The CEYLON MEDICAL JOURNAL

Established 1887

Vol. 35 MARCH 1990 No. 1

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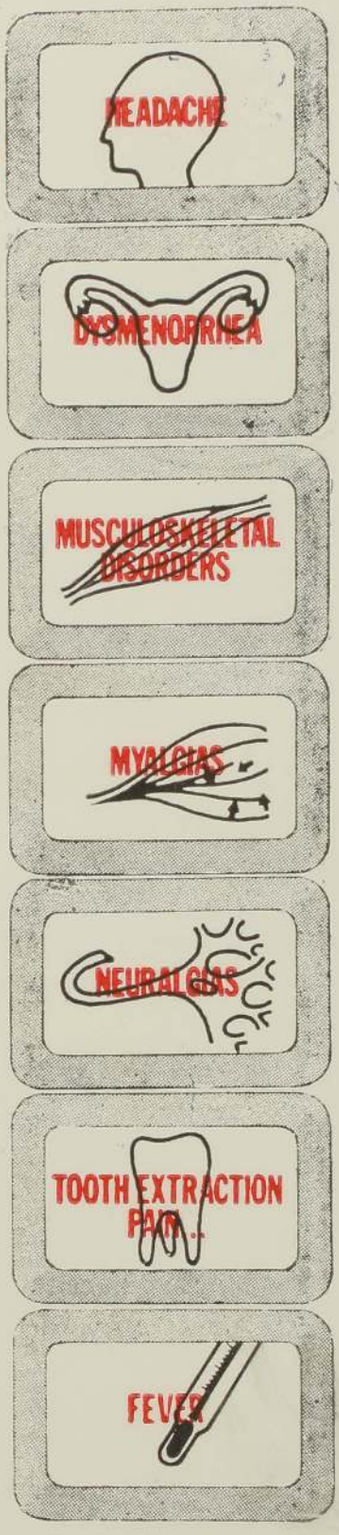

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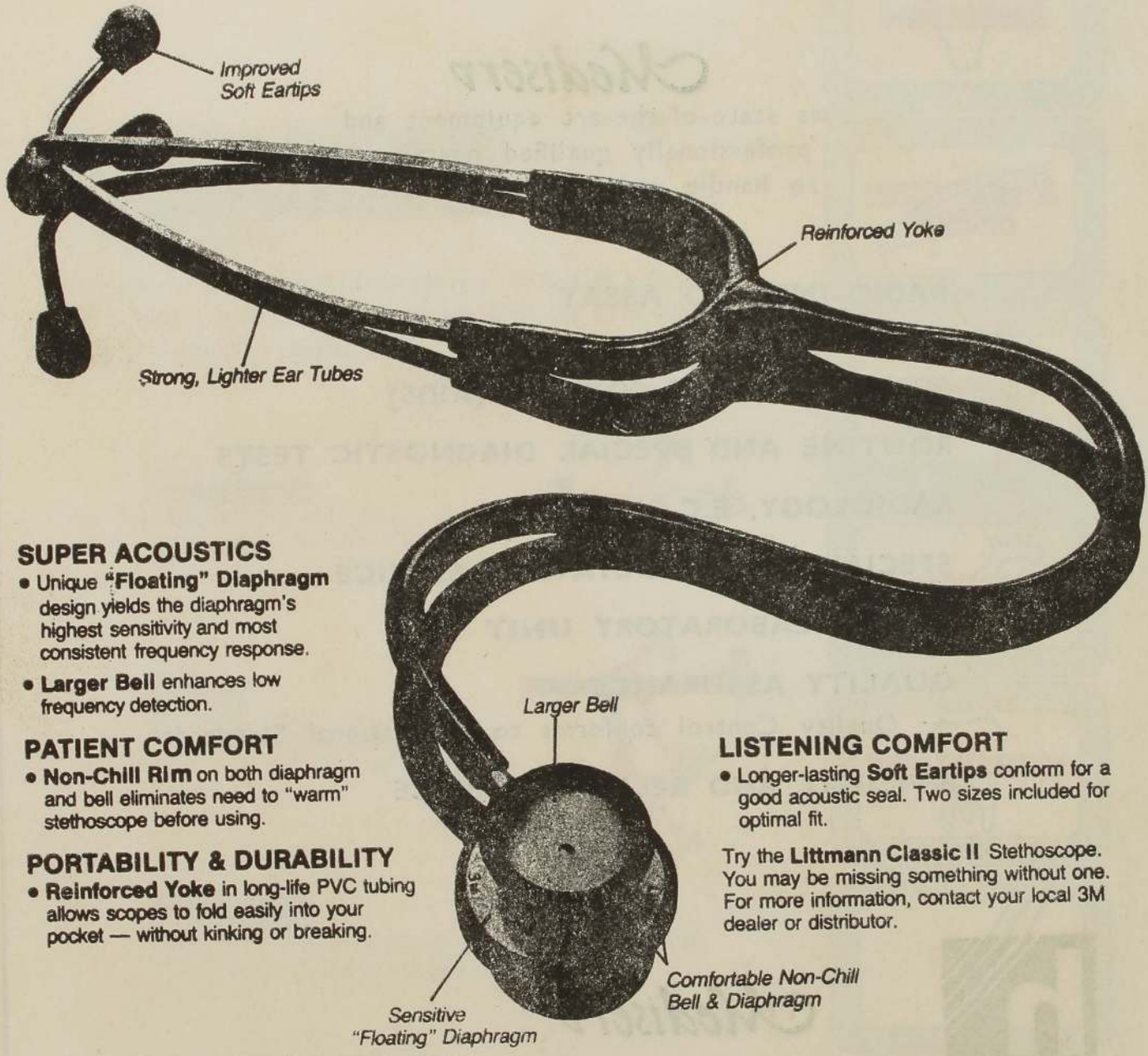

