

Free radicals: emerging challenge in environmental health research in childhood and neonatal disorders.

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Infants and children may undergo severe oxidative stress due to disease state, pre-existing nutritional status, frequent use of oxygen, and lower levels of antioxidant defenses. Antioxidant defenses, made up of intracellular and extra-cellular components, work synergistically to prevent oxidative damage. Total antioxidant activity (TAA) was analyzed by method of ferric reducing antioxidant power assay (FRAP). Patients admitted in Pediatric Dept, RNT Medical College, Udaipur, India were selected for these studies. TAA level in neonates with hypoxic-ischemic-encephalopathy (HIE) stage III and in poor outcome cases was significantly low. Erythrocyte SOD activity level was low in pre-term neonates. TAA level in severely malnourished children at the time of hospital admission was low. This low antioxidant level in severely malnourished children could be multi-factorial viz. low zinc, selenium, vitamin A & C deficiency, recurrent infections, elevated free iron and chronic starvation stage. Delayed recovery of oxidant injury may lead to delayed incomplete recovery at cellular level. In a study of 29 tuberculosis patients TAA level was found to be low in tubercular patients compared with control. TAA level decreased more in CNS tuberculosis compared with other system tuberculosis. In a study of nutritional tremor syndrome TAA, ascorbic acid and alpha-tocopherol levels were low during pre-tremor phase compared with tremor phase (ATS). Pre-term neonates have incompletely developed antioxidant defenses and are deficient in vitamin E, which is normally derived from maternal circulation at the end of 3rd trimester. Therefore, decreased TAA level in HIE with poor outcome indicates addition of antioxidants in therapeutic strategy. Since rise in TAA in antioxidant supplemented group of severely malnutrition children was higher with good outcome compared with nonsupplemented group it would be prudent to supplement antioxidant during nutritional management. These studies have shown that health benefits can be obtained by children with a reduced risk of disease from supplements of antioxidant nutrients. The amounts of optimal supplements in these disorders, whether pharmacologic or large, are to be determined. Further work is needed to show whether modest increases in nutrient intakes in children with these disorders will delay or prevent the complications and improve the outcome. Therefore, available evidence regarding health benefits to be achieved by supplementing antioxidant nutrients is encouraging. Free radical injury and antioxidant deficiency is more common than what we think. Severely malnourished children and children suffering from chronic infections and diseases are at several fold increased risk of antioxidant deficiency and likely to suffer from free radical injury. Appropriate interventions are required in reducing the risk associated with these observations.

Responding to the crisis in sub-Saharan Africa: the role of nutrition.

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In the chapter dealing with education and health, the report of the influential Commission for Africa prioritises basic health systems, HIV/AIDS, malaria and tuberculosis. In contrast, nutrition is given less than half a page and is reduced to parasite control and micronutrient support. Such neglect of nutrition is hard to understand in the context of increasing hunger and malnutrition across the continent. Sub-Saharan Africa is the only region in the world where the proportion of underweight children has stagnated and the absolute numbers have actually increased in the last decade. It has been pointed out that if current trends continue sub-Saharan Africa will achieve the Millennium Development Goal for child mortality around 2115 - one century after the target date. Quite clearly those concerned with nutrition need to more powerfully advocate the role of nutrition in lifting Africa out of the spiral of poverty. The present paper argues that to achieve this requires an understanding not just of the critical role of nutrition for health and development (both individual and national), but also of how recent global changes are interacting with changes in food production and supply, other determinants of maternal and child health, and the role and capacity of the state to tackle malnutrition in Africa. It

Community-based therapy for children with multidrug-resistant tuberculosis.

