

Journal Abstracts

EDITOR: ANNETE ROBERTSON*

1. Pre-eclampsia. Walker, J. *Lancet*. 2000. 356:1260-65.

In many parts of the world, the morbidity and mortality associated with pre-eclampsia continues to be high. International comparisons are difficult given the varying definitions and degrees of accuracy of diagnosis. Pre-eclampsia is more common in primigravid women and in women with donor eggs. A change in partners appears to increase the risk in multiparous women and certain men seem to be associated with fathering pre-eclamptic pregnancies. The role of genetics in its pathophysiology remains unclear. There is an initial placental trigger, maladaptation of maternal spiral arterioles and poor villous development. It appears that a strong maternal systemic inflammatory reaction produces the signs and symptoms characteristic of the disorder. Initial diagnosis is generally based on the presence of hypertension, whether Korotkoff phase IV or V classification is used; and/or proteinuria, although some women may present with convulsions; abdominal pain or general malaise. The fall in incidence of neurological sequelae are directly related to the use of antihypertensive medication and magnesium sulphate. Posterior leucoencephalopathy syndrome (PLES) is a radiological description of cerebral oedema associated with convulsions, which may be seen in severe cases. A stepwise protocol for management of pre-eclampsia as well as antihypertensive and anticonvulsant therapy, fetal assessment and management were discussed. There is still no consensus on which antihypertensive medication and what threshold of blood pressure is required for most effective treatment. Trials indicate that hydralazine is inferior to labetalol and nifedipine for blood pressure above 170/110 mmHg while methyldopa is equally effective as them for mild to moderate pre-eclampsia. Substantial care is necessary during and after the delivery to determine blood pressure readings, signs of fluid overload, especially pulmonary

oedema, and renal function.

Editorial comment. This is an excellent review of pre-eclampsia covering aspects from epidemiology to management for medical students and practising doctors. It is clearly written and contains updated information pertaining to management. While variations in hypertension classification may be important epidemiologically, on a clinical level it is vital that all women with elevated blood pressure readings are closely monitored and managed. Improvement in antenatal care and maternity services are vital to decreasing the morbidity and mortality associated with pre-eclampsia.

2. Paternal and Maternal Components of the Predisposition to Pre-eclampsia. Esplin, M.; Fausett, M.; Fraser, A.; et al. *The New England Journal of Medicine*. 2001. 334(12):867

Although an inherited maternal predisposition to preeclampsia has been described, the paternal contribution to the condition has not been well investigated. A study was conducted using the Utah Population Database to determine whether the offspring of men and women who themselves were the product of pregnancies involving preeclampsia were more likely to be the product of pregnancies that were complicated by preeclampsia. A total of 298 male study subjects and 237 female study subjects whose mothers had preeclampsia were recruited. A total of 596 male control subjects and 474 female control subjects who were not the product of

pregnancies complicated by preeclampsia were recruited for comparison, matched to gender, county of birth, maternal age, year of birth and birth order. Outcomes of all pregnancies producing offsprings were identified using three different methods. The percentages of offspring born of pregnancies complicated by preeclampsia were calculated in the four groups

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and further analyses adjusting for potential confounders was conducted using logistic regression. Approximately 2.7 percent of the male study group were born of pregnancies complicated by preeclampsia while 1.3 percent of the male control group were born of the preeclampsia. Similarly, in the female study group, approximately 4.7 percent were born of pregnancies complicated by preeclampsia and only 1.9 percent were born of such pregnancies. Among the male groups, father being born of a pregnancy complicated by preeclampsia was found to be an independent risk factor in the offspring. Among the female groups, being the product of a pregnancy complicated by preeclampsia was also an independent risk factor.

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Editorial Comment. This well designed study suggests that there is both a maternal and a paternal genetic contribution to the development of preeclampsia. It supports another epidemiologic study, which though different in design and analyses, has pointed to a paternal role in this disorder. The maternal role has been suggested in several studies. Because of the cohort nature of this study design, the choice of the study population and methods of analyses, ascertainment bias and confounding appear to be minimized. This is an excellent study for students trying to understand study design and analyses as it is a simple, well-conceived study. Other health personnel should also find this an interesting article. Further genetic studies may shed light on the genetic nature of preeclampsia.

