacterium lactis* to **NAN 1**. This probiotic has been clinically proven to promote early gut colonisation with bifidobacteria and increase IgA secretion, thereby enhancing immune protection.[5,6] **New NAN 1 with *B. Lactis*** meets the nutritional needs of all infants from birth to 6 months,[7] and activates the immune system in those infants who are not breastfed, including those born via caesarean section.[8]

INFORMATION FOR HEALTH CARE PROFESSIONALS ONLY IMPORTANT NOTICE The World Health Organisation (WHO*) has recommended that pregnant women and new mothers be informed on the benefits and superiority of breastfeeding – in particular the fact that it provides the best nutrition and protection from illness for babies. Mothers should be given guidance on the preparation for, and maintenance of, lactation, with special emphasis on the importance of a well-balanced diet both during pregnancy and after delivery. Unnecessary introduction of partial bottle-feeding or other foods and drinks should be discouraged since it will have a negative effect on breastfeeding. Similarly, mothers should be warned of the difficulty of reversing a decision not to breastfeed. Before advising a mother to use an infant formula, she should be advised of the social and financial implications of her decision: for example, if a baby is exclusively bottle-fed, more than one can (450 g) per week will be needed, so the family circumstances and costs should be kept in mind. Mothers should be reminded that breastmilk is not only the best, but also the most economical food for babies. If a decision to use an infant formula is taken, it is important to give instructions on correct preparation methods, emphasising that un-boiled water, unsterilized bottles or incorrect dilution can all lead to illness. * See: International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Resolution WHA 34.22, May 1981.

INFORMATION FOR HEALTHCARE PROFESSIONALS ONLY

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Don't underestimate the impact of early nutrition on health

Prof Atul Singhal | Deputy Director | MRC Childhood Nutrition Research Centre | Professor of Paedatric Nutrition at the Institute of Child Health in London

Research over the last 20 years has highlighted the increasing importance of the role of infant nutrition and its long-term health implications, particularly with regard to cardiovascular disease and obesity. Prof Atul Singhal, Deputy Director, MRC Childhood Nutrition Research Centre and Professor of Paediatric Nutrition at the Institute of Child Health in London, provided insights into these concepts.

The importance of early nutritional programming *in utero* and in early life in preventing micronutrient deficiencies and cardiovascular disease (CVD) should not be underestimated, according to Prof Singhal, adding that there were a few misconceptions and issues that needed to be addressed.

Misconceptions

The first issue relates to the benefits of breastfeeding. "We are all aware that breastfeeding is the best form of nutrition for a newborn, but our research shows that it is also the best form of nutrition to ensure long-term health," said Prof Singhal. The impact of breastfeeding should not be trivialised as it has huge impact on bone health and cognitive function, as well as the risk of obesity, diabetes and CVD.

The second misconception relates to the pattern of growth and its influence on long-term health. Paediatricians and mothers are erroneously taught that the faster and larger the child grows, the healthier the child. However, in the last 10 years, researchers have discovered that this is not the case – babies have an optimal growth pattern that is defined by the normal growth rate of a breastfed infant, and this is the basis on which most countries map their growth charts. "It has been proven that faster growth rates have adverse consequences. For example, a higher-than-normal growth rate explains 30% of a person's risk of obesity, compared to the <5% role that genes may play," asserted Prof Singhal. This reiterates the importance of programming the integral role of infant feeding and determining the right growth rate and weight gain over time.

Breastfeeding guidelines

The World Health Organization (WHO) guidelines on breastfeeding are designed to maximise the benefits for short-term health, and are also the best practice for ascertaining long-term health in adulthood. The WHO advocates exclusive breastfeeding for the first six months, which coincides with the fact that the programming effect is most effective during this period of infancy. There is some evidence which shows that this effect persists into childhood, as older children who gain weight too quickly are more susceptible to developing type 2 diabetes later in life.

UK studies reveal that by the second week of life, the breastfeeding rate decreases to 45% in favour of formula feeding. Possible reasons cited include cultural aspects, aesthetic reasons, logistics and practicality for career women; as well as the fact that mothers are apprehensive that their child is not ingesting enough milk as they are unable to gauge how much is being taken in. "It is vital for the paediatrician to guide the parents and rectify this type of thinking. However, it is important not to judge mothers who choose not to breastfeed. Rather educate them on the scientific facts and benefits of breastfeeding in order to empower them to make an informed decision," advised Prof Singhal.

The role of formulas

Formulas are an invaluable substitute for mothers who cannot or choose not to breastfeed. Extensive research and scientific advancements have been responsible for the rapid evolution of formulas over the last few decades. "Manufacturers are dedicated to trying to match the growth patterns associated with formula to that of breastfeeding, through ongoing research. At present, formula contains approximately 75 nutrients, while breast milk contains at least 300, so manufacturers are continuously striving to improve.

"Historically, within the context of 'the bigger the baby, the better,' formulas included a higher protein content under the assumption that high-protein formulas were more beneficial," said Prof Singhal, adding that when research subverted this way of thinking, formula manufacturers were quick to act in reducing the protein content.

"The ultimate aim is to produce formula that is as similar to breast milk as possible, and breast milk has a much lower protein content. Another pertinent factor is that amino acid matching between breast milk and cow's milk is extremely difficult, as the latter has a different amino acid structure in its various proteins which are in varying concentrations when compared to breast milk.

"Because the proteins aren't a proper match, shortages of certain amino acids may arise because we are trying to manufacture something using a product from another species of animal essentially. However, well-researched formulas are the closest substitute we have for infant feeding," he asserted.

Micronutrient deficiencies

Breastfed infants do not generally exhibit micronutrient deficiencies in the absence of an underlying pathology and provided the mother's diet was balanced during pregnancy.

After breastfeeding cessation, which usually occurs after the first six months of life, micronutrient deficiencies become increasingly evident in both developing and developed countries. The younger the child, the greater the micronutrient deficiency due to the limited types of food babies are able to eat in terms of textures and consistencies.

According to Prof Singhal, in developing countries, weaning and complementary feeding may be problematic in terms of including a variety of foods or maintaining an adequate protein intake which may result in stunting, wasting and malnutrition. Even Western countries such as the UK have vitamin and micronutrient deficiencies, including vitamins A and D and minerals such as zinc, iron and iodine. This is attributed to the difficulty of including these vitamins into the diet of a 6-12-month-old baby. "Iron is contained in meat and infants don't eat meat, for example; or zinc is prevalent in seafood and meat and babies are unable to eat these at young ages. Therefore, in the UK, standard government policy recommends that children under five years should receive vitamin A, D and C supplementation," Prof Singhal states.

"The overall issue is that it is difficult to provide optimal nutrition through complementary feeding when breastfeeding is curtailed at six months. Most parents begin the complementary feeding process with foods such as rice and bananas, but they lack a variety of vitamins," continued Prof Singhal, adding that all regulatory authorities in the UK, Europe and US do not advocate cow's milk in the first year of life – not because of allergy, but due to the resulting iron loss and iron deficiency risk. Cow's milk has a low concentration of iron and causes microscopic blood loss from the gut.