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OBJECTIVES: The goals were to describe the management of multidrug-resistant tuberculosis among children, to examine the tolerability of second-line antituberculosis agents among children, and to report the outcomes of children treated for multidrug-resistant tuberculosis in poor urban communities in Lima, Peru, a city with high tuberculosis prevalence. **METHODS:** A retrospective analysis of data for 38 children <15 years of age with multidrug-resistant tuberculosis, either documented with drug sensitivity testing of the child's tuberculosis isolate or suspected on the basis of the presence of clinical symptoms for a child with a household contact with documented multidrug-resistant tuberculosis, was performed. All 38 children initiated a supervised individualized treatment regimen for multidrug-resistant tuberculosis between July 1999 and July 2003. Each child received 18 to 24 months of therapy with > or =5 first- or second-line drugs to which their Mycobacterium tuberculosis strain was presumed to be sensitive. **RESULTS:** Forty-five percent of the children had malnutrition or anemia at the time of diagnosis, 29% had severe radiographic findings (defined as bilateral or cavitary disease), and 13% had extrapulmonary disease. Forty-five percent of the children were hospitalized initially because of the severity of illness. Adverse events were observed for 42% of the children, but no events required suspension of therapy for >5 days. Ninety-five percent of the children (36 of 38 children) achieved cures or probable cures, 1 child (2.5%) died, and 1 child (2.5%) defaulted from therapy. **CONCLUSIONS:** Multidrug-resistant tuberculosis disease among children can be treated successfully in resource-poor

settings. Treatment is well tolerated by children, and severe adverse events with second-line agents are rare.

The effect of multi-vitamin/mineral supplementation on mortality during treatment of pulmonary tuberculosis: a randomised two-by-two factorial trial in Mwanza, Tanzania.

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Malnutrition is common in pulmonary tuberculosis (TB), and may impair survival. The objective of this study was to assess effects of multi-vitamin/mineral (MVM) and zinc (Zn) supplementation during TB treatment on mortality. Patients diagnosed with sputum-positive pulmonary TB in Mwanza, Tanzania, were randomised, using a two-by-two factorial design, to Zn (45 mg) or placebo, and MVM (vitamins A, B, C, D, E, and selenium and copper) or placebo. Survival status was ascertained at the end of the 8-month TB treatment and supplementation period. Of 499 TB patients, 213 (43 %) had HIV. The mean weight gain at 7 months was 6.88 kg (95 % CI 6.36, 7.41). Zn and MVM combined, but neither alone (interaction, $P=0.03$), increased weight gain by 2.37 kg (95 % CI 0.91, 3.83), irrespective of HIV status. Survival status at 8 months was determined for 422 patients (84.6 %), of which fifty-two (12.3 %) had died. Among fifty-two deaths, there were no effects of MVM (relative risk (RR) 0.73; 95 % CI 0.43, 1.23) and Zn (RR 0.76; 95 % CI 0.46, 1.28). However, among HIV co-infected patients, marginally significant effects of both MVM (RR 0.60; 95 % CI 0.34, 1.05) and Zn (RR 0.63, 95 % CI 0.37, 1.08) were seen, and MVM and Zn combined reduced mortality (RR 0.29; 95 % CI 0.10, 0.80; interaction ratio 0.52). In conclusion, supplementation with MVM, including Zn, during treatment of pulmonary TB may reduce mortality in those co-infected with HIV. A randomised trial of the effect of the combined intervention used in this study should be conducted in a different setting to confirm the finding.

Clinically directed selective screening for HIV infection in hospitalized children.

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BACKGROUND: As HIV infection presents with several manifestations, none of which is specific, several children are subjected to HIV testing. Very few studies have examined the issue of probability of HIV infection with a given clinical manifestation. **AIM:** To determine the probability of HIV infection when a child is hospitalized with at least one of the selected manifestations. **MATERIAL AND METHODS:** Children aged 18 mo and above, admitted to a tertiary care center in Mumbai, India with chronic diarrhea, severe

malnutrition, persistent cough, generalized lymphadenopathy, oral thrush, hepatomegaly, repeated common infections, generalized dermatitis, chronic parotid swelling, recurrent bacterial infection, disseminated tuberculosis and/ or Pneumocystis carinii pneumonia were enrolled in a prospective study after obtaining informed consent. They were subjected to HIV testing using WHO-UNAIDS strategy II. The data obtained was analyzed using the Statistical Package For Social Sciences (SPSS) software program. RESULTS: Twenty-three (20 PERCENT) of the 115 children enrolled tested positive for HIV. The seropositivity rate for various features ranged from 9.1 PERCENT for chronic diarrhea to 83.3 PERCENT for chronic dermatitis. Oral thrush, generalized dermatitis and generalized lymphadenopathy were the significant independent clinical risk factors for predicting HIV seropositivity. The probability of HIV infection was higher in children who had higher number of risk factors present concomitantly CONCLUSIONS: The probability of HIV infection in a child is dependent upon the nature and number of manifestations present.