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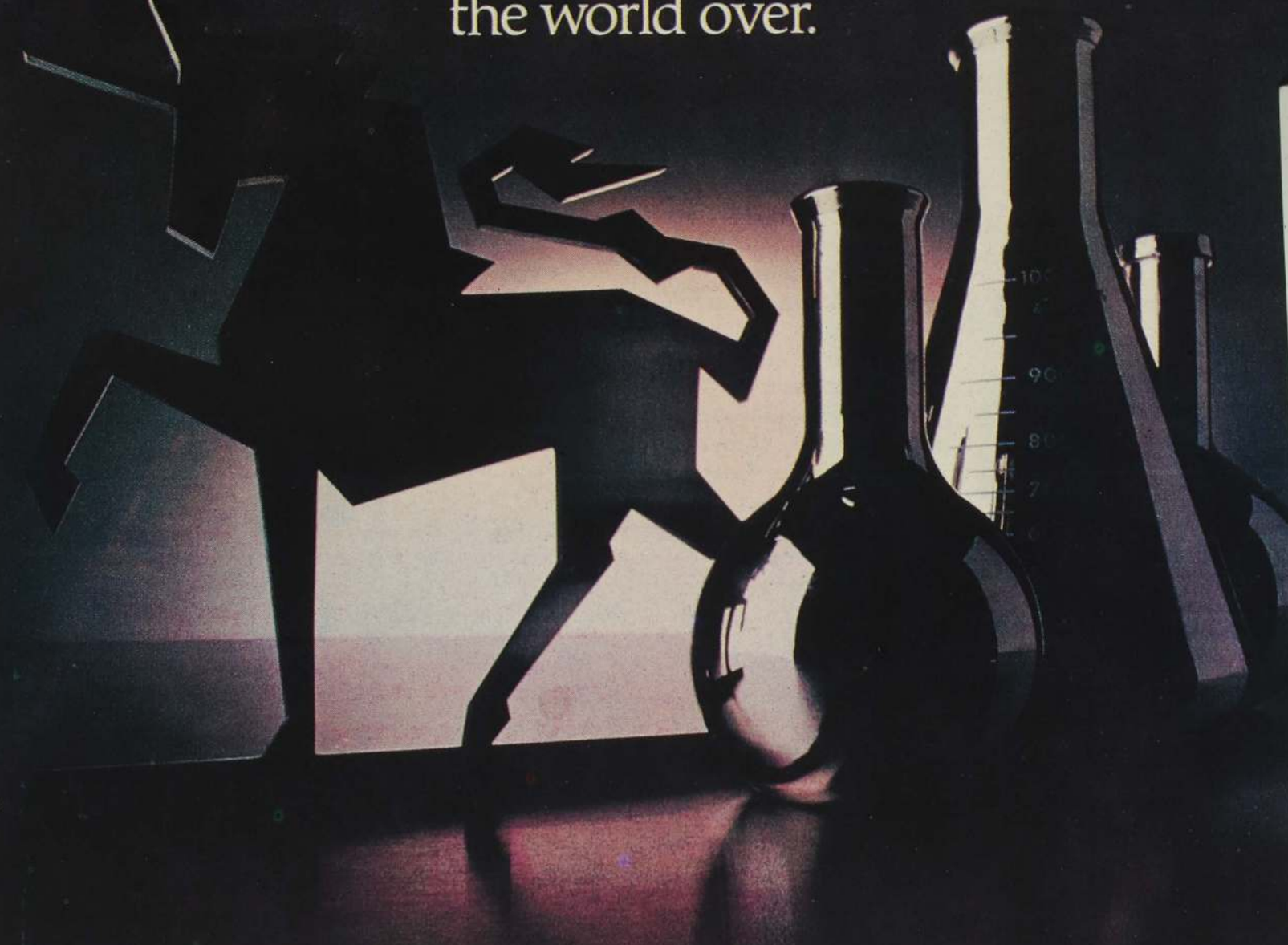

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All authors must give signed consent for publication, and the posts held at the time they did the work reported

Three copies should be submitted **typed** on one side only of A4 paper with double spacing and 5 cm margins at the top and left hand side.

Only **standard abbreviations** of units should be used in the text.

References should be indicated by a superscript number in the order in which they appear in the text, and listed in this order at the end of the article.

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Tables and illustrations should be separate from the text of the paper. Tables should be simple and should not duplicate information in the text of the article.

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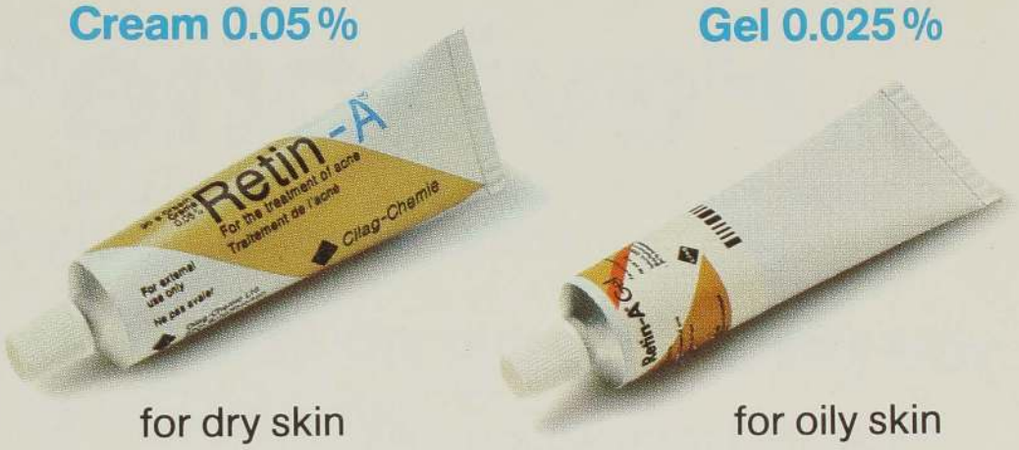

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Leading Article

Shigellosis: a Killer Disease

Ceylon Medical Journal, 1990, **35**, 1–4

Shigellosis is undoubtedly one of the foremost diarrhoeal diseases causing heavy morbidity and mortality amongst children in Third World countries; adults are not spared and sporadic cases are found in developed countries as well. It is an ancient disease, descriptions of it dating back to the time of Hippocrates.

Shigella species belong to the family Enterobacteriacea and are gram-negative non-motile organisms. Strains of Shigella can be characterised by specific cell wall antigens and there are four serologic groups responsible for disease in man. The clinically important species within the respective groups are S. dysenteriae type 1 (shiga bacillus), S. flexneri, S. boydii and S. sonnei. Usually S. boydii and S. sonnei are responsible for mild disease whereas S. flexneri and especially S. shigae are responsible for more virulent infections and epidemics. Shigellosis is world-wide in distribution, occurring in arctic, temperate and tropical climates. Over the last decade S. sonnei has accounted for most of the Shigella isolations in the USA, UK, Western Europe, Japan and Korea. It has been suggested that the predominance of S. sonnei within a particular country is associated with increasing industrialisation, economic development and a higher standard of living[1].

During the last 20 years serious epidemics have occurred in Central America, Africa and South Asia, due predominantly to S. shigae. From 1969 to 1971 more than half a million cases of shigellosis occurred in Central America (Guatemala, Belize, El Salvador, Honduras, Nicaragua and Costa Rica) causing about 20 000 deaths. In some villages the case fatality rate was as high as 10 to 15%[2]. The high mortality during this epidemic was due to delayed diagnosis because of difficulties in culturing the organism and Entameoba being wrongly implicated as the causative agent. Although Shigella affects pre-school children predominantly, no age group is immune. It has been mentioned that during times of war, shigellosis perhaps contributes to more disability and death among soldiers than those caused by armaments[3].

In Sri Lanka, shigellosis became a problem after 1976; at present health care workers in every province have become familiar with it due to frequent epidemics at times of drought and floods. The South Asian epidemic had its origins in Bangladesh and spread southwards via Tamil Nadu to Sri Lanka, where the first outbreak occurred in the Jaffna peninsula in 1976[4]. Thereafter it spread through the length and breadth of our country rapidly. In Sri Lanka also initially some cases were misdiagnosed as cases of amoebic dysentery due to difficulties in culturing the organism and mis-identification of motile macrophages with ingested red cells in stool smears as amoebic trophozoites.