Because very few mothers breastfeed for the first year of life, formulas play a vital role as a stand-alone meal and as a supplement to complementary feeding, to keep up with the growing child's changing nutritional requirements. After six months, vitamins A and D, and iron and zinc are required in greater quantities.

Important considerations

Some UK dietitians argue that it is best to modify one's diet and ensure that all the right nutritional elements are included. Many believe there is no need for micronutrient supplementation as this can be addressed by an adequate diet.

An adequate diet requires having extensive knowledge about nutrition and impeccable planning; and it depends on numerous factors affecting one's ability to change one's diet. Parents find this difficult to achieve in their children's diets, necessitating the use of supplements, in the form of fortified foods, or powders, drinks or pills.

Many manufacturers are altering their mindsets and responding to the changing trends and demands in society, such as decreasing the amount of salt in children's food products.

Formulas are heavily regulated as this is the sole diet of many babies, therefore, they must be carefully monitored. Children's food is less regulated and there are campaigns that advocate increased regulation in terms of food labelling and an increased responsibility of manufacturers.

Undernutrition may prevail once breastfeeding has stopped and non-desirable complementary feeding ensues, such as tea, which prevents iron absorption, or a primarily maize-based diet, which does not provide all the nutrients. Dietary history and growth faltering should be taken into account. Most paediatricians are alert to identifying undernutrition, finding the root cause and remedying the problem.

Overnutrition may be overlooked by paediatricians as larger babies may not be viewed as a reason for concern. It is only in the last five years that UK health professionals have been taught to look out for this. This may be correlated to the high rates of obesity prevalent in these countries, so they are paying particular attention to prevention.

There is minimal research on complementary feeding, perhaps because the multitude of ways it is practised across cultures and countries. Each culture has its own complementary feeding pattern, which should be executed in a well-balanced manner in order to capitalise on the programming window.

Because many women are still the primary nurturers involved in food preparation in most countries, the mother's diet is adopted by the entire family, making adult dietary education vital.

Dietary practices should be adapted to ensure that the types of foods given are of sufficient nutrient density to provide all the micronutrients.

It is advisable to avoid allergenic foods – peanuts, eggs, or other foods where there is a family history of allergy.

If implemented in an informed manner, vegetarian diets are fine if the parents are enlightened on how to ensure an optimal micronutrient intake, such as lentils and pulses provide iron, and combining these with vitamin C encourages iron absorption.

Babies should not be overfed

It is very easy to overfeed a formula-fed baby, both in the amount and the composition of the formula. Furthermore, some mothers encourage their baby to finish his or her bottle or they tend to feed their baby every time he or she cries, despite the fact that babies cry for various reasons – not just hunger.

Researchers have not conclusively proven any particular mechanism, although there is ongoing research. "My favourite hypothesis is that babies who eat more or grow too quickly have a higher set point for appetite, so they don't get full as quickly (satiety levels), therefore when faced with more calorie-dense food, they are more likely to become obese. However, this can be controlled. If you exercise and control your calorie intake, you will not be susceptible to obesity, but people have different abilities to do this. This set point theory associated with appetite is relatively new, only surfacing in the last two year," advised Prof Singhal.

Final thoughts

It is important for parents, doctors, midwives and clinic sisters to understand that faster growth in infancy is not advocated. Rather ensure optimal nutrition to enhance nutritional programming. Nutrition does not obviate the need for exercise as the child gets older.

Positive interventions need to begin as early as possible to counter the fact that in most countries with an epidemic of child obesity, about 80% of cases are established when the children are around the age of five years. Childhood obesity increases the risk of CVD independently in adulthood.

Society is obesogenic and it is the health professional's duty to help counter this through providing optimal advice to parents and their children. Doctors can make a difference in optimising the health of the future generation.

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Important Notice: Breast milk is the best food for babies. Breast milk contains all the nutrients required for babies' growth and development. Breast feeding should be initiated immediately after birth or within one hour of delivery. Breast milk alone fulfills babies' total nutritional requirements during the first six months of life. A good maternal diet is important for the quality and maintenance of breast milk. The decision to avoid or discontinue breast feeding may be difficult to reverse. The introduction of partial bottle feeding may have a negative effect on breast feeding. Before using infant formula, a mother should be aware of the financial and social implications of formula feeding. Inappropriate food or feeding method may lead to health hazards. Working mothers should be encouraged to continue breast feeding even after they resume their full-time jobs. Mothers who are unable to breast feed should seek professional medical advice.

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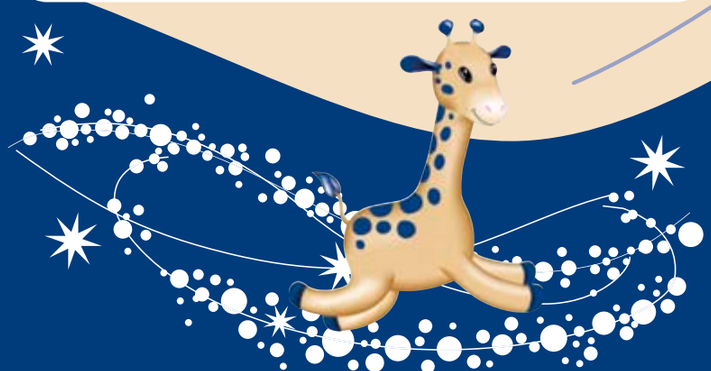