3. Effects of Maternal Smoking during Pregnancy and Environmental Tobacco Smoke on Asthma and Wheezing in Children. Gilliland, F.; Li, Y.; Peters, J. American Journal of Respiratory and Critical Care Medicine. 2001. 163:429-436.

This cross-sectional study involving 5,762 children was conducted to investigate the effects of maternal smoking during pregnancy and environmental tobacco smoke on asthma and wheezing in children. Self-administered questionnaires were completed by the parents or guardians of the children of selected class groups of selected areas in California. Information gathered related to asthma and wheezing status, and current and past household smoking status of all adult family and household members as well as atopic or allergic health problems and certain environmental factors. The prevalence of asthma was found to be higher in children exposed *in utero* to maternal smoking than children not exposed. It was also higher in children exposed to environmental tobacco smoke (ETS) than those not exposed. The likelihood of lifetime wheezing was also higher in the ETS group than the unexposed group. *In utero* exposure to maternal smoking without subsequent postnatal ETS exposure was associated with physician-diagnosed asthma and wheezing (Odds ratio 1.8; 95% Confidence Interval 1.1-2.9). Postnatal exposure to ETS in the absence of *in utero* exposure to maternal smoking was not associated with physician diagnosed asthma. (Odds ratio 1.1; 95% Confidence Interval 0.9-1.4). However, both *in utero* exposure to maternal smoking and ETS exposure were found to be independent risk factors for lifetime history of wheezing. The effects of *in utero* exposure to maternal smoking on wheezing appeared to be greater in the group with a negative family history of asthma or atopy than those with a positive history. This study estimates that the elimination of *in utero* exposure to maternal smoking would prevent 5 to 15 % of the asthma cases in children.

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Editorial Comment. This study does have some limitations by nature of its cross-sectional design, namely the inability to control for change over time in exposure, the inability to control for potential confounders, and the possibility of bias due to exposure misclassification. However, the authors well acknowledge the problems and try to project possible effects on the results. For some time now we have known that smoking during pregnancy had deleterious effects on the fetus. The exact nature of those effects are becoming increasingly better understood. Given the knowledge that *in utero* exposure adversely affects postnatal lung function and for numerous other reasons, it is vital that all women visiting antenatal clinics are continued to educated about the evidence against smoking during pregnancy and strongly urged not to smoke. However, effecting behavioural modification in the light of the knowledge is the real challenge.

4. Antimicrobial resistance in the tropics. Shears, P. Tropical Doctor. 2000. 30:114-16.

In most tropical countries, there is little local data depicting the bacterial patterns of resistance to different antimicrobial agents. Initial studies of antibiotic resistance were undertaken in the 1950s during shigella dysenteriae outbreaks in Japan. Subsequently, increasing resistance to tetracycline, streptomycin, sulphonamides, and chloramphenicol have been noted throughout the tropical regions. During the last two decades, resistance to nalidixic acid and ciprofloxacin has become evident. Throughout the world, the prevalence of penicillin resistant strains of *Neisseria gonorrhoea* is as high as 90% in some countries. Information related to antibiotic resistant strains of tubercle bacilli is recently becoming available in tropical countries with evidence of varying rates of resistance to rifampicin. Strategies to reduce the impact of increasing antibiotic resistance include restricting at least certain antimicrobials to prescriptions use only, increasing training programmes for all levels of health workers about locally agreed upon treatment schedules, and increasing community awareness about the dangers of improper use of antibiotics. The improvement of microbiological laboratory facilities at selected district hospitals to provide clinicians with information on antimicrobial resistance is more feasible than the implementation of widespread bacterial culture and sensitivity testing programmes. The establishment of a Global Programme for Antimicrobial Resistance Monitoring could be the impetus needed for improved surveillance at local, regional and global levels.

