Antibiotic usage in Pediatric Dentistry: A Comprehensive Review

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ABSTRACT

In recent years, there has been an increasing tendency to reduce the widespread use of antibiotics for prophylactic and therapeutic purposes. This is based, both on increasing scientific evidence and enhanced professional experience. The development of resistant strains of microorganisms, doubt on the efficacy of the proposed prophylactic regimens, possible toxic and adverse reactions to antibiotics and poor compliance by patients and dentists raised questions about risks and benefits. The administration of drugs to pediatric patients is further complicated by the necessity to adjust the dosages of medications to accommodate their lower weight and body size. Good knowledge about the indications of antibiotics is the need of the hour in prescribing antibiotics for dental conditions. Dental practitioners should know the protocol to be applied in their patients and should apply the most recent guidelines regarding antibiotic regimen.

Keywords: Pediatric patients, Antibiotics, Antibiotic resistance, Oral infections, Prophylaxis.


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INTRODUCTION

Proper use of antibiotics depends upon careful diagnosis of the patient’s oral disease, adequate knowledge of the patient’s systemic condition, and complete understanding of antibiotic therapy. While many articles appear in the literature each year concerning one antibiotic or another, there is a paucity of comprehensive information regarding the use of antibiotics in dentistry. Unwarranted use of antibiotics are reported in children; mostly for ear and dental infections. However, in children, increasing microbial resistance to antibiotics is a well-documented and is a serious global health concern.

Antibiotics are used in dentistry for two major reasons: to control oral infection, and to prevent a bacteremia precipitated by dental manipulations from causing severe systemic sequelae. Antibiotics commonly are prescribed by dentists, and the uses and abuses of these drugs should be familiar to all practicing clinicians. It has long been accepted that children have different susceptibilities to oral and systemic diseases than adults, and that the metabolism of drugs is often vastly different in the pediatric patient, there are few sources emphasizing the use of antibiotics by dentists treating children.

PHYSIOLOGICAL CHANGES IN PEDIATRIC PATIENTS

Unlike adults, children are constantly growing and developing. This fact should be taken into account whenever any drugs are given to children. There is a large differences in body surface area as well as hepatic and renal function depending on age.

Absorption

Various host factors like—surface area available, gastric and duodenal pH, gastric emptying time, size of bile salt pool, bacterial colonization of gastrointestinal tract, presence and extent of underlying diseases influences drug absorption.

Distribution

The factors influencing the volume of distribution are the size of various body parts, protein binding properties, hemodynamic factors including cardiac output, local blood flow, membrane permeability.

Metabolism

Most important organ is liver. Liver cells are involved in 2 types of enzymes reaction for the biotransformation of drugs.
Phase I
Anonsynthetic process and includes oxidation, reduction, hydrolysis and hydroxylation for functional preparation of drugs.

Phase II
A synthetic process and includes conjugation with glycine, glucuronide and sulfate for the enhancement of drug excretion.

The enzymes involved in reactions differ between children and adults and there exists high interindividual variability.

Excretion
The amount of drug filtered by glomeruli depends on glomerular function, renal blood flow and drug protein binding. Renal tubular function matures at about 30 weeks of age and glomerular rate between 3 and 5 months. Thus, the development and maturation of the glomerular filtration rate is important in determining the appropriate drug dosage.

These peculiarities result in differences in therapeutic efficacy and toxicity of various antibiotics used in children.

Although numerous pharmacokinetic differences in pediatric patients are known, little information has been published concerning pharmacodynamic changes.

Other Factors to be Considered in the Pediatric Age Group

Growth and Development
Because childhood is a period of continuous growth and development, administration of antibiotics in children may cause peculiar neurologic an physical abnormalities. It may not be immediately evident but if becomes obvious after long term administration. Especially since the central nervous system is continuously developing, antibiotics may cause severe neurodevelopmental dysfunction.

The best known adverse drug influence on physical development would be that of tetracycline, it forms tetracycline—calcium orthophosphate complex and cause enamel dysplasia, hypoplasia and discoloration of teeth and dysfunction in bone growth.

Quinolones are reported to cause reversible arthralgia.