Clinical features and outcome in children admitted to a TB hospital in the Western Cape--the influence of HIV infection and drug resistance.

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BACKGROUND: The Western Cape has a high incidence of tuberculosis (TB) and a rising prevalence of HIV infection. Children form 15-20% of this TB burden. OBJECTIVE: To document the clinical features and outcome of TB among children admitted to a regional TB hospital. METHOD: A retrospective, descriptive study was undertaken of children under 15 years of age admitted to Brooklyn Hospital for Chest Diseases from January 2000 to December 2001. Demographic and clinical details of children were recorded routinely in a register that formed the basis of this review. RESULTS: Two hundred and thirty-eight of the 250 children admitted had TB, of whom 120 (50.4%) were boys. The median age was 25 months. Reasons for admission were disease severity in 99 cases, social reasons in 36, and a combination in 103. Adult source cases were identified in 138 instances; 9 had drug-resistant TB, 31 drug-susceptible TB and in 98 cases susceptibility was unknown. TB was confirmed by culture in 119 children. Of 79 in whom susceptibility testing was done, 10 had isoniazid-resistant TB and 8 multidrug-resistant TB. HIV serology was positive in 43 of 138 children tested (31%). Previous antituberculosis treatment, severe malnutrition and weight under the 3rd percentile for age, a negative Mantoux test, and mortality were significantly more common in the HIV-infected children. Twenty-two of 41 previously negative Mantoux tests (< 5 mm induration) were positive on retesting. CONCLUSIONS: HIV infection is common in children with TB and malnutrition, and mortality in this group is high. Repeat Mantoux tests may show an increased number of positive results.

Nutrition and HIV in the international setting.

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HIV infection has become increasingly prevalent globally, with more than 40 million infected individuals worldwide, the majority of whom live in the resource-limited world, especially sub-Saharan Africa and Asia. There are nutritional and metabolic issues that significantly impact morbidity and mortality in HIV-infected populations. In addition, malnutrition has been associated with an increased risk of transmission of HIV from infected mothers to infants, and malnutrition may further compromise HIV-infected individuals who have tuberculosis or persistent diarrheal disease. The introduction of highly active antiretroviral therapy will have a significant impact on the mortality of HIV, but will not completely alleviate the malnutrition associated with HIV infection in the global setting.

[Risk factors for developing tuberculosis]

[Article in Serbian]

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INTRODUCTION: Application of modern achievements in the field of medicine such as organ transplantation, long-term immunosuppressive therapy in treatment of numerous diseases, dialysis, successful treatment of malignant diseases prolonged duration of life and consequential continuation of long-term immunodeficiency. RISK FACTORS FOR DEVELOPING TUBERCULOSIS: HIV infection currently represents a major risk factor for reactivation of tuberculosis with its associated relative risk being 30-170 times higher in comparison to the control group, in regard to the number of CD4 T-lymphocytes. Malignant diseases (hematological, lung and breast carcinomas) are important immunocompromising conditions affecting reactivation of tuberculosis, whereas the relative risk is 16. METABOLIC DISORDERS AS RISK FACTORS: Development of tuberculosis among diabetics is considerably more frequent in comparison to general population (relative risk 2-4). Prominent glycoregulation disorders point to greater liability to development of tuberculosis. Alcoholism is characterized by general reduction of resistance, resulting from alcohol intoxication, malnutrition, irregular life style, etc. In malabsorption, immunosuppression is induced by deficiency of nutritive components and thus, relative risk for reactivation of tuberculosis is 5-12 in gastrectomy and 27-63 in jejunoileal bypass. In patients with chronic renal failur the relative risk ranges from 10 (nephropathies) to 37 (transplantation). Numerous patients use long-term immunosuppressive therapy that contributes to increased risk for developing tuberculosis (relative risk 12) as early as one month after application of a dose above 15 mg/day. CONCLUSION: There are numerous of risk factors that have frequently combined effects responsible for immunologic imbalance and development of tuberculosis.

Micronutrient malnutrition and wasting in adults with pulmonary tuberculosis with and without HIV co-infection in Malawi.