Shigella is a unique organism because it is adapted to virtually one host, namely man; primates and dogs are occasional victims. Because the host-parasite relationship is limited, shigellae depend on direct or indirect human-to-human contact to perpetuate themselves in nature. Thus maintenance of infection in a population depends on effective faeco-oral transmission which is related to environmental sanitation and personal hygiene. Some strains of shigellae induce mild and occasionally asymptomatic infections, ensuring their maintenance in the community. An asymptomatic carrier state exceeding one year has been documented for some strains.

The number of organisms needed to cause disease is small (between 10 to 100) in shigellosis, compared to non-invasive toxigenic pathogens such as V. cholerae and E. coli (10^8 organisms). Classically a patient develops fever, abdominal pain, painful defaecation (tenemus) and passes many stools per day (usually more than 20) which are of small volume and bloody-mucoid in appearance. It is important to remember that the initial presentation may be that of a watery diarrhoea which is clinically indistinguishable from a rotavirus or toxigenic E. coli diarrhoea in young children. However the watery phase lasts only a few hours to a few days before the classic dysentric phase appears. As S. shigae causes the most virulent infection, the watery phase may be overlooked because of rapid progression to dysentery.

Shigellae elaborate many toxins such as enterotoxin, cytotoxin and neurotoxin. As the ingested organisms pass through the ileum, the enterotoxin induces a watery diarrhoea. Once the bacilli reach the colon, they invade the colonic mucosa causing intense inflammation and superficial ulceration. As the shigellae invade the colon but not the jejunum it is postulated that a site-specific receptor mechanism is responsible which selectively recognises virulent bacteria and promotes bacterial penetration of the colonic mucosa. The cytotoxins are responsible for the destruction of colonic mucosal cells. The inflammatory response is limited to the superficial mucosa and it is rare for shigellae to invade the blood stream and cause a bacteraemia. The cytotoxins and the neurotoxins are responsible for the systemic complications which are thought to be mediated through immunological mechanisms.

Complications include neurological manifestations (seizures, altered levels of consciousness), haemolysis, haemolytic-uraemic syndrome, acute renal failure, prolapse of rectum, toxic megacolon, protracted diarrhoea, hyponatraemia, and an arthropathy affecting the knee joints in adults. Reiter's syndrome has been described in individuals who have the specific histocompatibility antigen HL-A B 27. The protracted diarrhoea contributes to gross marasmus in many children. The haematological changes consist of a leukaemoid reaction, thrombocytopaenia, presence of burr cells, helmet cells (schistocytes) in peripheral blood, and anaemia. A leukaemoid reaction (over 50×10^9/litre) has been observed in young children with S. shigae infection and is associated with an increased mortality[4 5 6]. Most deaths are due to renal failure. Many patients who develop renal failure require peritoneal dialysis. In Tamil Nadu, the commonest

cause of acute renal failure in children under 5 years was shigellosis in 1977[7]. Recently hyponatraemia has been documented in haemolytic-ureamic syndrome associated with bloody diarrhoea[8]. We have observed this phenomenon in Galle during a recent epidemic. As hyponatraemia is difficult to detect clinically, it should be remembered as a potential cause for seizures in a child with dysentery.

How should cases of shigellosis be treated? As in any other diarrhoeal illness, hydration should be looked after. Oral hydration fluid (*Jewanee*) should be given to patients who are able to drink. Intravenous fluids would be required in patients with evidence of severe dehydration. The WHO has recommended that antibiotics should be used in suspected cases of shigellosis with moderate to severe illness[9]. However, shigella is notorious for developing antibiotic resistance. This phenomenon has been reported in many countries in Central America[10], Africa[11], Bangladesh[12] and Sri Lanka[13]. In 1976 during the initial epidemic in Sri Lanka, the organisms were found to be resistant to antibiotics such as ampicillin and cotrimoxazole but sensitive to furazolidone and nalidixic acid[4]. Furazolidone was extensively used because it was the cheaper antibiotic. Few years later, the shigellae became resistant to it and nalidixic acid was used, only for it to develop resistance to that drug as well[13]. During the epidemic in 1989, studies in Galle showed that S. dysenteriae has become sensitive to furazolidone again but remains resistant to nalidixic acid (Dr. C. Perera, personal communication). The surest way to promote antibiotic resistance is to treat patients with inadequate doses for too short a period. It is prudent to be guided by the correct local antibiotic sensitivity patterns when choosing an antibiotic to treat a suspected case of shigellosis, and to use it for a minimum of five days. Anti-diarrhoeal agents are contraindicated in the management of acute bacillary dysentery[9]. Fresh blood transfusions are a useful adjuvant when there is evidence of haemolysis.

In Sri Lanka, hundreds of patients have succumbed to shigellosis since 1976. No effective vaccine is available as yet because of the presence of numerous serotypes, the need for booster vaccination and the brief period of immunity. Therefore, personal hygiene and environmental sanitation are important tools in its prevention. Hand-washing with soap has been shown to be effective in preventing person to person spread[14]. During outbreaks of shigellosis it is of paramount importance for the local health authorities to chlorinate wells, encourage people to drink boiled water and improve environmental sanitation. As stated earlier, from a microbiological point of view, when S. sonnei overtakes S. shigae as the more prevalent organism in Sri Lanka, we would know that we are progressing in the correct direction!

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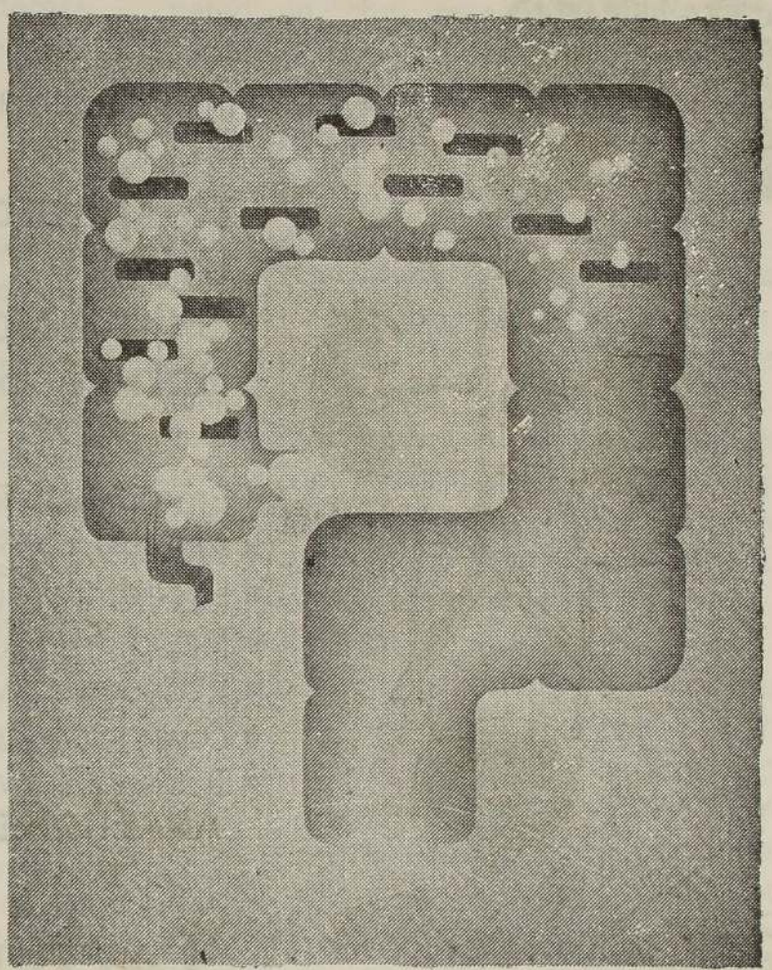