Drug Administration
The oral route is preferred for pediatric patients. An important factor to be considered for oral administration is in relation to meals. For antibiotics such as penicillin G, ampicillin, cloxacillin, lincomycin, drug absorption is significantly decreased when given with food. Tetracycline should not be given with milk, dairy products or food containing calcium and magnesium, which interfere with absorption of drug. A liquid form is available for most preparations and should be used, if the young patient is unable to swallow the tablet or capsule.

Intravenously administered drug seem to reach the site of action quickly. It depends of intravenous fluid infusion, the dead space of infusion set and volume of fluid in which drug is diluted. Since, most intravenous infusion sets are manufactured for adult use, they have a large dead space and since the rate of infusion in children is slow.

Intramuscular injection may be used when there is no accessible venous route, but the site of injection should be chosen cautiously. There are a number of factors influence the rate and amount of drug absorption when the intramuscular route is used. Especially in severely sick, the blood circulation at the site of injection is often poor and it may diminish the effect of intramuscular administered drug.

Prescription
Taste, smell and color of drugs should not be overlooked when drugs are prescribed to children.

SELECTION OF ANTIBIOTICS
The goal of antibiotic treatment is to use the smallest amount of the agent most effective against the microorganism causing the infection. It is desirable to choose an agent with a narrow, specific spectrum of activity with as few adverse effects as possible. The surest way to determine which antibiotic will be most effective is to isolate the offending organism with culture and sensitivity tests of the infected area.

However it is not always possible to secure an uncontaminated sample from the diseased part, particularly when it is located in the mouth (with its own endemic diverse flora). Moreover, there will be certain instances when it is prudent to begin an immediate course of antimicrobial therapy. In such circumstances, a knowledge of the most likely organism is invaluable.

The duration of drug therapy should extend at least 5 days past the point of substantial improvement or resolution of symptoms. The importance of completing a full course of antibiotic therapy must be emphasized to the patient. Should the antibiotic be discontinued prematurely, the surviving bacteria can restart an infection that may be resistant to the original antibiotic.

The advantages of antibiotic use are obvious, and the disadvantages should be accorded equal attention. With each antibiotic usage there is a possibility of:

1. Sensitizing the patient to the drug
2. Hypersensitivity reaction
3. Toxic reaction
ADJUSTMENT OF DOSAGES IN
PEDIATRIC PATIENTS

In general, pediatric patients cannot be given adult dosages of drug. The primary reason for this is the difference in body size (Table 2). Several rules exist to compute the dosage of a drug for a child; the most common is the Clark’s rule and the Young’s formula. Current dosage recommendation are usually based on the basal metabolism of the child. Some formulas for calculating drug dosage are:27

- Based on body weight (Clark’s formula) – child dose = weight (kg)/70 × adult dose
- Based on body surface area – child dose = body surface area (m²)/1.7 × adult dose
- Based on age (Young’s formula) – child dose = age of child/age + 12 × adult dose

Table 2: Dosage guidelines for commonly used antibiotics in children

<table>
<thead>
<tr>
<th>Antibiotic generic name</th>
<th>Daily oral dose</th>
<th>Drug interval</th>
<th>Dosage form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>50 mg/kg/day</td>
<td>8 or 12 hours</td>
<td>125 and 250 mg/5 ml susp.</td>
</tr>
<tr>
<td></td>
<td>90 mg/kg/day (high dose)</td>
<td>12 hours</td>
<td>250 and 500 mg cap.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>125 and 250 mg chew. tab.</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate potassium</td>
<td>45-50 mg/kg/day (amoxicillin)</td>
<td>8 hours</td>
<td>125 and 250 mg (amoxicillin)/5 ml susp.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>250 and 500 mg tab.</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>20-30 mg/kg</td>
<td>12 hours</td>
<td>100, 200, 250, 500, 750 mg tab. and 20 mg/10 ml cap.</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>25-50 mg/kg</td>
<td>6 hours</td>
<td>250 mg tab. and 125/5 ml, 250 mg/5 ml susp.</td>
</tr>
<tr>
<td>Cefixime</td>
<td>8 mg/kg</td>
<td>12 hours</td>
<td>125 mg/5 ml susp.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>250 and 500 mg tab.</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>30-50 mg/kg</td>
<td>6 hours</td>
<td>125, 250 mg tab. and 125/5 ml susp.</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>30-50 mg/kg</td>
<td>6 hours</td>
<td>125 mg/5 ml susp.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>250 and 500 mg tab.</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>50-100 mg/kg</td>
<td>6 hours</td>
<td>125, 250 mg tab. and 125 mg/5 ml susp.</td>
</tr>
<tr>
<td>Penicillin V</td>
<td>25-50 mg/kg</td>
<td>Every 6 hours</td>
<td>125, 180, 250 and 300 mg/5 ml susp.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>every 12 hours</td>
<td>300 mg tab.</td>
</tr>
</tbody>
</table>