Editorial Comment. It is hoped that regional and national co-ordinated efforts to combat the problems of antibiotic

resistance should facilitate increased community awareness and eventual change in practice related to antibiotic usage in the Pacific. Strategies to educate healthworkers of all levels about locally agreed upon strategies of treatment against infections are an integral part of this endeavor for eventual behavioural modification. The improvement of existing microbiological laboratory facilities in Pacific island nations should facilitate the provision of information regarding patterns of bacterial resistance to antimicrobials that would guide healthworkers in treatment.

5. Diarrhoeal Disease. Hart, A. *Tropical Doctor*. 2000. 30:170-2

Diarrhoeal disease, primarily a disease of infants in developing countries, was the fourth leading cause of death in the world. As many as forty different pathogens are known to cause diarrhoeal diseases. Viruses and especially rotavirus, which account for at least 870,000 deaths in children under five years, continue to be the dominant pathogen. A vaccine against rotaviral infections has been shown to be effective but cost, potential side effects and possible ineffectiveness against new strains of rotavirus have limited its use. The cholera pandemic caused by *Vibrio cholerae* 01 El Tor and the emergence of a new serotype of cholera in India, *V. cholerae* 0139, were discussed. Two new toxins; Zot(Zonula occludens toxin) and Ace(accessory cholera endotoxin) have recently been reported. *V. cholerae* may continue to exist for a long time even in chlorinated water. *E. coli* 0157 can cause haemorrhagic colitis and antibiotic therapy can precipitate haemolytic uraemic syndrome. *Cryptosporidium* is responsible for a substantial number of cases of chronic diarrhoea and while there is no effective treatment, paromycin and nitazoxanide are potential candidates. *Cyclospora cayatanensis*, discovered in 1993 and associated with waterborne and foodborne outbreaks, is unlikely to be spread from person to person and responds to co-trimoxazole. Decreases of diarrhoeal diseases have been shown to be related to fly control in the Gambia and the drinking of water exposed to sunlight in plastic bottles among Maasai children.

Editorial Comment. An overview of the major diarrhoeal diseases encountered in the world today and some of the more recent issues that relate to investigation and management of these diseases were discussed briefly. Although there are specific issues of management that relate to individual pathogens, the overall principles of management involve appropriate rehydration and adequate nutrients supply. Prevention through consumption of potable water, personal hygiene, environmental sanitation and fly control may appear to be relatively simple measures. However, in many countries its implementation has not been possible

and diarrheal diseases continue to be a substantial cause of morbidity and mortality.

6. Epidemiology of post-shigellosis persistent diarrhea in young children. Ahmed, F.; Ansaruzzaman, M.; Haque, E.; et al. *Pediatric Infectious Disease Journal*. 2001. 20: 525-30.

Dysentery, of which the principal organism is shigella, is associated with approximately 20 percent of the 4.6 million diarrhoea-related deaths in children from developing countries. A community-based study of Bangladeshi rural children younger than five years old was conducted to determine if there was an increased risk of persistent diarrhea in children with shigella infections and to investigate the nature of the postshigellosis persistent diarrhea. A total of 1259 children with shigellosis, *Shigella*-negative bloody diarrhea, and *Shigella*-negative non-bloody diarrhea were followed up for a one month period over two years

to determine the likelihood of developing persistent diarrhea. There was a 23 percent risk of developing persistent diarrhea in children with culture-confirmed diarrhea and a 13 percent risk in shigella-negative epi-

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sodes, thus children with *Shigella*-positive diarrhea were almost twice as likely to develop persistent diarrhea as compared to children with *Shigella*-negative diarrhea. Results revealed that children with multiply antibiotic-resistant shigellosis episodes (resistant to ampicillin, trimethoprim-sulfamethoxazole and nalidixic acid) were almost four times more likely to develop persistent diarrhea than children with other shigella forms of diarrhea. Dysenteric shigellosis episodes were more likely to become persistent than nondysenteric episodes. A significant association was also detected between unsanitary hanging latrines and persistent diarrhea. Infancy was associated with an increased risk of persistent diarrhea and appropriate use of nalidixic acid was associated with a decreased risk of persistent diarrhea.