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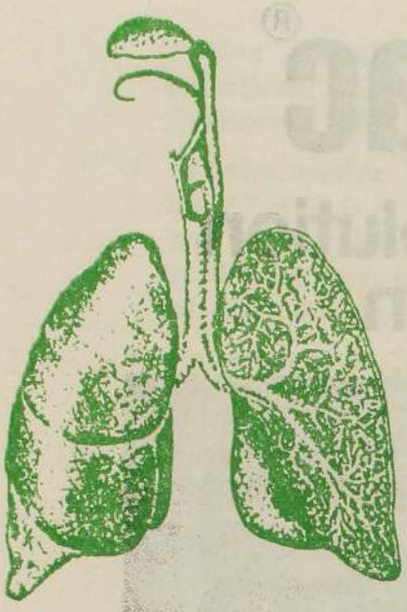

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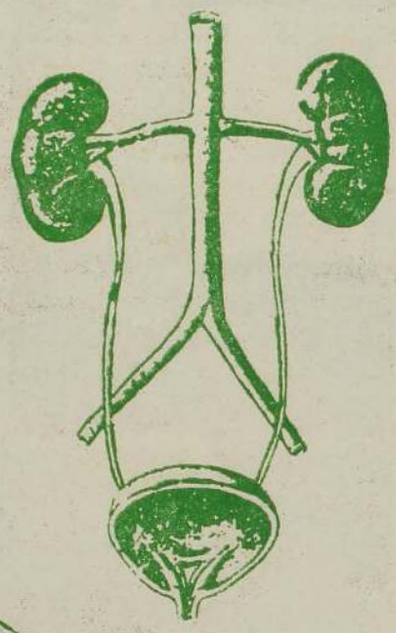

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cause of acute renal failure in children under 5 years was shigellosis in 1977[7]. Recently hyponatraemia has been documented in haemolytic-ureamic syndrome associated with bloody diarrhoea[8]. We have observed this phenomenon in Galle during a recent epidemic. As hyponatraemia is difficult to detect clinically, it should be remembered as a potential cause for seizures in a child with dysentery.

How should cases of shigellosis be treated? As in any other diarrhoeal illness, hydration should be looked after. Oral hydration fluid (*Jewanee*) should be given to patients who are able to drink. Intravenous fluids would be required in patients with evidence of severe dehydration. The WHO has recommended that antibiotics should be used in suspected cases of shigellosis with moderate to severe illness[9]. However, shigella is notorious for developing antibiotic resistance. This phenomenon has been reported in many countries in Central America[10], Africa[11], Bangladesh[12] and Sri Lanka[13]. In 1976 during the initial epidemic in Sri Lanka, the organisms were found to be resistant to antibiotics such as ampicillin and cotrimoxazole but sensitive to furazolidone and nalidixic acid[4]. Furazolidone was extensively used because it was the cheaper antibiotic. Few years later, the shigellae became resistant to it and nalidixic acid was used, only for it to develop resistance to that drug as well[13]. During the epidemic in 1989, studies in Galle showed that S. dysenteriae has become sensitive to furazolidone again but remains resistant to nalidixic acid (Dr. C. Perera, personal communication). The surest way to promote antibiotic resistance is to treat patients with inadequate doses for too short a period. It is prudent to be guided by the correct local antibiotic sensitivity patterns when choosing an antibiotic to treat a suspected case of shigellosis, and to use it for a minimum of five days. Anti-diarrhoeal agents are contraindicated in the management of acute bacillary dysentery[9]. Fresh blood transfusions are a useful adjuvant when there is evidence of haemolysis.

In Sri Lanka, hundreds of patients have succumbed to shigellosis since 1976. No effective vaccine is available as yet because of the presence of numerous serotypes, the need for booster vaccination and the brief period of immunity. Therefore, personal hygiene and environmental sanitation are important tools in its prevention. Hand-washing with soap has been shown to be effective in preventing person to person spread[14]. During outbreaks of shigellosis it is of paramount importance for the local health authorities to chlorinate wells, encourage people to drink boiled water and improve environmental sanitation. As stated earlier, from a microbiological point of view, when S. sonnei overtakes S. shigae as the more prevalent organism in Sri Lanka, we would know that we are progressing in the correct direction!

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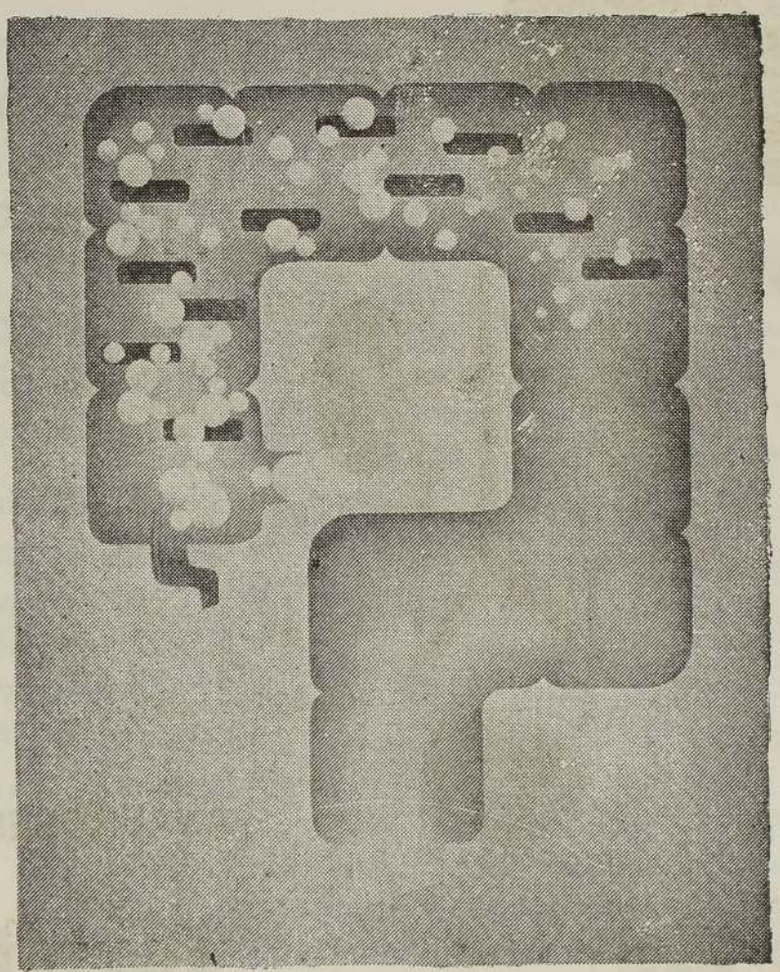