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BACKGROUND: Wasting and micronutrient malnutrition have not been well characterized in adults with pulmonary tuberculosis. We hypothesized that micronutrient malnutrition is associated with wasting and higher plasma human immunodeficiency virus (HIV) load in adults with pulmonary tuberculosis. **METHODS:** In a cross-sectional study involving 579 HIV-positive and 222 HIV-negative adults with pulmonary tuberculosis in Zomba, Malawi, anthropometry, plasma HIV load and plasma micronutrient concentrations (retinol, alpha-tocopherol, carotenoids, zinc, and selenium) were measured. The risk of micronutrient deficiencies was examined at different severity levels of wasting. **RESULTS:** Body mass index (BMI), plasma retinol, carotenoid and selenium concentrations significantly decreased by increasing tertile of plasma HIV load. There were no significant differences in plasma micronutrient concentrations between HIV-negative individuals and HIV-positive individuals who were in the lowest tertile of plasma HIV load. Plasma vitamin A concentrations <0.70 micromol/L occurred in 61%, and zinc and selenium deficiency occurred in 85% and 87% respectively. Wasting, defined as BMI<18.5 was present in 59% of study participants and was independently associated with a higher risk of low carotenoids, and vitamin A and selenium deficiency. Severe wasting, defined as BMI<16.0 showed the strongest associations with deficiencies in vitamin A, selenium and plasma carotenoids. **CONCLUSIONS:** These data demonstrate that wasting and higher HIV load in pulmonary tuberculosis are associated with micronutrient malnutrition.

A study of tuberculosis, malnutrition and gender in Sri Lanka.

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This study assesses the nutritional status of tuberculosis (TB) patients in Sri Lanka and differences in the nutritional presentation between males and females. In May-June 2002, cases from Colombo hospitals and controls from both the Sri Lankan Air Force Base and audience members at a 'better health' presentation in Colombo were assessed for nutritional status using a modified Standard Global Assessment. Fifty cases and 49 controls were recruited. Nutritional examinations revealed the cases to have significantly lower nutritional values than the controls (body mass index 16.2 vs. 24.0 kg/m²); arm circumference 20.7 vs. 28.4 cm; muscle wasting [temples 56% vs. 0%; shoulders 46% vs. 0%]. The nutritional history revealed the cases to have higher levels of anorexia, vomiting, nausea and diarrhoea within the preceding fortnight. Differences between the genders were minimal other than an increase of 23 and 19% in the frequency of female

cases having suffered with vomiting and nausea respectively. Consequently, both male and female TB patients in Sri Lanka are significantly malnourished. It is recommended that patients receive nutritional support during their treatment, with studies of the exact nutritional deficiencies at the micronutrient level and their effect on the immune system being required.

Diagnosis of pulmonary tuberculosis by score system in children and adolescents: a trial in a reference center in Bahia, Brazil.

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Since 2002, the Brazilian Ministry of Health has recommended a score system for tuberculosis diagnosis of children and adolescents that does not need bacteriological positivity, because most cases in this age group have few bacteria. An observational, transversal study was carried out at the outpatient health care service of the reference medical service in Salvador, Bahia, including 164 patients with pulmonary tuberculosis, with ages ranging between 1 and 15 years of age, who were treated from 1990 to 2001. The gold standard used to establish the diagnosis was clinical, radiological, epidemiological and based on follow-up data. The score system for diagnosis purposes was tested retrospectively. The median age and the average age of the 164 patients were 6 and 6.62 years (SD +/- 4.33), respectively. About 65% of the sample reported a history of close contact with a tuberculous adult. The BCG vaccine coverage was 70.7% (116/164). It was found that 26% (43/164) of the patients had severe malnutrition. Out of this group, 26/43 (60.47%) were < 5 mm reactive to the tuberculin test. On the other hand, out of the 91 patients with tuberculin test < 5 mm, 29% (26/ 91) had severe malnutrition. The use of the score gave the following distribution: a) TB very likely in 81.7% (134/164) of the patients; b) possible TB in 15.9% (26/164) and TB unlikely in 2.4% (4/164). Among patients who had been vaccinated more than 2 years before, there was a 9 times higher risk of finding a tuberculin test above 10 mm in individuals with probable TB in comparison with the patients with possible or unlikely TB.