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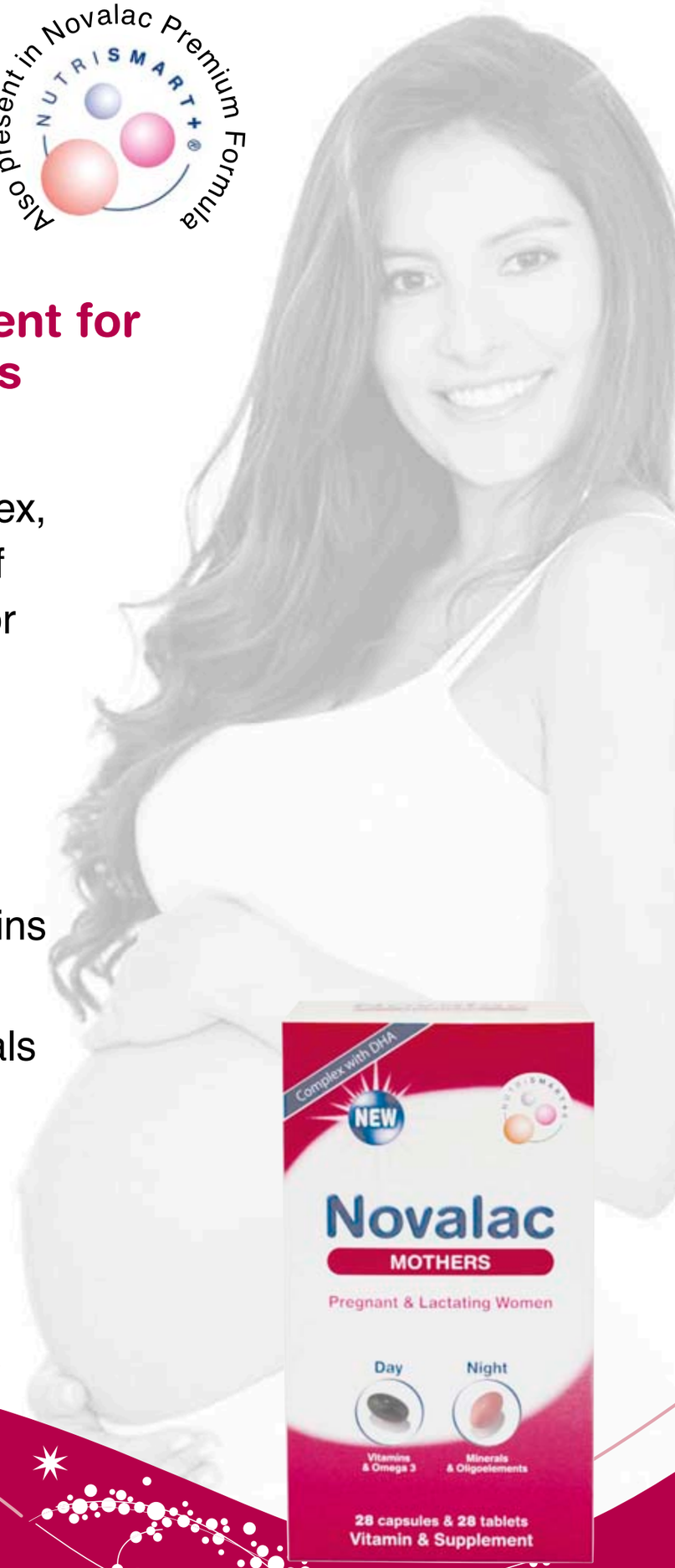

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** Arachidonic acid
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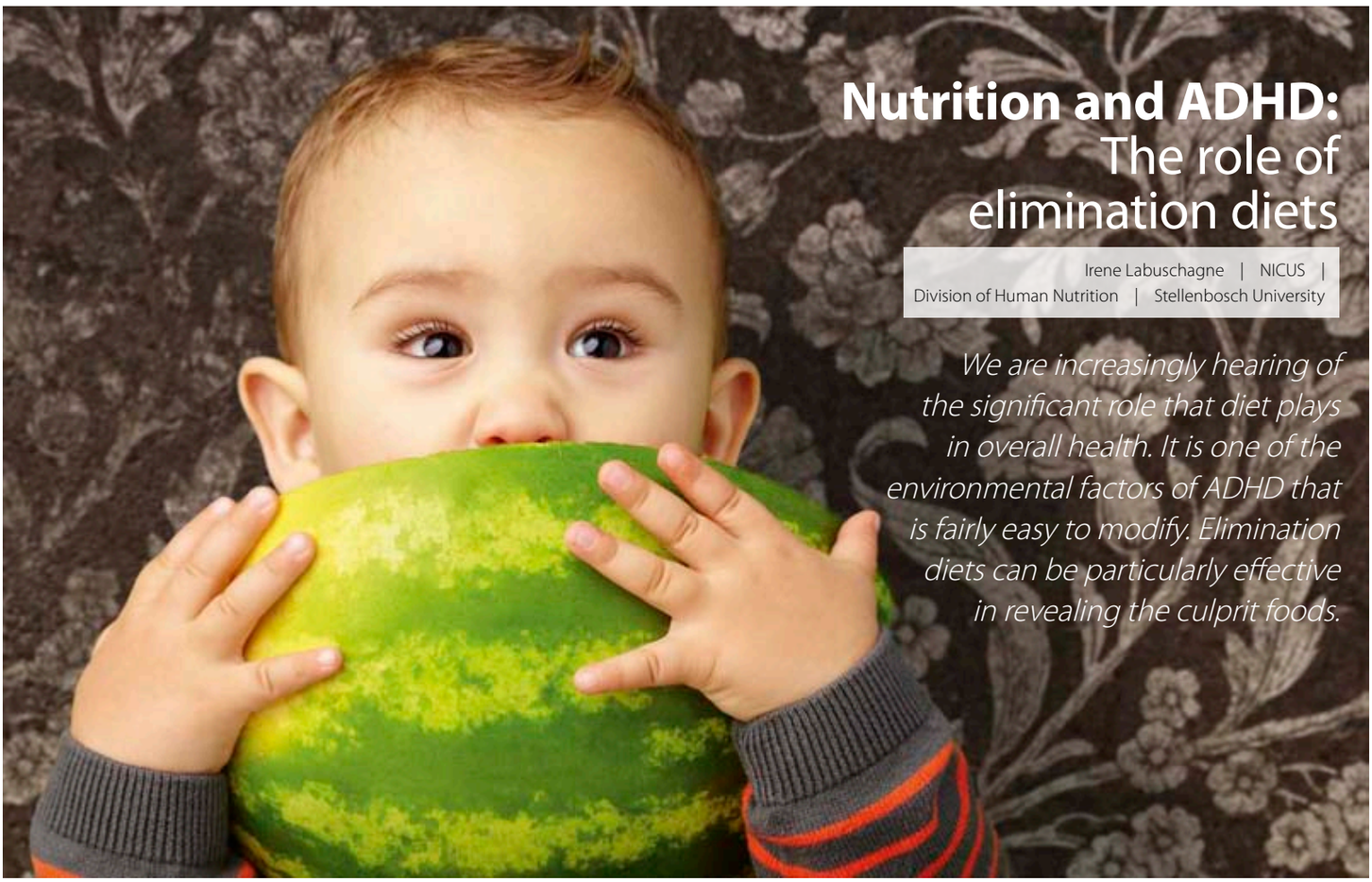

Nutrition and ADHD: The role of elimination diets

Irene Labuschagne | NICUS |
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We are increasingly hearing of the significant role that diet plays in overall health. It is one of the environmental factors of ADHD that is fairly easy to modify. Elimination diets can be particularly effective in revealing the culprit foods.

The successful treatment of attention deficit hyperactivity disorder (ADHD) depends on the adoption of a holistic approach, which addresses the known cause of the disorder. Parents who are caught up in the enthusiasm for dietary intervention may overlook the other forms of intervention to the detriment of the child. Therapeutic approaches, such as nutritional supplementation and restricted elimination diets (RED) might contribute to better management of children with ADHD. The aim of this brief review is to discuss the issues concerning the role of the diet in the treatment of the children with diagnosed ADHD.

Introduction

Diet is one environmental aetiology of ADHD that is amenable to modification. There are still many questions to be answered concerning the course, outcome and treatment of ADHD. The stimulant medications methylphenidate and amphetamine are the most frequently used treatments for ADHD, but these can be associated with variable efficacy and undesirable side effects such as: loss of appetite and weight, growth inhibition, abdominal pain, headaches, sleeping problems and increased blood pressure. The indications for diet therapy include the following: medication failure or adverse reaction, parent or patient preference, symptoms or signs of mineral deficiency, and the need to substitute an ADHD-free healthy diet for an ADHD-linked diet. Clinical and biochemical evidence suggests that deficiencies of polyunsaturated fatty acids (PUFA) could be related to ADHD. Furthermore, chronic deficiencies of certain minerals such as zinc, iron, magnesium and iodine may have a significant impact on the development and deepening of the symptoms of ADHD in children.