This clinical guide is provided for information purposes and is not a substitute for the practitioner’s judgment.

THE DECISION TO USE
ANTIBIOTICS—STATUS OF INFECTION

The use of antibiotics mandates a tentative analysis of a wide range of clinical parameters. An infection must either be persistent or systemic to justify the need for antibiotics. Pain alone or a localized swelling does not require antibiotic treatment. Most dental pain can be managed using nonnarcotic analgesics, such as nonsteroidal anti-inflammatory drugs.24

The evaluation of the following signs and symptoms may assist in determining the status of an infection.

1. **Patient’s health:** Patients in poor health, including immunocompromise, (i.e. a white blood cell count less than 1,000 mm⁢³, are more likely to need antibiotics.
2. **Severity of symptoms:** Swelling, cellulitus, or fever that escalates with time may indicate that an infection is spreading.
3. **Extent of soft tissue inflammation:** If an intraoral swelling is localized, the infection may be managed by surgical drainage. However, if the swelling spreads into extra oral musculofascial spaces or impedes breathing or swallowing, the patient should immediately be referred for emergency care. A large, diffuse swelling may require antibiotics as well as surgical drainage.25
4. **Benefits vs risks:** An antibiotic allergic reaction may present as a minor rash or a significant life-threatening anaphylaxis. Patients may also develop adverse side effects, such as gastrointestinal problems and secondary infections. Pregnant women should be evaluated with extra care due to a developing fetus.26

### Table 1: Decision making sequence for antibiotic selection in pediatric dental patients

1. Is an antibiotic really needed?
2. Correlate with the patient’s drug history
3. Identify the causative organism by culture and sensitivity
4. Use a specific narrow spectrum antibiotic as far as possible
5. Decide the route for administration of antibiotic
6. The appropriate duration and dosage of drug depending on the severity of the infection

4. The development of stains of microbes resistant to the drug
5. Super infection by other organisms.15-17,20,21

The dentist must always consider whether using or not using an antibiotic constitutes the greater danger.1 The antibiotic prescribed most frequently is penicillin or an analog, especially amoxicillin.22 However, other newer-generation antibiotics are becoming more widely used because of the belief that these are more effective, and they are more expensive. This belief may be based more on marketing than on the fact, as their effectiveness has not been demonstrated in clinical trials.23
CONDITIONS THAT MAY NECESSITATE THE PRESCRIPTION OF ANTIBIOTICS IN PEDIATRIC PATIENTS

Odontogenic Infections

Most orofacial infections are of odontogenic origin. Dental pulp infection, as a result of caries, is the leading cause of odontogenic infection. The major pathogens identified in dental caries are members of the viridens (alpha-hemolytic) streptococci family including Streptococcus mutans, Streptococcus sobrinis and Streptococcus milleri. Once bacteria invade the dental pulp an inflammatory reaction results in necrosis and a lower tissue oxidation-reduction potential. At this stage, the bacterial flora changes from predominately aerobic to more anaerobic flora. Anaerobic Gram-positive cocci (Peptostreptococcus) and anaerobic Gram-negative rods (Bacteroides, Prevotella, Porphyromonas and Fusobacterium) predominate. The infection progresses forming an abscess at the apex of the root, resulting in bone destruction. Depending on host resistance and bacteria virulence the infection may spread into the marrow, perforate the cortical plate and spread to the surrounding tissues.