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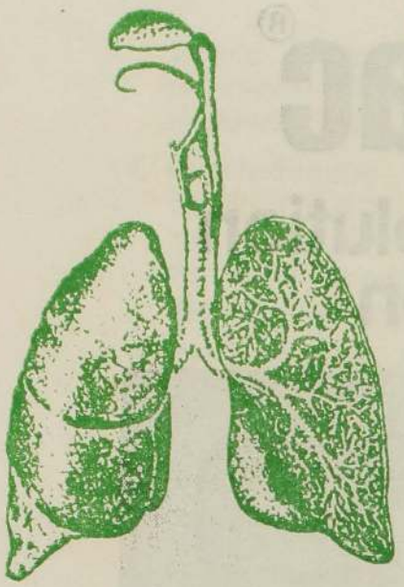

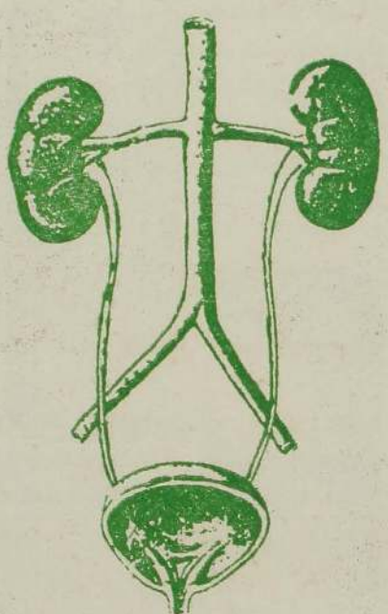

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Leading Article

Platelet Anti-aggregatory Therapy in Pregnancy: Another Role for Low Dose Aspirin ?

Ceylon Medical Journal, 1990, **35,** 5–9

Pregnancy induced hypertension (PIH) (or pre-eclampsia), foetal intra-uterine growth retardation (IUGR), and foetal death-in-utero (DIU) are universal problems in obstetric practice. They raise questions regarding the prevention of serious complications in current and subsequent pregnancies.

Some pathophysiological events causally related to the above conditions have been clarified during the past decade, though gaps still remain [1 2 3]. New prophylactic interventions evolved on the basis of such pathophysiological events seem to provide a hope of success in the management of these conditions, which generally carry a poor prognosis for the foetus [4 5].

Clinically significant levels of hypertension should be managed with anti-hypertensive drugs. This therapy helps to prevent more serious maternal complications while maintaining optimum peripheral tissue perfusion. Adequate placental perfusion is vital for foetal survival and growth, and is determined by normal changes in the structure and behaviour of the placental bed decidual spiral arteries[3]. In fact PIH may be a "physiological" response to compensate for the impaired placental bed perfusion caused by the failure of normal placentation[1]. This is similar to other diseases resulting from coagulation and vascular phenomena which occur in coronary and cerebro-vascular occlusion[5].

The discovery of prostacyclin (PgI_2) and thromboxane (TxA_2) was an important step in clarifying the pathophysiology of these conditions. PgI_2/TxA_2 ratio is known to play a central role in the above disorders[5], and the use of low dose aspirin to shift the balance in favour of the latter is now an established mode of treatment[7].

Links between prostaglandins and the reproductive system date from the time their actions were first described by Kurzrob and Lieb[8]. The implication of such potent vaso-active agents in PIH was therefore inevitable[3]. In normotensive pregnancies the PgI_2/TxA_2 ratio is weighted towards the former, but remains biased towards thromboxane production in pregnancies destined to eventually develop PIH and IUGR[1 6], and as in coronary artery disease, prophylactic low dose aspirin therapy has been used in an attempt to reverse this effect[6].

Commonly practiced management involves the use of bed rest to prevent IUGR and anti-hypertensive drug therapy to contiol hypertension. Foetal outcome however, has not improved as much as expected. Bed rest improves uterine perfusion, but the enhanced flow may not reach the placental bed. Locally produced prostanoids play a significant part in the distribution of blood within the uterus as they do in the kidneys[1]. Their production and distributron within the uterus can vary in a number of ways[9].

Intra-uterine tissues are sites of prostanoid synthesis, particularly during pregnancy[1]. Foetal blood vessels, placenta and membranes produce more of vasodilatory prostaglandins (PgE_2 PgI_2) while the decidua synthesises more of vasoconstrictor prostanoids, ($PgF_{2\alpha}$ TxA_2). In PIH there is a relative decrease of vasodilator prostanoids in the placenta[10] and liquor amnii[11], which is reflected in the metabolites in the urine[13]. A similar trend is observed in the foetus in PIH and IUGR[12]. Amniotic fluid endogenous factors affecting prostaglandin synthesis are also altered during PIH[14]. A net vasoconstrictor effect results, causing poor placental perfusion. The role of prostanoids in chronic hypertensive disease has not been extensively studied although similar changes could be expected if normal placentation fails. Analysis of results in this instance has to be made in relation to IUGR in addition to the hypertension.

Presently available data suggest that platelet anti-aggregatory therapy improves foetal prognosis by dilating the "feeder" blood vessels of the placental bed[4 15] by a mechanism similar to prophylactic therapy in coronary and cerebral vascular disease[7]. Aspirin and other non-steroid anti-inflammatory drugs irreversibly block the cyclo-oxygenase enzyme in all mammalian tissues[16]. The vascular endothelium can regenerate the blocked enzyme while the platelets, which are anucleate, cannot do so[17]. Thus the PgI_2/TxA_2 ratio shifts towards the former until the re-entry of fresh platelets, while low dose aspirin therapy can shift the PgI_2/TxA_2 balance towards the former. A long term high dose can nullify this effect by blocking even the freshly generated cyclo-oxygenase in the vascular endothelium.

A general impression has been created recently that low dose aspirin therapy has a good potential as an anti-hypertensive agent[4 5 15]. Closer examination of the data from available studies only suggests that it may be of benefit in the prophylaxis against developing PIH later on in pregnancy. The study by Wallenburg and co-workers[5] is particularly relevant, as the subjects were selected by the angiotensin II infusion test, which is the only accepted method for predicting a tendency for PIH in any particular pregnacy. No statistically significant difference in the foetal outcome has been noted. Treatment had been commenced after 28 weeks of gestation.

In contrast Beaufils and his group[4] selected subjects with a poor obstetric history in the past and platelet anti-aggregatory treatment was given as a prophylactic measure from the end of first trimester. The possible benefits of platelet anti-aggregatory therapy in preventing PIH are also shown here. Of greater significance is the better foetal outcome noted in the test group. The analysis however, seems to be incomplete as the foetal outcome and the incidence of PIH should be further studied after excluding the subjects with previous early abortions. This study illustrates the benefits of early commencement of platelet anti-aggregatory therapy at a stage when it may influence the important changes of the second phase of placentation.