Aging and infectious diseases in the developing world.

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Although demographic aging does not remain restricted to industrialized countries, the medical challenge arising from the aging population will be distinct in the developing world. This is particularly true with respect to infectious diseases, which have a distinct spectrum in the elderly population, as well as a greater overall relevance in the developing world. Tropical diseases have a specific presentation and epidemiology in

elderly patients. Infectious diseases with a worldwide distribution impact elderly patients in the developing world in a specific manner, which is most obvious with respect to human immunodeficiency virus and tuberculosis but is also true with respect to "trivial" manifestations of infection, such as diarrhea and pneumonia. Malnutrition contributes in a major way to the immunodeficiency of elderly patients in the developing world. Poorly controlled use of antimicrobial drugs leads to multidrug-resistant microorganisms, which, together with the limited resources available for drug treatment, makes appropriate treatment of infections in elderly patients in developing countries very difficult. Infections in elderly patients will have an increasing impact on the public health and economy of developing countries.

A view on antimicrobial resistance in developing countries and responsible risk factors.

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Antimicrobial resistance is one of the biggest challenges facing global public health. Although antimicrobial drugs have saved many lives and eased the suffering of many millions, poverty, ignorance, poor sanitation, hunger and malnutrition, inadequate access to drugs, poor and inadequate health care systems, civil conflicts and bad governance in developing countries have tremendously limited the benefits of these drugs in controlling infectious diseases. The development of resistance in the responsible pathogens has worsened the situation often with very little resource to investigate and provide reliable susceptibility data on which rational treatments can be based as well as means to optimise the use of antimicrobial agents. The emergence of multi-drug-resistant isolates in tuberculosis, acute respiratory infections and diarrhoea, often referred to as diseases of poverty, has had its greatest toll in developing countries. The epidemic of HIV/AIDS, with over 30 million cases in developing countries, has greatly enlarged the population of immunocompromised patients. The disease has left these patients at great risk of numerous infections and even greater risks of acquiring highly resistant organisms during long periods of hospitalisation. This review discusses antimicrobial resistance in developing countries and the risk factors responsible.

A social disease/a social response: lessons in tuberculosis from early 20th century Chile.

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During the 1930s, Chile reported the world's highest mortality rate due to tuberculosis. In this pre-antibiotic era, the attention of the biomedical community frequently turned to the underlying social inequalities and deficiencies that created conditions of heightened risk for Chile's rapidly expanding working class. With the recognition that crowded housing, chronic malnutrition and substandard working conditions fostered an environment in which the disease developed and spread with virulent rapidity, physicians frequently

became vocal advocates for widespread and significant social reform. However, by the time of the introduction of efficacious pharmaceutical agents in the 1940s and with the overall rapid development of biomedicine in the mid-20th century, the larger medical discourse became more rigidly defined and characterized by the promotion of the new antibiotics and treatments. These factors increased the depth of the self-defined medical territory but substantially reduced its breadth. Accompanying this shift was an increasing focus on individual behaviors that were seen as deficient and were both socially censored and used as explanations for increased susceptibility. In the midst of the current worldwide epidemic of tuberculosis, this disease and its epidemiological pattern heightens our awareness of the significance and consequences of global inequalities. It also draws our attention to the importance of intervention within the social conditions from which these patterns emerge.

Malnutrition and the severity of lung disease in adults with pulmonary tuberculosis in Malawi.

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SETTING: Zomba Central Hospital, Zomba, Malawi. OBJECTIVE: To examine the relationship between malnutrition and the severity of lung disease in human immunodeficiency virus (HIV) positive and negative adults with pulmonary tuberculosis (PTB). DESIGN: Cross-sectional study. METHODS: Chest radiographs and anthropometric measurements were obtained and bioelectrical impedance analysis was conducted in sputum-positive patients with pulmonary tuberculosis. Lung disease in chest radiographs was graded as normal, minimal, moderately advanced and far advanced according to a conventional classification system. RESULTS: Among 319 adults with PTB with or without HIV co-infection, body mass index (BMI), fat mass and phase angle were independently associated with increasing severity of lung disease. Multiple logistic regression analyses showed that BMI, fat mass and phase angle were associated with increasing severity of lung disease among 236 HIV-positive adults, when adjusted for sex, age, and plasma HIV load. CONCLUSION: The severity of lung disease in adults with PTB is associated with the extent of malnutrition, as reflected by BMI and body composition studies using bioelectrical impedance analysis.