Additionally, the anaerobic bacteria inhabiting the periodontal tissues may provide an additional source of odontogenic infection. The most common anaerobes are Actinobacillus actinomycetemcomitans, Prevotella intermedii, Porphyromonas gingivalis, Fusobacterium nucleatum and Eikenella corrodens.

Most odontogenic infections (70%) contain mixed aerobic and anaerobic bacteria. Pure aerobic infections have less than a 5% incidence. Pure anaerobic infections have a 25% incidence. The consensus by researchers is that in early odontogenic infections, bacteria are aerobic with Gram-positive, alpha-hemolytic streptococci (S. viridens) predominating. As the infection matures and increases in severity the microbial flora becomes a mix of aerobes and anaerobes. The anaerobes found are determined by the site of origin; pulpal or periodontal. As the host defenses begin to control the infection process the flora becomes predominately anaerobic.

Orofacial Lacerations

There is a high incidence of perioral and intraoral lacerations throughout childhood. In most instances, intraoral wounds, although contaminated by the oral flora, will heal well without the developing infection, provided the wound is clean, no foreign bodies are left within the cut surfaces, and sutures are placed to approximate the tissues where needed. However, wounds involving the skin surface, particularly those with skin-to-oral mucosa communication, are most likely to develop infection, and Shira states that patients with these injuries should receive prophylactic antibiotics. When antibiotics are prescribed after traumatic injury, it must be kept in mind that organisms not endogenous to the oral cavity may have been seeded into the wound, particularly if the wound is ‘dirty’. At the first sign of infection, a culture and sensitivity test should be attempted.

Dental Trauma

The local application of antibiotic to the root surface of an avulsed tooth (doxycycline 1 mg/20 ml) reduces root reabsorption and increases pulp vascularization. The administration of systemic antibiotics is a coadjuvant measure (penicillin and its derivatives at high doses, or normal-dose doxycycline).

Prophylactic Antibiotics for Medically Compromised Patients

Antibiotic prophylaxis may be indicated if the infection to be prevented is common but not fatal or if it is rare but carries an unacceptably high mortality rate. The principles of antibiotic prophylaxis include the following:

1. Satisfactory risk and cost-benefit ratios should exist in which benefit to the patient significantly outweighs medical and financial risks.
2. The antibiotic must be in high concentrations at the target site (blood or tissue) before the onset of the bacteremia or surgery.
3. An antibiotic loading dose (2 to 4 times the maintenance dose) must be used.
4. The antibiotic chosen should be active against the single most likely microorganism to cause the infection (antibiotic prophylaxis is not effective against polymicrobial infections).
5. The antibiotic is continued only as long as microbial contamination of or from an operative site continues.

There still is much controversy over which procedures do or do not require antibiotic prophylaxis. The dental procedures which required antibiotic prophylaxis are dental extractions, periodontal procedures including surgery, scaling, root planning and probing, dental implant placement, re-implantation of teeth, endodontic instrumentation or surgery beyond the tooth apex, subgingival placement of antibiotic fibers or strips, initial placement of orthodontic bands but not brackets, intraligamentary local anesthetic injections and prophylactic cleaning of teeth or implants with anticipated bleeding.

Protocol for Antibiotic Prophylaxis

In recent years several changes were made to the most widely used protocols. These can be summarized as follows:
Intravenous administration has been replaced by oral administration, the oral dose has been reduced from 3 to 2 gm of amoxicillin, the follow-up dose has been discontinued and erythromycin has been substituted by other antibiotics as alternatives for penicillin. It was shown that bacterial isolates recovered in cases of bacteremia following oral surgical procedures in children are susceptible to most of the antibiotics recommended for antibiotic prophylaxis. Whenever possible, sugar free preparations should be used when liquid medicines are prescribed in order to prevent the development of dental decay.

Acute Primary Herpes Infection

This acute infectious disease occurs most often in young children who may become extremely debilitated with high fever and malaise. It is important that fluid intake be continued to avoid dehydration. The etiologic agent in this condition is a virus, and antibiotics have no role in treatment of the primary disease. Penicillin is definitely contraindicated, as it will fix the virus and prolong the disease. McDonald and Avery report that topical application of tetracyclines to ulcerated areas will aid in the control of secondary (bacterial) infection.