Editorial Comment. Once again, the difficulty in studying the effects of inappropriate antibiotic use and multiple antibiotic resistance was evident. Methodologically the difficulty in determining the independent effects is compounded by the fact that the antibiotic use is highly correlated with multiple antibiotic resistance. Although substantial discussion has centred on the difficulty of statistically separating the effects of highly correlated covariates, it continues to be an important issue that warrants further attention. The prevention of shigellosis to reduce the burden of persistent diarrhea in the Pacific should be aimed at infants and children and of course include other diarrheal diseases. While there has been some improvement in sanitary conditions over the past few decades, there is still a need for substantial improvement.

7. Evidence Assessment of Management of Acute Otitis Media: 1. The Role of Antibiotics in Treatment of Uncomplicated Acute Otitis Media. Takata, G.; Chan, L.; Shekelle, P. et al. *Pediatrics*. 2001. 108: 239-247.

Treatment of uncomplicated otitis media is controversial. To investigate the role of antibiotics in the treatment of acute otitis media, a literature search was undertaken of seven electronic databases for articles published between 1966 and March 1999 and reference listings in proceedings, published articles, reports and guidelines. This evidence assessment was limited to children between the ages of four weeks and eighteen years and guided by a panel of eleven multidisciplinary experts, including two physicians who independently reviewed each article. Seventy four of the 3461 citations located were accepted for analysis. Analysis in terms of natural history of the disease revealed that 78% of children would have experienced clinical resolution within 4 to 7 days of diagnosis in the absence of antibiotic usage. The clinical failure rate at 2-7 days among those receiving ampicillin or amoxicillin was 12% less than among those on placebo. While there were no significant differences in clinical failure rates between those using ampicillin/ amoxicillin or trimethoprim-sulfamethoxazole and other antibiotics, those on cefixime had an 8% higher rate of diarrhea compared to those on amoxicillin. There was also a higher rate of side effects detected in children on amoxicillin-clavulanate versus those on azithromycin. There was no significant difference detected in the clinical failure rates between those on twice a day versus three times a day regimes of amoxicillin.

Editorial Comment. Although a large number of studies have been conducted to investigate the role of antibiotics in acute otitis media, synthesizing that information into recommendations for clinical practice is extremely difficult. Investigators face several epidemiological-related problems that include the lack of consensus on diagnostic criteria and potential misclassification bias; the diversity of influencing factors on outcome; and the inconsistencies in definitions of outcomes. Furthermore, as an extension of the discussion in one of the previous abstracts, the issue of antibiotic resistance and its role on outcome also needs to be better addressed in future studies.

8. Stability of insulin in tropical countries. Gill, G. *Tropical medicine and International Health*.

In tropical countries where insulin is expensive and difficult to attain, problems with storage of insulin for persons without refrigeration is a source of concern and

an apparent barrier to treatment for diabetic persons. A literature search of standard medical literature and diabetes specialists in tropical countries was conducted to investigate the issue concerning insulin stability. Ranges of rates of refrigerator access varied between 26% in Addis Ababa and 77% in Tripoli in studies reviewed. The majority of patients who did not have their own refrigerator facilities used those of their neighbours, friends, local shopkeepers or butchers. Cool storage for insulin was sought in shady corners of rooms, holes in grounds, boxes outside houses and in clay pots with sand and water inside. In studies reviewed, soluble porcine insulin stored at 25 degrees C lost 5% of its potency in 31 months and intermediate-acting insulins lost 5% of their potency in 14 weeks. At 40 degrees C, soluble porcine insulin lost 5% of its bioactivity in 14 weeks and lente insulin lost 5% in 4

weeks. In a study conducted in Mali, there were no significant differences between the potencies of various soluble insulins stored at temperatures between 25 and 34 degrees C compared with those stored at 4 degrees C over a similar time period. During the lifespan of vials of insulin in current use, there is little evidence that insulin preparations will lose substantial bioactivity at ambient temperatures.

Editorial Comment. While it may seem an important problem for diabetics who require insulin and live in warm tropical environments with little access to refrigeration, local means of maintaining cool temperatures are possible. The relative stability of insulin in ambient temperatures is reassuring. Further research on the temperatures attained by the widely used method of porous clay pots with sand and water inside would be interesting. Similar methods used by communities in the Pacific who live on outlying islands and have little access to refrigeration no doubt exist.

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