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Responding to the crisis in sub-Saharan Africa: the role of nutrition.

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In the chapter dealing with education and health, the report of the influential Commission for Africa prioritises basic health systems, HIV/AIDS, malaria and tuberculosis. In contrast, nutrition is given less than half a page and is reduced to parasite control and micronutrient support. Such neglect of nutrition is hard to understand in the context of increasing hunger and malnutrition across the continent. Sub-Saharan Africa is the only region in the world where the proportion of underweight children has stagnated and the absolute numbers have actually increased in the last decade. It has been pointed out that if current trends continue sub-Saharan Africa will achieve the Millennium Development Goal for child mortality around 2115 - one century after the target date. Quite clearly those concerned with nutrition need to more powerfully advocate the role of nutrition in lifting Africa out of the spiral of poverty. The present paper argues that to achieve this requires an understanding not just of the critical role of nutrition for health and development (both individual and national), but also of how recent global changes are interacting with changes in food production and supply, other determinants of maternal and child health, and the role and capacity of the state to tackle malnutrition in Africa. It concludes by suggesting some responses that nutritionists could now be making.

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Exemption policies and community preferences for tropical endemic diseases in the Bamako initiative programme in Nigeria.

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We determined the actual written policies/guidelines and practices of fee exemptions aimed at the primary health-care level for tropical diseases treatment within the Bamako initiative system and the community's and decision makers' preferences for exemption in Nigeria. Health policy documents from the federal and state ministries of health were reviewed to determine the guidelines for exemptions, services, goods and category of people to receive exemptions. The records of the local government areas, health centres and community health committees were also reviewed to check who had received exemptions and modalities for doing so. In addition, household surveys using questionnaires was conducted. There is no clear-cut national policy regarding exemption. In areas where exemption exists, these are largely unofficial, as no official documents exist to support exemption. A total of 1594 individuals were surveyed. Community members prefer pregnant women, children and patients with TB, malaria, onchocerciasis and leprosy to be exempted from payment of fees: decision makers prefer the poor, children and patients with malaria, TB and leprosy to be exempted from payment for drugs, registration, consultation and preventive services such as immunization and antenatal services. One area of divergence

between the preferences of the community and decision makers is the issue of exempting people with malaria and HIV/AIDS.

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From chloroquine to artemisinin-based combination therapy: the Sudanese experience.

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BACKGROUND: In Sudan, chloroquine (CQ) remains the most frequently used drug for falciparum malaria for more than 40 years. The change to artemisinin-based combination therapy (ACT) was initiated in 2004 using the co-blister of artesunate + sulfadoxine/pyrimethamine (AS+SP) and artemether + lumefantrine (ART+LUM), as first- and second-line, respectively. This article describes the evidence-base, the process for policy change and it reflects the experience of one year implementation. Relevant published and unpublished documents were reviewed. Data and information obtained were compiled into a structured format. **CASE DESCRIPTION:** Sudan has used evidence to update its malaria treatment to ACTs. The country moved without interim period and proceeded with country-wide implementation instead of a phased introduction of the new policy. The involvement of care providers and key stakeholders in a form of a technical advisory committee is considered the key issue in the process. Development and distribution of guidelines, training of care providers, communication to the public and provision of drugs were given great consideration. To ensure presence of high quality drugs, a system for post-marketing drugs surveillance was established. Currently, ACTs are chargeable and chiefly available in urban areas. With the input from the Global Fund to fight AIDs, Tuberculosis and Malaria, AS+SP is now available free of charge in 10 states. **CONCLUSION:** Implementation of the new policy is affected by the limited availability of the drugs, their high cost and limited pre-qualified manufacturers. Substantial funding needs to be mobilized by all partners to increase patients' access for this life-saving intervention.

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Pharmacovigilance of antimalarial treatment in Africa: is it possible?