Acute Necrotizing Ulcerative Gingivitis (ANUG)

Spirochetal organisms have been isolated from the involved gingivae of patients with ANUG. This disease may occur in young children but the highest incidence is in late adolescence and early adulthood. The patient with severe ANUG will present systemic complications, such as fever, malaise and associated lymphadenopathy. Bear and Benjamin state that only with massive necrosis or systemic effects is systemic antibiotic therapy indicated in addition to the more conservative measures of removing local irritants, improving oral hygiene, and using oxidizing mouthwashes recommended by other authors. The use of metronidazole (a nitroimidazole antimicrobial which is cidal against anaerobic microorganisms) has been reported for treatment of ANUG. However, penicillin is the drug of choice, utilizing erythromycin if the patient is allergic to penicillin.

Eruption and Exfoliation of Teeth

Although it is a common belief that children present systemic symptomatology during the ‘teething’ period, studies have not correlated fever or elevated white cell counts with normal tooth eruption. If fever and other systemic disturbances are present at the time of eruption, the source of the infection should be investigated. There is no evidence of a need for antibiotic coverage of tooth eruption or normal exfoliation even in a child susceptible to SBE.

Pediatric Periodontal Disease

In periodontal disorders associated with neutropenia, Papillon-Lefèvre syndrome and leukocyte adhesion deficiencies, the immune system of children is unable to control the growth of periodontal pathogens. Antibiotic treatment is therefore needed in such cases. Cultures and susceptibility testing are useful for selecting the most appropriate drug in each case. Prolonged antibiotic therapy is indicated for the management of chronic periodontal disease.

Patients with Compromised Immune System

In the absence of an adequate host immune system, patients are at increased risk for developing bacteremia progressing to septicemia. Immunosuppression can be the direct result of a disease process and/or the result of the treatment for the specific condition. However, consensus guidelines are lacking for this type of patients. The use of antibiotic prophylaxis or coverage must be considered on an individual case basis in the following conditions: neutropenia, HIV infection, organ transplantation, long-term immunosuppression (e.g. corticosteroid use). Consultation with the treating physician is mandatory in order to evaluate the immune status of the patient, the risks of the planned dental procedure, the choice of antibiotic and the duration of antibiotic coverage.

- Antibiotic coverage is required in patients with reduced neutrophil counts because these individuals are at risk of bacterial infection. When neutrophils are less than one thousand cells per ml, antibiotic coverage is mandatory.
- Children undergoing chemotherapeutic treatment are in need of antibiotic coverage when dental extractions or deep periodontal scaling are necessary.
- Children who have deficiency in humoral or T-cell mediated immunity, such as children who receive immunosuppressive medication that they take for prevention of graft rejection or for an autoimmune disease need antibiotic coverage.
- Children infected with the human immunodeficiency virus (HIV) and AIDS need antibiotics if the neutrophil counts are low.
- Children with diabetes (especially the insulin-dependent type) often exhibit some degree of leukocyte dysfunction. Therefore antibiotic coverage is usually recommended for invasive dental procedures when their condition is poorly controlled or uncontrolled.
- There is still much debate regarding the need for antibiotic coverage in chronic intravenous drug abusers and after splenectomy.
DURATION OF ANTIBIOTIC THERAPY

The ideal duration of antibiotic treatment is the shortest cycle capable of preventing both clinical and microbiological relapse. Most acute infections are resolved within 3 to 7 days. When oral antibiotics are used, a high dose should be considered to secure faster therapeutic levels.\textsuperscript{22}

MISUSE OF ANTIBIOTICS

Resistance is an inevitable consequence of antibiotic use. It is considered that the benefits of antibiotic use to society are so great that some level of evolved resistance is both tolerable and accepted as a social cost. The concern lies with the rate at which resistant strains of bacteria are emerging, and with the human behaviors that foster faster resistance. Intuition, mathematical models, and empirical observations predict and provide evidence that the rate at which resistance will evolve in a community or hospital is directly related to the magnitude of antibiotic use. It is not by chance that the frequency of antibiotic-resistant bacteria among countries is proportional to their relative rates of antibiotic use.\textsuperscript{41}