Several studies also demonstrated the positive impact of the elimination food products containing synthetic food additives, like artificial food dyes and preservatives and salycilates on the behaviour of children with ADHD.

Elimination diets

Feingold first introduced the idea that many children are sensitive to dietary salicylates and artificially added food colours, flavours and preservatives. Some examples of foods containing dietary salicylates include apples, peaches, oranges, tea and Worcester sauce. Food additives can be found in cold meats, sausages, hot dogs, jams, sweets, cake mixes and flavoured cold drink. Thus, the aim of the Feingold diet was to remove such substances from the diet. Food products containing additives are labelled by law so as to enable the consumer to avoid their consumption in case they experience any adverse effects. Recently, evidence from population-based studies has reported behavioural sensitivity to artificial food colours (active exposure period 20mg daily total content consisting of sunset yellow 5mg, tartrazine 7.5mg, carmoisine 2.5mg and ponceau 4R 5mg and sodium benzoate 45mg daily) and preservatives in children with or without ADHD.

In line with these findings, a 2012 meta-analysis concluded that an estimated 8% of children with ADHD may have symptoms related to synthetic food colours. A restriction diet benefits some children with ADHD and the investigation of diet and ADHD is warranted with approximately 33% of children responding to a dietary intervention. However, the source of most of the dietary response remains unclear.

According to Pellser *et al*, children with ADHD that respond favourably to a five-week restriction elimination diet may be diagnosed with food-induced ADHD (FI-ADHD). In these children, ADHD may be considered a hypersensitivity disorder triggered by food. Parents with children diagnosed with FI-ADHD are advised to enter a RED challenge period to identify the problem foods, eventually resulting in a diet as varied as possible. Children with ADHD not responding favourably to a RED may be diagnosed with Classic ADHD (C-ADHD) and may start or continue medical treatment as usual.

Table 1: Food items associated with ADHD

ADHD associated foods	Healthy foods for ADHD
Take-away fast food	Fish (steamed, grilled, canned)
Red meat	Vegetables
Processed meat	Fresh fruit
Crisps, potato chips	Whole grains
High fat dairy products	Low-fat dairy products
Soft drinks	

Healthy diet patterns

Park *et al*, recently investigated the associations between a wide range of measures of dietary behaviours and ADHD in 986 Korean school children (507 boys, 479 girls) with a mean age of 9.1 (SD 0.7) years. Children's dietary behaviours were assessed by the mini-dietary assessment for Koreans. They reported that after adjusting for potential confounders, a high intake of sweetened desserts, fried food and salt is associated with more learning, attention and behavioural problems. A balanced diet, regular meals, and a high intake of dairy products and vegetables, however, is associated with less learning, attention and behavioural problems.

Howard *et al* proposed various food items to avoid (food items that are associated with ADHD prevalence) and foods that can be given to ADHD children (***see Table 1***).

Recommendations

Children with ADHD need to:

- Follow a healthy balanced diet based on fresh, home-cooked, whole foods. Nutrition interventions such as added snacks, adjusted meal times and an increase in energy intake can prevent a low weight accretion.
- Any decisions in the management of an ADHD child in the form of a RED, i.e. free of colourants and preservatives, should only be taken by a health professional. The restricted diet can be tried for 2–5 weeks. If there is no benefit, the restricted foods can be added back weekly, one food component at a time, to identify the problem foods to be excluded from a less restrictive permanent diet. This diet may, in certain cases, not be nutritionally complete and may, therefore, not be used for longer than the prescribed time period. Micronutrient supplementation will be prescribed by the dietician or doctor in case of a risk for deficiencies.

Based on: The Food Intolerance Network and Tygerberg Hospital Diet Pamphlets

After completion of the elimination period, food should be re-introduced. A symptom diary should be used.

Medication may cause a lack of appetite in more than 60% of cases with most of the catecholamine-based medications used for ADHD. Nutritional supplements such as balanced meal replacement drinks can be used as snacks to promote weight gain and growth. More frequent meals throughout the day may be useful, especially in the evening when the child may be more relaxed and in the home environment.

A multivitamin and mineral supplement at recommended dietary allowance (RDA) doses may be indicated to prevent micronutrient deficiencies. Preservative- and additive-free products should ideally be chosen. Therapeutic doses of iron and or zinc may be indicated in confirmed deficiencies (low serum levels).

A 2012 Cochrane review compared the efficacy of PUFA to other forms of treatment or placebo in treating the symptoms of ADHD in children and adolescents. The authors concluded that the majority of data showed no benefit of PUFA supplementation, although there was limited data that did show an improvement with combined omega-3 and omega-6 supplementation.

Children should eat up to 360g (two average meals, smaller portions for young children) a week of a variety of fish and shellfish that are lower in mercury and high in omega 3 fatty acids.

References available on request.

Table 2: Example of a restricted elimination diet

FOOD GROUP	FOODS ALLOWED	FOODS TO AVOID
MILK AND DAIRY PRODUCTS	Hypoallergenic milk formula Peptamen Junior (Nestlé) Recommendation: 500ml-750ml/day Other alternatives: Alfaré (Nestlé), Alimentum (Abbott), Neocate (Nutricia), Nutramigen (Mead Johnson)	Cow's milk and products - Yoghurt - Cheese - Ice cream - Chocolate - Deserts - Baked products - Custard
GRAINS AND CEREALS	Rice and products originating from rice Oats Maize porridge, mealie fritters, cornflakes	Wheat and wheat-containing products
FRUIT AND VEGETABLES	Most fruit and vegetables are allowed except those mentioned in the adjacent table Cooked fruit and vegetables are even better alternatives during the period this diet is followed	Citrus fruits e.g. oranges, naartjies, grapefruit and lemons Apples, peaches, oranges, strawberries Tomato Celery Peas Potato Additional fruits and vegetables only need to be excluded if a reaction for a specific item is confirmed or expected.
MEAT AND MEAT PRODUCTS	Lamb Fish Chicken Turkey	Beef Pork Egg and egg-containing products Processed meat Shellfish Soy and soy-containing products
FATS AND OILS	Sunflower oil, canola oil and olive oil Dairy-free margarine	Nuts and peanut butter Butter Dairy-containing margarine Mayonnaise
DRINKS AND MISCELLANEOUS	Rooibos tea Water Honey (if pasteurised) Corn- and maple syrup Salt Cane- or beet sugar	Chocolate Colas and other soft drinks English tea and coffee Fruit-dairy blends and fruit nectar Raw honey Worcester sauce Jams, sweets, cake mixes, flavoured cold drink
PRESERVATIVES, COLOURS, SALICILASTES, FLAVOUR ENHANCERS	Whole foods not containing the substances. Read food labels carefully	Processed foods Artificial colours; natural colour annatto 160b Processed foods e.g. bread, drinks, dried fruit, ham MSG, inosinates, guanylates, ribonucleotides 600-635, HVP, yeast extract, natural glutamates

'The yeast connection'

Vanessa Ascencao | Nutritional Consultant for OTC Pharma SA and OTC Pharma International

With candida on the rise in young children, we have to focus on building healthy lifestyle habits from a young age. A correctly balanced diet not only goes a long way in treating common ailments, but affects immunity as well as mental and emotional wellbeing. This article looks at the link between asthma, food allergies, ADHD and candidiasis.