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Pharmacovigilance, defined as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug related problem", is increasingly being recognized in Africa. Many African countries have simultaneously adopted artemisinin derivative based combination therapy (ACT) as first-line treatment for uncomplicated malaria, offering an opportunity to assess the safety of these drugs when used widely. While ACTs appear to be safe and well-tolerated, there is little experience with these medicines in Africa, outside clinical trials. Pharmacovigilance for ACTs and other combination treatments in Africa is essential. Malaria transmission intensity is high and antimalarial medicines are used frequently. Presumptive treatment of fever with antimalarials is common, often in the absence of a confirmed diagnosis, using drugs obtained without a prescription. Informal use of antimalarial drugs may increase the risk of incorrect dosing, inappropriate treatment, and drug interactions, which may impact negatively on drug safety. Furthermore, the administration of antimalarial treatments in patients with a concomitant illness, including HIV/AIDs, tuberculosis and malnutrition, is a concern. African countries are being encouraged to establish pharmacovigilance systems as ACTs are rolled out. However, pharmacovigilance is difficult, even in countries with a well-developed health care system. The rationale for pharmacovigilance of antimalarial drugs is discussed here, outlining the practical challenges and proposing approaches that could be adopted in Africa.

History of nutritional immunology: introduction and overview.

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Nutritional immunology is a newly recognized subdiscipline of vast clinical and public health importance. Its history began in 1810 with recognition of lymphoid tissue atrophy due to malnutrition. Discovery of vitamins in the early 1900s was followed by reports on their contribution to immunity and other host defenses. A hiatus in immunonutritional progress occurred during World War II and the "antibiotic era," but a worldwide rebirth of interest began in the 1960s and early 1970s. The current logarithmic growth of nutritional immunology was triggered by increased medical interest, plus the introduction of new concepts and investigative research methodologies from both parent sciences.

1: J Nutr 1996 Oct;126(10 Suppl):2611S-2615S

Nutrition in pediatric HIV infection: setting the research agenda. Nutrition and immune function: overview.

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Malnutrition can have adverse, even devastating effects on the antigen-specific arms of the immune system and on generalized host defensive mechanisms. Protein/energy malnutrition and/or deficiencies of single nutrients that assist in nucleic acid

metabolism generally lead to atrophy of lymphoid tissues and dysfunctions of cell-mediated immunity. Deficiencies of single nutrients can impair production of key proteins. Trace element deficiencies are often multifactorial. Essential fatty acid deficiencies can reduce or perturb the synthesis of cytokine-induced eicosanoids. Arginine deficiency can diminish the production of nitric oxide, and deficiencies of antioxidant nutrients can allow increases in the damaging effects of free oxygen radicals. Humoral immunity continues to be maintained, although new primary responses to T-cell-dependent antigens are generally subnormal in both magnitude and quality. Immunological dysfunctions associated with malnutrition have been termed Nutritionally Acquired Immune Deficiency Syndromes (NAIDS). Infants and small children are at great risk because they possess only immature, inexperienced immune systems and very small protein reserves. The combination of NAIDS and common childhood infections is the leading cause of human mortality. NAIDS can generally be corrected by appropriate nutritional rehabilitation, but from a viewpoint highly important to this Workshop, AIDS and NAIDS are intensely synergistic. AIDS-induced malnutrition can lead to the secondary development of NAIDS, with its much broader array of additional immunological dysfunctions. The complex and far reaching insults to the immune system caused by NAIDS, and the synergistic combination of NAIDS and AIDS, thereby hasten the demise of many victims of AIDS. Aggressive nutritional support for children with HIV infections could delay, or lessen, the development of NAIDS and avoidance of NAIDS would improve both quality and length of life.

Fatal infections in protein-calorie malnourished children with thymolymphatic atrophy.

Comment in J Infect Dis. 1995 Feb;171(2):502-4

Purtilo DT, Connor DH.

The clinicopathological features of 25 children who died with protein-calorie malnutrition were studied. All but four subjects were found at necropsy to have nutritional thymectomy and all but 3 died of infectious diseases. The infectious agents were chiefly intracellular micro-organisms including miliary tuberculosis, Herpes simplex, varicella, measles, Pneumocystis carinii, and Plasmodium falciparum. Staphylococcal infections, salmonellosis, shigellosis, strongyloidiasis, and hookworm were other significant infectious agents. Nutritionally acquired defective immunity, especially cell-mediated immunity, probably permitted these infectious agents to multiply and to disseminate widely.

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