During the second phase of placentation which commences at the end of the first trimester, trophoblastic invasion of the decidual spiral arteries

is extended into its myometrial segment[16]. This important change fails to occur in pregnancies destined to result in PIH, IUGR and DIU irrespective of the presence of hypertension[3 15]. The poor placental perfusion that results would therefore cause an impairment of foetal growth and the systemic hypertension during the third trimester has been postulated to occur to compensate for this lack[1].

The possible role of prostanoids in establishing a normal second phase is supported by some clinical[4] and experimental[20] evidence. Prostacyclin appears to be necessary for the establishment of a normally functioning placental unit[20]. Platelet anti-aggregatory therapy, by shifting the PgI_2/TxA_2 balance in favour of prostacyclin should be able to achieve this. Preliminary results from an on-going study at the Obstetric and Gynaecology Unit of the University of Colombo seems to support this view. Women with the highest possible risk ie. with chronic hypertensive disease and a history of repeated foetal deaths or IUGR, were offered treatment with low dose aspirin. When therapy was started after the 23 week the foetus did not survive beyond the 32 week, but commencement of the drug in the early second trimester resulted in a successful foetal growth and survival until term, and a healthy neonate.

Although there are many pharmacological methods of controlling prostaglandin synthesis[21] the use of cyclo-oxygenase inhibitors acting at the pre-endoperoxide stage is the most convenient one[7]. Of all the cyclo-oxygenase inhibitors available aspirin is the one most extensively used so far for platelet anti-aggregation, although other non-steroid anti-inflammatory drugs could also be used clinically. To inhibit platelet aggregation further, dipyridamole has also been added[4]. Many dosage regimes of aspirin have been used during pregnancy and in the non-pregnant state with good results [4 5 15]. In non-pregnant subjects a daily dose of 40 mg is sufficient to inhibit thromboxane production within the veins while maintaining adequate prostacyclin synthesis[21]. *In vitro* experiments performed two hours after the administration of the drug gave the 50% inhibitory dose of aspirin for platelet aggregation as 2.5 to 3.2 mg/kg of body weight[17]. During pregnancy, varying daily doses ranging from 40 to 150 mg have been used. Since this therapy depends on the adequate recovery of prostacyclin production it is essential that the lower doses be used. If doses greater than 150 mg are used they could be administered every other day. It is important to ensure that the lower doses are used, as no facilities for biochemical monitoring or assessment of platelet aggregation with an aggregometer are available in Sri Lanka.

In summary, what we would like to emphasise strongly on the basis of the available data is that platelet anti-aggregatory therapy during pregnancy should be reserved for use only as a prophylactic measure in cases selected on the basis of previous IUGR and DIU with or without hypertension. The lower doses of aspirin should be used, and careful clinical assessment should precede any increase in dosage. The use of this therapy as an anti-hypertensive regime is irrational, and

the dose should not be increased merely to treat non-responsive hypertension which is better managed with appropriate anti-hypertensive drugs. It is essential that foetal growth and well-being are monitored carefully. It is advisable to stop the drug 24 hours before delivery so as to avoid post-partum haemorrhage due to coagulation impairment. The neonate also should be examined carefully for any adverse effects of the drug.

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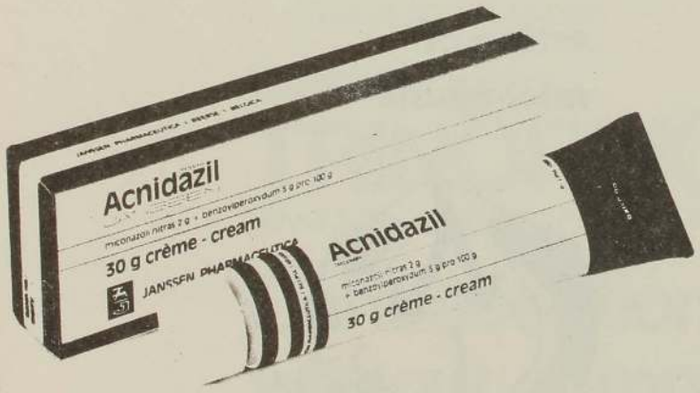

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Cryptosporidiosis – Oocyst Shedding and Infection in Household Contacts

JENNIFER PERERA[1] and G N LUCAS[2]

Ceylon Medical Journal, 1990, **35**, 11-14

Summary

The incidence of cryptosporidiosis in children with acute diarrhoea when compared with age-matched controls was 6.1% in a paediatric unit. Studies were made on eight immunocompetent children with cryptosporidiosis to determine the period of oocyst shedding after cessation of diarrhoea. The majority (75%) shed oocysts for less than ten days after cessation of diarrhoea. There was considerable variation among patients, some eliminating oocysts more quickly than others. This was not related to the severity or duration of diarrhoea. The sucrose floatation technique was found to be more sensitive than direct smear for detecting small numbers of oocysts present at the end of the shedding period. Studies on household contacts showed infection in 43%, which suggests a subclinical infection or a transient carrier state, and confirms the occurrence of person to person transmission.

Introduction

Cryptosporidia are coccidian parasites which have been identified in animals since 1907[1]. The first description of disease in humans however, was not until 1976[2]. Most earlier reported cases have occurred in immunodeficient patients in whom cryptosporidial infection causes prolonged watery diarrhoea which is often fatal[3]. There have been several recent reports of acute gastroenteritis associated with *Cryptosporidium* occurring in apparently immunocompetent adults and children[4].

Although infection in immunocompromised patients may be life-threatening, it is likely that infection in the immunocompetent is numerically more important. Little is known of the epidemiology of this infection, including the infective dose of *Cryptosporidium* mode of spread, source of infection, incubation period and duration of excretion of oocysts. One of us ha previously reported the clinical details of 11 children with cryptosporidiosis[5]. We now present the results of a prospective study of stool examination for *Cryptosporidium* oocysts from children with diarrhoea compared with a control group who did not have diarrhoea. The incidence of infection in family contacts, and the speed and efficiency with which the patients eliminate oocysts are discussed.

Materials and methods

The patients were 162 children with acute diarrhoea admitted to Ward 8 of Lady Ridgeway Hospital from April to August 1987. The controls were 98 patients admitted to the same ward for other conditions. The age

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Table 1

Age distribution of the study group

No.	*Age range*	*Mean age ± SD*	*Median age*
Patients 162	2m to 10y	2y 5.5m ± 2y 7.3m	1y 5m
Controls 98	2m to 10y	2y 5.9m ± 2y 9m	1y 5m

m = months y = years SD = standard deviation.

distribution of the study group is shown in Table 1.

Stools were collected soon after admission to hospital and examined for *Cryptosporidium* oocysts by a direct smear method[5], and if this was negative, by the sucrose phenol concentration method[6], which is widely accepted as the most sensitive technique for the detection of small number of oocysts[7]. From positive cases samples of faeces were collected every 4 to 5 days, during and particularly after the illness, and further information was obtained from the mother with the aid of a questionnaire. Specimens of stools were also obtained from household contacts of these index cases within seven days of diagnosis.

Results

Incidence. *Cryptosporidium* oocysts were detected in stools from 10(6.1%) children out of 162 children with diarrhoea and only from one out of 98 age-matched controls. The control patient with cryptosporidia had wheezy bronchitis but was otherwise well and never had gastrointestinal symptoms or a contact history of diarrhoea in the recent past. A second specimen of stool obtained after five days from the control patient did not contain oocysts. All positive cases were detected on the direct smear.