Vanessa Ascencao

Our ability to digest, absorb and assimilate nutrients is finely tuned to the health of our internal flora and gastrointestinal health. Candida is naturally occurring yeast that resides within the mucous membranes of the gastrointestinal tract. If 'fed', candida can manifest into serious health conditions later.

If children are exposed to antibiotics, corticosteriods, or prednisone, and a high sugar diet, the good bacteria that normally keep candida in check are killed off, causing some internal challenges.

When the candida yeast gets out of control, it morphs into a mycelial fungal form, becomes invasive and grows rhizoids. These rhizoids leave microscopic holes in the intestinal wall allowing toxins such as undigested food particles (specifically sugar), bacteria and yeast into our blood stream. This systemic yeast infection is called candidiasis.

Severe diaper rash, rectal rashes or infections, rashes in the genital area and colic are the most common symptoms in babies, but thrush, general skin rashes, infections of the ear, nose and throat, gas, diarrhoea or constipation are also possible symptoms.

BEHAVIOUR

Dr Bernard Rimland noted that a small, but significant, proportion of children diagnosed as autistic are in fact victims of a severe candida infection. He linked this to a series of ear infections, which are routinely treated by antibiotics. Soon thereafter, speech development stops and then regresses, often to the point of muteness. Within a few weeks or months, the child may become unresponsive and lose interest in his parents and surroundings. The concerned parents then consult with various specialists and finally come up with a diagnosis of 'late-onset autism'.

Medical experts and authors Dr William Crook, a paediatric allergist and Dr C Orian Truss (*The Missing Diagnosis*) have also linked yeast infection in children to chronic ear infections and the antibiotics prescribed causing yeast infections. I would rather advise parents to opt for homeopathic remedies such as Similasan Children's Earache Relief to be used at the onset of any ear discomfort.

Ear infections can be caused by the overproduction of mucus as a result of dairy or, to a lesser extent, grain foods. This mucus plugs the eustachian tube that runs from the inner ear to the oral cavity.

Food allergies are common these days; there is continuous progressive research in terms of understanding the nutritional and immunological connection. Often, the reactions to food are as a result of excess yeast growth.

Research is starting to notice that the symptoms of an attention deficit hyperactivity disorder (ADHD) child are the same as that of a child with candida. The real difference between the ADHD child and the child with the yeast overgrowth is that yeast-infected children are sick more often. They get headaches, stomach aches, more allergies, diarrhoea, constipation and so on. They tend to whine a lot and are often considered 'hypochondriacs', which is not the case.

Interestingly, the symptoms of a systemic yeast infection are much the same and include trouble remembering facts, inability to concentrate and jumping from one thing to the next.

Asthma and eczema are also common indicators of candida, brought on by diets high in sugar and carbohydrates, repeated use of antibiotics that may impair the immune system, steroid hormone therapy and copper imbalance.

Even in those children who have not had repeated doses of antibiotics, residues of these drugs may be ingested today in commercial meats and dairy products.

Dr Crook stated: "Children with learning disabilities, dyslexia, hyperactivity, ADD, food allergies, drug abuse and a variety of delinquent and emotional disorders, had often received repeated courses of antibiotics for recurrent ear infections, bronchitis and other conditions – including prolonged courses of tetracycline for acne."

A wide spectrum of allergic disorders, from classical hay fever to chronic, delayed-onset type food allergy and petrochemical sensitivity, have improved following antiyeast therapy.

CAUSES

There are many causes and lifestyle-based environmental conditions, besides those previously mentioned, that could upset the balance of good intestinal flora, including heavy metals and environmental toxins, drinking chlorinated water and cortisone and other anti-inflammatory drugs.

A combination of yeast overgrowth and hypoglycaemia may cause a physical addiction to sugar or sugary foods. This can affect childhood behaviour, and lead to more serious conditions such as alcoholism in later years.

ACTION PLAN

Allopathic drugs have side effects. For example, Nystatin, which is the mainstay of conventional candida treatments, is not advisable for neonatal thrush (candidiasis of the oral cavity). Prevention is better than cure, especially for infants and young children. Baby hygiene plays a critical role in reducing risk of candida.

Probiotics found in vegetables help to keep the balance of intestinal flora intact. Garlic is a natural antifungal and antibacterial herb, and should be used liberally in cooking. In the event of candida infection in children, homeopathic remedies are a better option, as they are safer and devoid of any side effects. It is vital that a child starts taking a good-quality probiotic to replace the good bacteria into the system.

Many studies have shown Spirulina to be a great supplement for children due to its excellent immune-boosting nutrients. Echinacea also provides anticandida benefits. It supports the immune system in the fight against candida as well as other infections.

Yeast-prone kids are greatly affected by dust mites. Use a plastic cover that surrounds the entire mattress, top and bottom, to reduce susceptibility. Limit the amount of stuffed animals in their room. Take care to wash baby underclothes with a good detergent and dry them completely, preferably in the sun.

References available on request.

The humbling experience – **paediatric intravascular access**

Dr Lara Goldstein | Specialist Emergency Physician | Helen Joseph Hospital

The first time it happens, you are surprised. Pride certainly does come before the fall and that is when you realise that there is nothing as humbling as trying to obtain paediatric intravascular access in an emergency (or non-emergency) situation. Although 'acupuncture is a well-founded form of therapy', no-one wants to poke a patient more than is necessary.