Antibiotic resistance driven mainly from the over use of antibiotics, particularly in children, is increasingly becoming a major public health problem globally. In other words; the once effective and inexpensive treatment for infections will soon become increasingly ineffective; consequently increasing morbidity, mortality and healthcare costs. Although most of the common childhood infections such as diarrhea and upper respiratory tract infections are caused by viruses, large volumes of antibiotics are prescribed for these infections in children in the primary care settings. It is a well-known fact that these common infections in children (with the exception of acute otitis media) are mostly viral and self-limiting (including Bronchitis—a lower respiratory tract infection), thus antibiotics are most often unnecessary.\textsuperscript{44}

There are two possible alternatives available for physicians treating a child with uncomplicated URTI:

i. Not prescribing antibiotics

ii. Delaying antibiotic prescription.

There is strong evidence to suggest that this treatment approach is both safe and effective in reducing antibiotic prescribing from major clinical trials.\textsuperscript{35-47}

In 2010, the National Institute for Health and Clinical Excellence (NICE) guidelines endorsed this policy and recommended either delayed or no prescribing for five common diagnoses; acute otitis media, acute sore throat, acute cough/bronchitis, acute sinusitis and common cold. The evidence supporting the guidelines suggests that delayed prescribing can reduce antibiotic use for the above conditions by up to 80%. Similarly, the guidelines are also applicable for adult patients.\textsuperscript{48}

Currently, there is overwhelming evidence to follow one of these treatment options when treating a child with one of the conditions previously outlined. Otherwise, in a child who is well with no pre-existing comorbidities, such as heart/lung/liver diseases or Immunosuppression; it would be advised not to prescribe any antibiotic, however the natural course of the illness and advice pertaining to the course of action if symptoms persist must be clearly communicated. A description of the illness is more vital than the prescription of an antibiotic in most cases. Thus, delayed prescribing is a very safe alternative and offers a safety net; the policy is likewise important in the sense that it can protect physicians in the rare occurrence of complications. With respect to the waiting period for delayed prescription; approximately 2 to 3 days of wait-and-see approach is safe for acute otitis media, 5 days estimated for sore throat, and 10 to 14 days for acute cough. Young children (less than 2 years) with bilateral otitis media or otorrhea with otitis media may require an immediate antibiotic prescription. For the most part, it was interesting to note in most trials on delayed prescribing, that only a few patients resorted to antibiotic therapy.\textsuperscript{44}

According to Dr Thomas J Pallasch\textsuperscript{49} antibiotic misuse in dentistry mainly involves prescribing them in ‘inappropriate situations’ or for too long, which includes, giving antibiotics after a dental procedure is complete in an otherwise healthy patient to ‘prevent’ an infection, which in all likelihood will not occur:

- Using antibiotics as ‘analgesics,’ particularly in endodontics;—employing antibiotics for prophylaxis in patients not at risk for metastatic bacteremias.
- Using antimicrobials to treat chronic adult periodontitis, which is almost totally responsive to mechanical treatment.
- Using antimicrobial therapy in lieu of mechanical therapy for management of periodontitis.
- Using antibiotics and antimicrobials chronically in periodontitis.
- Using antibiotics instead of surgical incision and drainage of infections.
- Using antibiotics to ‘prevent’ claims of negligence.\textsuperscript{14}

CONCLUSION

The decision to use or not use antibiotics, and the potential to misuse these drugs, is a routine issue in dental practice. Complications associated with bacterial resistance to antibiotics dictate that clinicians do not prescribe antibiotics unless they are clearly indicated. When treating a patient with any of the conditions discussed in this article, the dentist must seek to avoid systemic infection originating from the oral cavity. Selection of proper antibiotic agent and its judicious use is the need of the hour to avoid the
risk of bacterial resistance. A team work with a pediatrician is important when dealing with pediatric patients with systemic ailments. Utmost care is required when dealing with the pediatric population as negligence or slightest ignorance can affect their productive and disease free future as an adult.

REFERENCES