Duration of oocyst shedding. The mean duration of diarrhoea was 7(SD 3.5) days with a range from 5 to 21 days. The beginning of oocyst shedding was not known for all patients. Therefore we concentrated on the duration of oocyst shedding after cessation of diarrhoea. Eight patients were followed up further during and after illness by examining specimens of stools. When direct smear technique was used to detect oocysts, the last positive and the first negative specimens were detected at mean periods of six and ten days after cessation of diarrhoea respectively. However, there was considerable variation among patients, the range being 2 to 20 days after cessation of diarrhoea. With the floatation method oocyst shedding was detected for slightly longer periods as shown in Table 2. Thus the general superiority of the floatation technique to detect small numbers of oocysts was evident.

In general the duration of oocyst shedding was not related to the duration of diarrhoea. None of the features examined, namely age, sex, severity of diarrhoea or of other symptom, correlated with the pattern of oocyst shedding.

Contacts. Contact with animals: none of these patients had close contact with domestic pets or farm animals.

Household contacts : Specimens of stools were examined from 23 family members of the eight index cases

Table 2

Duration of oocyst shedding after cessation of diarrhoea in eight patients

Method	*Last positive specimen* days ± SD (range)	*Last negative specimen* days ± SD (range)
Smear	5.6 ± 4.3 (2 to 16 days)	10.7 ± 4.0 (8 to 20 days)
Float	10.4 ± 5.8 (6 to 24 days)	14.9 ± 5.7 (10 to 28 days)

Ten (43%) contacts from five households were excreting *Cryptosporidium* oocysts. Out of them 7(70%) were children and 3(30%) had mild gastrointestinal symptoms such as abdominal pain and loose stools. The number of oocysts excreted was less than in symptomatic patients and in a few we found excretion to be transient.

Discussion

The incidence of cryptosporidiosis was 6.1% which confirms our earlier finding in a study conducted on random stool samples[5]. So far little information has been collected about the duration of oocyst shedding in human cryptosporidiosis. In infected lambs and calves shedding coincides with diarrhoea and ceases shortly afterwards[8]. Although recognition of oocysts in suitably stained smears of faeces is a convenient method for laboratory diagnosis of cryptosporidiosis, the sucrose phenol floatation technique is more sensitive for monitoring the shedding of oocysts. Baxby and co-workers[9] used sucrose floatation method and found that 60% shed oocysts for less than one week after cessation of diarrhoea. A study[10] carried out in Finland used modified Ziehl-Neelsen staining of faecal formalin -ether concentrates. In this study it was found that 73% had positive stools after cessation of symptoms for a mean period of 6.9 days. In our study when the sucrose floatation technique was used for monitoring, a majority (75%) of cases shed oocysts for less than 10 days after cessation of diarrhoea, and this generally agrees with findings of other workers.

From an epidemiological point of view oocyst shedding after cessation of diarrhoea is important. Consequently, it would be reasonable to regard patients as infective until oocyst shedding ceases. Although initially considered as a zoonosis, there is evidence now of person to person transmission[11 12]. Infection in family members suggests either a common source of exposure or person to person transmission. Symptomless infection in household contacts may have been either a subclinical infection or a carrier state. Symptomless infection with *Cryptosporidium* and other intestinal pathogens have been reported in studies carried out in India[13] and Thailand[14]. Repeated stool examination should be done in symptomless carriers to detect whether the carriage is long term or transient. In developing countries multiple infections of the gut are common. Microbial synergism could be at work in mixed infections. Thus the influence of other intestinal pathogens on cryptosporidial infection requires investigation.

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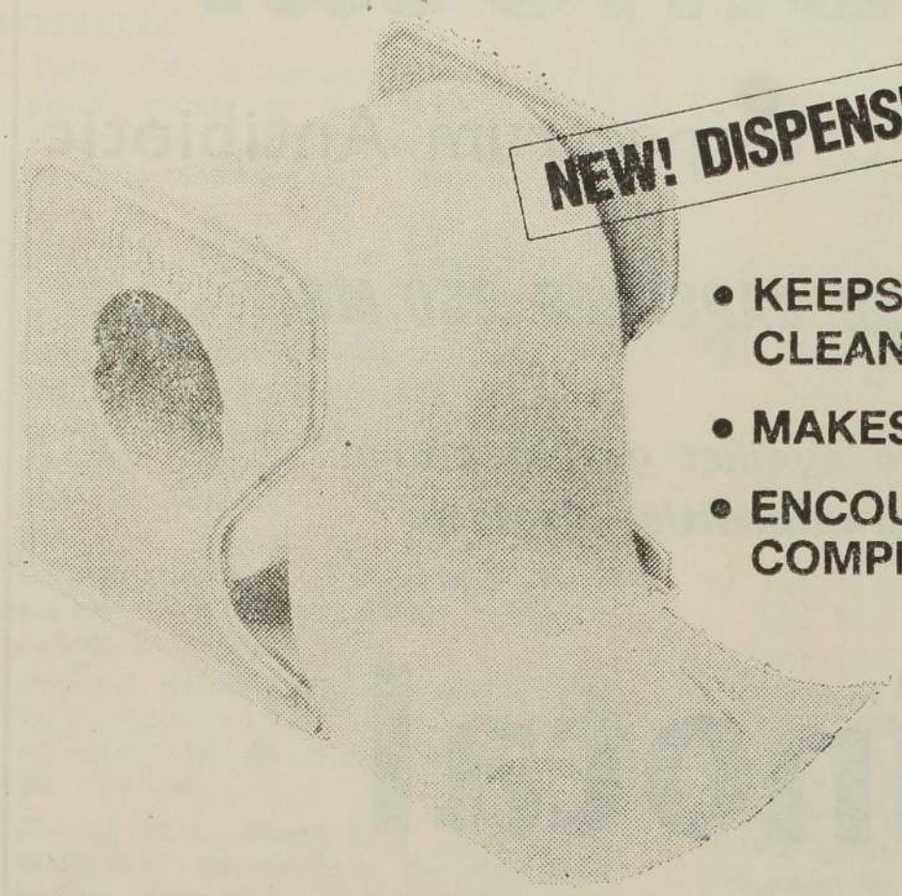

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Effectiveness of Mass Treatment with Mebendazole in the Control of Soil Transmitted Helminths in Sri Lanka

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Ceylon Medical Journal, 1990, **35**, 15-20

Summary

The efficacy of a single large dose of mebendazole was compared with the three-day multiple dose in mass treatment. The subjects were selected from among plantation workers of a tea estate in Kandy. The multiple dose regime showed consistently better egg reduction rates and cure rates when compared to the single large dose in subjects harbouring one or more soil-transmitted helminths.

Introduction

Soil-transmitted helminthiasis is one of the major public health problems in Sri Lanka[1]. Despite the high prevalence of helminthiasis there have been no serious efforts made to launch a well organised control programme in this country. Some progress has been made in the education of the public in the use of latrines, and in the provision of sanitary latrines in communities where these were scarce. However, one of the most important aspects of helminthiasis control programmes, mass chemotherapy, has not been attempted on a significant scale in Sri Lanka in recent times.