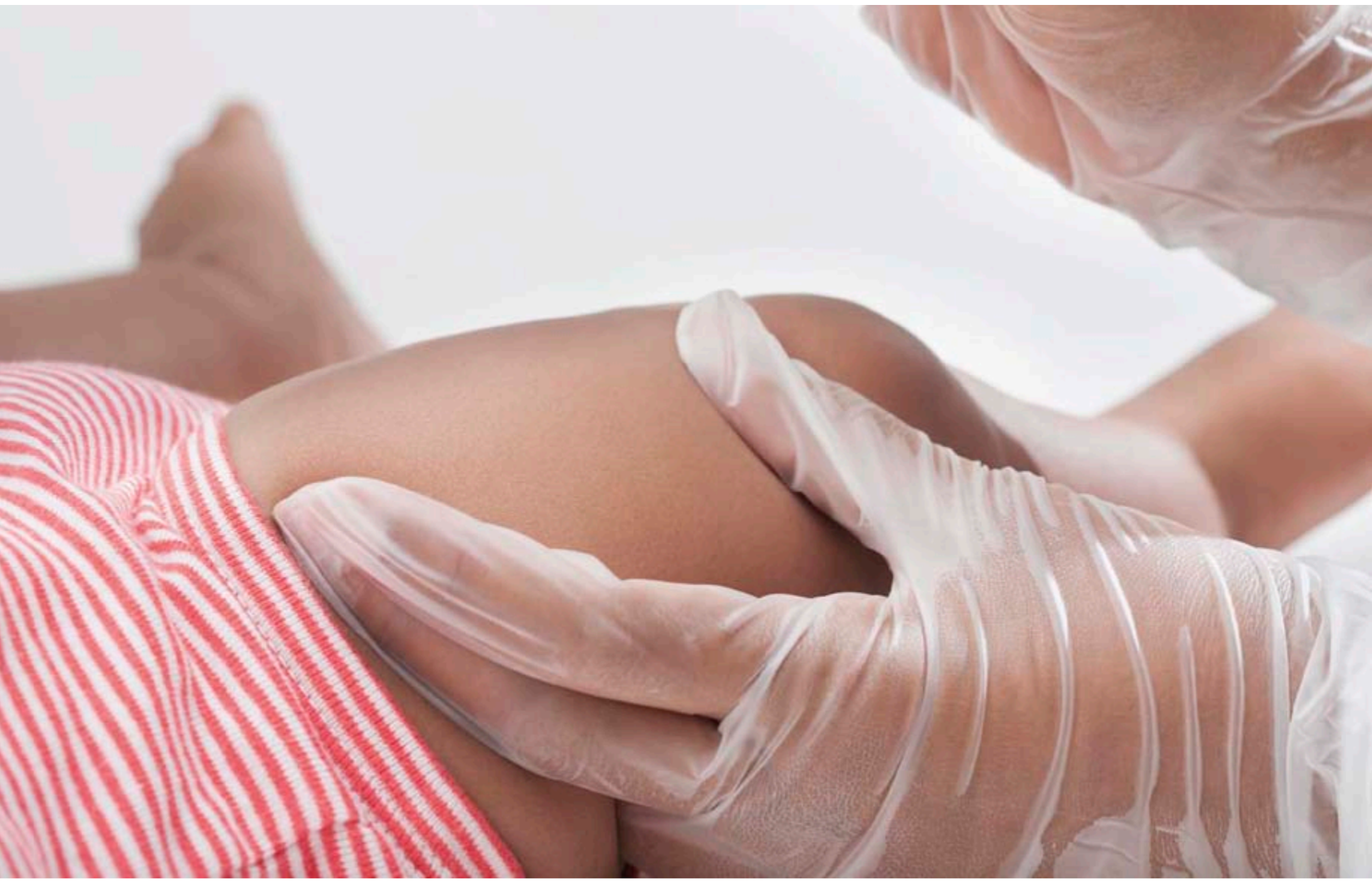
Intravascular (IV) access may be needed for patient management ranging from the life-saving intervention of fluid administration in a dehydrated, shocked child to obtaining a blood sample.

The resuscitation setting

As fate would have it, the more urgently a patient requires IV access, the more difficult it is to establish. In the critically ill or injured child, this can be exacerbated due to the technically challenging aspects of obtaining IV access.

- What options are available to us?
- Peripheral vein cannulation
- Intraosseous cannulation
- Central venous cannulation
- Venous cutdown.

The pre-ultrasound literature reports low success rates for central venous access in the paediatric population. Pneumothorax, haemothorax, arrhythmias and arterial puncture or haematoma are also potential complications from this procedure. While ultrasound guidance has assisted in increasing the success rate and decreasing the complication rate, the procedure still takes valuable time to perform, which may not be available to the patient who is in extremis. Venous



cutdown is also time consuming (averaging 24 minutes for placement in one study) with a higher infection rate and has, therefore, fallen out of favour.

Current guidelines suggest that after three attempts or two minutes spent in the search for a peripheral vein, that healthcare providers progress to intraosseous (IO) cannulation in the resuscitation setting.

The first scientific research on IO cannulation dates back to 1922. It became popular in the 1940s and 1950s, especially with wartime usage, but mainly in the pre-hospital environment. Its use, however, seemed to decline secondary to the introduction of plastic intravenous catheters. Renewed interest was sparked in the early 1980s after a paediatrician published an article on his experience during a cholera epidemic and IO access subsequently became standard of care in the paediatric advanced life support guidelines.

Microanatomy and physiology

Long bones consist of a shaft (diaphysis) and two ends/epiphyses. The epiphyses consist of a sponge-like cancellous bone surrounded by a cortex, whereas the diaphysis has a hollow medullary cavity. The epiphysis and diaphysis are separated by the epiphyseal growth plate. The medullary cavity and cancellous bone form part of the 'non-collapsible vein network' known as the intraosseous space within the bone. They are connected to the central circulation by the Haversian and Volkmann canals, which contain arteries and veins. These vessels do not collapse, even when the patient is shocked. Despite the fact that the IO space is filled with bone marrow, both fluids and medications rapidly reach the central circulation. The blood pressure in the IO space is approximately one third of systemic arterial pressure – roughly 35/25mmHg.

Anatomy

The preferred sites for paediatric IO cannulation include:

- The proximal tibia just medial and distal to the tibial tuberosity
- The distal tibia just proximal to the medial malleolus
- The distal femur proximal to the epicondyles anteriorly.

Devices

There are a variety of needle options for IO access. A needle with a central stylet is preferred in order to prevent cannula obstruction by bony spicules.

If a commercial IO device is not available, an 18G paediatric 35mm spinal needle is a convenient substitute although technically more difficult. Bone-marrow or Jamshidi needles can also be used.

Newer, commercial IO devices make it potentially easier to obtain IO access. The EZ-IO is a battery-powered, hand-held drill used with specially designed detachable needles. The drill tip rotates into the IO space to a pre-set depth. There are three needle lengths available for different size patients. The Bone Injection Gun (BIG) is a spring-loaded device designed for single deployment.

Technique

- The chosen site must be identified and disinfected.
- The limb must be stabilised, but the operator's hand should not be placed behind the intended site in case of through-and-through puncture.
- The needle must be inserted through the skin until the bone is felt with the tip of the needle.
- The IO needle must enter the bone perpendicularly.
- The needle should then be advanced through the bony cortex with firm pressure and slight twisting motion until a loss of resistance is felt as the medullary cavity is penetrated.
- The needle should stay in place without support.
- Remove the stylet (if present) and attach a syringe with saline.
- Attempt to aspirate blood – this may or may not be possible even if the needle is in the correct place.
- The IO line should flush easily and without signs of swelling around the administration site.
- Free-flow of IV fluid may be slow therefore the line should either be connected to a pressure infusion bag or alternately, administer fluid manually via a three-way stop-cock push-and-pull method.

"Newer commercial IO devices make it potentially easier to obtain IO access. The EZ-IO is a battery-powered, hand-held drill used with specially designed detachable needles. The drill tip rotates into the IO space to a pre-set depth. There are three needle lengths available for different size patients."

- The needle can be secured with commercially available devices or by surrounding the exposed needle with gauze padding and securing with a crepe bandage or holding the needle in place with an umbilical cord clamp and crepe bandage.
- All fluids and medication that can be administered IV can be given IO.
- Hypertonic solutions should be diluted prior to administration.

Contraindications

- Fracture of the bone proximal to the insertion site
- Previous, recent (24-48 hours) IO attempt in the same bone
- Signs of infection at the intended site
- Bone diseases e.g. osteogenesis imperfect.

Complications

While, in theory, there is the danger of the IO needle penetrating the epiphyseal growth plate and interfering with bony growth or causing bone deformity, this has not been demonstrated in experimental models or clinical practice. Fat embolism is also a consideration, but there are no documented occurrences in the paediatric population. Osteomyelitis is reported to occur in one in 200 cases of IO insertion. No IO-related cases of osteomyelitis have to date caused death or incurable infection. Compartment syndrome must be considered in patients where extravasation has occurred. Pain on fluid and medication infusion can occur, however most patients who need IO access are unconscious. Pain can be controlled with a small amount of IO administration of IV lignocaine. Bone fracture is a possibility.

The non-resuscitation setting

Healthcare providers who need to obtain IV access in children in the non-emergency situation should make use of methods which can help attenuate the pain associated with the procedure.

A local anaesthetic cream or patch e.g. eutectic mixture of local anesthetics (EMLA) can be applied to the prospective insertion site an hour prior to the procedure. This achieves analgesia to a depth of 3mm. Some emergency departments have instituted protocols to allow this to be done in triage in order to try to prevent subsequent treatment delays. If local anaesthetic cream is used, the area must be sealed with an impervious dressing after a 3-5mm layer of cream is applied with a tongue spatula. The cream should not be applied to a large surface area of skin due to the risk of systemic toxicity.

Engorgement of the veins can be achieved with a tourniquet, dependent positioning of the limb, gentle tapping on the vein, pumping via muscle contraction and local heat application.

A recent device designed to be used to decrease the pain of injection and double up as a tourniquet is called the Buzzy®. It is a handheld, battery-powered device that can be secured to the child's limb with a Velcro strap. It vibrates when switched on which distracts the nerves, thereby reducing pain perception. This is augmented with the use of ice wings which aid in numbing the prospective injection site.

Ultrasound has been shown to be a useful tool in order to obtain IV access. The literature shows that if a vein cannot be identified with the use of an ultrasound machine then IV cannulation will not be feasible at that site.

Intravascular access is a pivotal skill needed in the resuscitation of a critically ill or injured child. Newer modalities have been developed in order to make this procedure easier to perform in that stressful situation. It is also, however, a necessary skill for the non-emergency management of the paediatric patient. In either setting, techniques should always be employed to make the procedure as atraumatic and analgesic as possible.

Instead of hunting high and low ... rather just go IO.

Coughs and colds

Daynia Ballot | Associate Professor | Department of Paediatrics and Child Health | University of the Witwatersrand

As winter approaches, we are once again presented with the prospect of miserable children with coughs and runny noses. Colds are extremely common among children, ranging from 6-10 per year in preschool children to 12 per year in those in day care, decreasing to around four colds per year in adolescents.

Risk factors for colds include the winter season, low humidity indoors, psychological stress, contact with infected people, weakened immunity, chronic illness and allergic conditions of the sinuses and throat. Prevention of the common cold includes handwashing and avoiding respiratory irritants, particularly tobacco smoke. A healthy, balanced diet decreases the chance of catching a cold. There is some evidence in systematic literature reviews that prophylactic zinc and vitamin C reduce the chance of catching a cold. Prophylactic treatment with montelukast did not prevent the occurrence of URIs in preschool-aged children. There is no vaccination against rhinovirus.

Causes

The common cold is usually caused by rhinovirus and coronavirus, although less commonly by the influenza viruses A, B and C, parainfluenza virus, respiratory syncytial virus, adenovirus and coxsackievirus.

Rhinovirus can survive for several hours on fomites such as telephones and stethoscopes, and is spread through hand contact, as well as coughing and sneezing. The incubation is between one and four days and children present with nasal congestion, sore throat, runny nose and sneezing. Fever is less common than with other respiratory viruses. However, up to 15% of infected children are asymptomatic.

Diagnosis

Diagnosis is easily made on clinical grounds and special investigations are not required, unless complications such as otitis media, sinusitis or pneumonia are suspected. Cold symptoms can persist for up to 10 days in children and the virus can be shed for up to three weeks. Rhinovirus-associated wheezing is a risk for the subsequent development of asthma.

Treatment

Colds are self-limiting and usually resolve within a week or two, although a slight cough can continue for a few weeks, particularly at night. There is no evidence to suggest that antibiotic therapy is of benefit in treating the common cold. Antibiotics should be reserved for complications such as bacterial pneumonia, sinusitis or otitis media. Over-the-counter (OTC) medicines including decongestants, antitussives and antihistamines may provide some symptomatic relief, but their safety in infants and young children is currently being questioned. Symptoms can be relieved with nasal aspiration in young infants, saline nose drops and humidification.

There are several systematic reviews of randomised controlled trials (RCTs) looking at various treatments for the common cold. There is evidence to support the use of zinc in the treatment of common cold symptoms – the duration and severity of symptoms was reduced with the use of zinc, although there was an increase in the occurrence of bad taste and nausea. Similarly, prophylactic vitamin C is effective in reducing the duration and severity of common cold symptoms. The benefit of prophylactic vitamin C at 1-2g per day is greater in children than in adults. There was a trend towards improvement in cold symptoms in children treated with echinacea, although there was an increase

in skin rashes. RCTs of OTC antitussives show variable results – there is some benefit with mucolytics and antihistamine-decongestant combinations on the frequency and severity of coughs.

When to worry: Flu

Parents must be warned to seek medical care if symptoms worsen within three days, new symptoms appear or the child does not get better within 14 days. Fever lasting longer than 72 hours, difficulty in breathing, severe headache, skin rashes, severe cough, earache or dental pain all suggest possible complications and the child should be seen by a health worker.

The term 'flu' is commonly used to describe the common cold, but influenza is a different and more serious illness. Influenza is caused by the influenza viruses A and B. It is spread predominantly by small particle aerosol. There are usually one or two predominant strains causing each annual epidemic. There is typically a short incubation of around 48 hours with a sudden onset of fever, malaise, chills, headache, anorexia, coryza, pharyngitis and dry cough. The systemic symptoms are usually more significant than those of the upper respiratory tract. The duration of the febrile illness is usually between two and four days. Infants and young children may appear febrile and toxic with no localising signs, which necessitates a full work up. Treatment of uncomplicated influenza in healthy subjects is essentially symptomatic and supportive, including rest, fluids and antipyretics. The prognosis for full recovery in healthy subjects is excellent. However, young children, those with chronic illness or immune compromise, pregnant women and the elderly are prone to complications, including pneumona, otitis media, myositis and myocarditis. Bacterial superinfection is common.

Treatment

Antiviral drugs, the neuraminidase inhibitors zanamivir and oseltamivir are effective against the influenza virus. Zanamivir is administered as an inhalation and is scheduled for use in children above seven years of age, while oseltamivir is administered orally and can be given to children above the age of one year. Amantadine and rimantadine are effective against influenza A. All antiviral medication must be commenced within 48 hours of the onset of symptoms.

Seasonal influenza vaccine is available. Recommendations for influenza vaccination are constantly being amended. In general, children between six months and four years of age, those with immune compromise or chronic illness, those in long-term care facilities and those on long-term aspirin therapy are candidates for annual influenza immunisation. Household contacts and caregivers of infants under the age of six months are also recommended to receive the vaccine. Secondary prevention can be achieved by chemoprophylaxis with the abovementioned antiviral drugs.

Final thoughts

It is normal for children to acquire many common colds. Handwashing, avoidance of tobacco smoke, avoiding infected individuals, a balanced diet, reducing psychological stress, zinc and vitamin C can reduce the chance of catching a cold. Influenza is a different illness characterised by systemic symptoms and fever, which can be treated with antiviral medication and prevented by immunisation.

References available on request.

Use of opioids in children

Dr Julia Ambler | Paediatric Palliatice Care Practitioner | King George V Hospital, Durban

Morphine has a very bad reputation, putting the fear of death into most doctors and nurses. Somewhere along the line, the fear of causing respiratory depression in children became so enormous, that health professionals frequently choose not to manage a child's pain effectively, rather than use morphine.

There are many reasons that pain is poorly managed in children; lack of resources and training, language barriers, cultural differences and negative staff attitudes are challenges that need to be faced in order to provide relief to this significant problem in our paediatric population.

Many associate morphine with 'terminal care' or 'end of life care' and although morphine is an excellent drug for terminal care, it can be used at any stage of a disease to control pain. Morphine can safely be withdrawn when the patient no longer needs it, for example in burn pain. Others are concerned that the patient may become addicted to it. Addiction does not develop in the management of true pain when the dose is titrated to manage the pain.

Doctors worry about causing respiratory depression. If used correctly, respiratory depression is very rare, as pain itself antagonises opioid-induced respiratory depression.

Pain guidelines

In 2012, new guidelines for the management of persisting pain in children were published, stating: 'Correct use of analgesic medicines will relieve pain in most children with persisting pain due to medical illness and relies on the following key concepts:

- Using a two-step strategy
- Dosing at regular intervals
- Using the appropriate route of administration
- Adapting treatment to the individual child

The original World Health Organization (WHO) three-step ladder has been abandoned now for children, in favour of a two-step approach'.

For mild pain, paracetamol and/or non-steroidal anti-inflammatory drugs (ibuprofen) should be offered. For moderate-to-severe pain, the second step now advocated is a strong opioid, thus leaving out weak opioids such as codeine or tramadol. The reason for this is that there is insufficient evidence supporting the use and safety of tramadol in children and the metabolism of codeine is complex and variable.

Codeine is a prodrug that needs to be metabolised to morphine. It has been shown that many young children are not able to convert codeine and, hence, may not enjoy the analgesic effects. Some children are ultra-rapid metabolisers of codeine and therefore run the risk of toxicity. Overall, it is believed that codeine should not be used for managing persisting pain in children.

This is not to say that both tramadol and codeine are now contraindicated in children, but until more robust evidence is available, low-dose strong opioids are preferred. There are health facilities where strong opioids are not available and in these circumstances, a trial of tramadol or codeine may be reasonable.

How to use morphine

Morphine is available as a short-acting syrup, long-acting tablets (MST) and intravenous preparation. One would start by using 0.2-0.4mg/kg/dose of morphine sulphate syrup (short-acting morphine). This allows for rapid and careful titration. In infants, the 5mg/5ml concentration is convenient as small doses (eg: 0.2mg) can be given using an insulin syringe (1mg = 1ml).

Morphine in this form has a half life (if given orally) of 2-3 hours and should be prescribed four hourly. In patients with delayed clearance (newborns, hepatic and renal dysfunction) it can be prescribed 6-8 hourly.

As per the WHO pain guidelines, morphine should be given regularly (by the clock) and not as required. Regular dosing controls pain better and ultimately results in lower doses than if given as needed.

If the patient experiences pain before the next dose (breakthrough pain) an extra breakthrough dose (BTD) of morphine may be given. A BTD is 50%-100% of the regular dose.

Increasing the dose

There are two ways to increase morphine as required for pain:

1. Increase the regular dose by 30%-50% of the previous dose if pain is not controlled. So, a patient receiving 5mg of morphine four hourly could have his/her morphine increased to 6.5mg (+30%)-7.5mg (+50%) four hourly.

2. Add up all BTD given in 24 hours and divide this by six, and add to the following day's, four-hourly regular doses.

Remember also to increase the BTD as the regular dose is being increased.

Converting to MST

Once pain is controlled with four-hourly, short-acting morphine, it can be converted to sustained release long-acting morphine tablets (MST) given 12 hourly for greater convenience. To determine the dose of MST, add up all the doses given in 24 hours and divide by two. This is the number of mg of MST to prescribe.

Conversion

When converting from oral morphine to intravenous, divide the oral dose by three.

When converting from oral morphine to subcutaneous, divide the oral dose by two.

Side effects of morphine

Morphine can be quite sedating in the first 24-48 hours, as the child relaxes with pain relief. This is not to be feared, as it should resolve quickly. There are many other causes for reduced consciousness in a child on morphine – especially if the child is in a terminal stage of disease. One must consider the underlying diagnosis of the child before using naloxone. The analgesic effect is reversed with naloxone. Stopping the analgesic effect of morphine leaves a child in pain.

Nausea and vomiting, although common in adults, only occurs in roughly 25% of children. Most patients become tolerant and the nausea disappears within 7-10 days. This side effect is easily managed with an anti-emetic such as haloperidol or metoclopramide.

Constipation is a common side effect that can and should be prevented by the prophylactic use of laxatives (lactulose, senna).

Rare side effects include urinary retention and pruritis. Patients with urinary retention may need to be catheterised. Pruritis is not an allergy and technically morphine does not have to be stopped. It is best treated with ultra-low dose naloxone (0,25ug/kg/hr) or opioid switch, but a trial of antihistamines may help.

If the side effects cannot be managed or are intolerable, consider switching to an alternative opioid such as fentanyl or methadone. Expert advice should be sought in these circumstances.

Withdrawing morphine

Physiological dependence with morphine use is likely and, therefore, if it has been given for more than 10-14 days, the dose should be weaned and not stopped abruptly. This will prevent withdrawal symptoms.

References available on request.

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REFERENCES: 1. Smith C, Goldman RD. Alternating acetaminophen and ibuprofen for pain in children. Canadian Family Physician 2012;58:645-647. 2. Falagas ME, Vouloumanou EK, Plessa E, Peppas G, Rafailidis PI. Inaccuracies in dosing drugs with teaspoons and tablespoons. Int J Clin Pract. 2010;64(9):1185-1189.

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