Periodic mass treatment of communities has been considered an important component of soil-transmitted helminthiasis control[2]. By effective mass treatment the number of parasites per person and consequently the total number of parasites in a given community are reduced. This would eventually lead to a smaller number of eggs polluting the soil, thus reducing the chances of re-infection.

Broad-spectrum anthelminthics play an important role in the treatment of poly-parasitism due to soil-transmitted helminths. These drugs are very effective against *Ascaris* infections where even a single small dose could give almost 100% egg reduction and cure rates[3,4]. However their efficacy against *Trichuris* infections in a single dose is much lower[4]. This is considered to be due to the mode of attachment of this parasite to the large intestinal mucosa.

Most broad-spectrum anthelminthics have to be administered in multiple doses over several days, with the exception of the relatively new drug albendazole. With some, such as pyrantel/oxental pamoate dosage is based on the body weight.

Drug regimes requiring multiple doses over several days and those based on

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body weight have no serious disadvantages when used in the treatment of individual patients. But they have distinct disadvantages when used in mass treatment programmes. Increase in the dose of a drug or in the duration of treatment leads to increased cost and decreased patient compliance. Consequently the use of a single dose regime has obvious advantages in such programmes.

The introduction of the 500 mg mebendazole tablets to the market in recent times was expected to overcome some of the major disadvantages of the earlier preparation of the drug (100 mg tablets) which had to be given as two doses a day for three days.

This study was undertaken to compare the efficacy of mebendazole 500 mg in a single dose with that of the multiple dose treatment in the field.

Materials and methods

Two hundred and twenty five apparently healthy people, excluding infants and pregnant mothers were selected for the study. They were plantation workers from two separate divisions of the Hantana Tea Estate situated 2 000 feet above sea level in the outskirts of Kandy.

Faeces collecting kits (plastic containers with lids fitted with scoops) were individually labelled with the name and a serial number. These were delivered to all households in the two study areas with clear instructions for collection of stool samples. Stool samples were collected and delivered to the laboratory at the Faculty of Medicine, Peradeniya, in batches of 50, on the dates of collection. These were examined by two experienced laboratory technicians using the Katz modification of the Kato's thick smear technique[5]. Quantitative estimation of eggs per gram faeces was carried out in all positive samples.

All subjects whose stools were positive for one or more soil-transmitted helminths were administered treatment. All positive subjects from one division of the estate were allotted to schedule A and those from the other division to schedule B.

Subjects in schedule A received a single tablet of 500 mg of mebendazole. There were 103 subjects in this group and they took the tablet under supervision. Those in schedule B were administered 100 mg mebendazole twice a day for a period of three days. There were 111 subjects in this group, and the compliance was not expected to be 100% as the drug was not taken under supervision.

Stool samples were collected between 11 and 17 days of the treatment. The same procedure for collection, despatch and examinations was followed as before.

Results

1. Initial prevalence

A total of 225 subjects from both groups gave a stool sample each for the pre-treatment examination. Of them 214 (95%) were found to contain one or more species of soil-transmitted helminths, showing that the area under study is one of heavy infestation. Of the 103 who were on schedule A, 69 (67%) were positive for *Ascaris*, 91 (88%) for *Necator*, and 68 (66%) for *Trichuris*. The corresponding figures for those on schedule B were 95 (86%) for *Ascaris* and 100 (90%) for *Necator* and 72 (65%) for *Trichuris*.

2. Response to treatment

The cure rate for *Ascaris* infestation was 88 and 95% for the schedules A and B respectively, as shown in Table 1. The difference in cure rates was not significant for *Ascaris*, but was highly significant ($P < 0.01$) for *Necator* and *Trichuris*. The egg reduction rates (ERR) for the two treatments are also given in Table 1. The mean eggs per gram (MEPG) faeces for those on schedules A and B are shown in Tables 2 and 3 respectively. The reduction in MEPGs was more pronounced with schedule B.

Both treatment schedules were found to be more effective against single infections than for multiple infections.

Table 1

Response to treatment

	Schedule A		*Schedule B*	
	Cure rate	*ERR*	*Cure rate*	*ERR*
Ascaris lumbricoides	88	91	95	98
Necator americanus	19	46	76	85
Trichuris trichura	29	49	79	95

ERR - Egg reduction rate

Table 2

Egg reduction rates and cure rates following treatment
Schedule A single dose mebendazole (500 mg)

Parasite species	*Total treated*	*Pre-treatment MEPG* (range)*	*Post-treatment MEPG* (range)*	*ERR** (%)*	*CR*** (%)*
Al	69	5849 (80 - 51880)	575 (0 - 22120)	57	88
Tt	91	232 (20 - 1520)	117 (0 - 1220)	49	19
Na	68	308 (20 - 1840)	166 (0 - 980)	46	19

* MEPG — Mean number eggs/g
** ERR — Egg reduction rate
*** CR — Cure rate
Al — *Ascaris lumbricoides*
Tt — *Trichuris trichura*
Na — *Necator americanus*

Table 3

Egg reduction rates and cure rates following treatment with 200 mg mebendazole for 3 days

Parasite species	*Total treated*	*Pre-treatment MEPG* (range)*	*Post-treatment MEPG* (range)*	*ERR** (%)*	*CR*** (%)*
Al	95	10054 (240 - 91240)	104 (0 - 620)	98	95
Tt	100	825 (20 - 7640)	38 (0 - 1240)	95	79
Na	72	397 (20 - 1720)	56 (0 - 560)	85	76

* MEPG — Mean number eggs/g
** ERR — Egg reduction rate
*** CR — Cure rate
Al — *Ascaris lumbricoides*
Tt — *Trichuris trichura*
Na — *Necator americanus*

Table 4

Response to treatment by treatment schedule and type of infestation

(Number treated in each group is given in parentheses)

	Cure rate %	
	Schedule A	*Schedule B*
1. Al only	100 (5)	100 (8)
2. Na only	0 (4)	— (0)
3. Tt only	20 (5)	75 (4)
4. Al + Tt	28 (25)	88 (27)
5. Tt + Na	8 (25)	75 (12)
6. Al + Na	67 (3)	66 (3)
7. Al + Na + Tt	19 (36)	59 (57)

Al — *Ascaris lumbricoides*
Na — *Necator americanus*
Tt — *Trichuris trichura*

Both schedules gave a 100% cure rate in subjects harbouring *Ascaris lumbricoides* only. The lowest cure rate of 0% was observed on treatment A in subjects harbouring *Necator* only. The lowest cure rate of 59% was observed on treatment B in subjects having all three parasites (Table 4). The number of single infestations observed in the present study is too small to draw definite conclusions. However, significance testing was un-

dertaken in groups where the sample size was adequate. This test shows that the schedule B is significantly superior ($P<0.01$) to schedule A for the treatment of multiple infections of *Ascaris* and *Trichuris, Trichuris* and *Necator* and *Ascaris*, *Necator* and *Trichuris*.

Discussion

The efficacy of the broad-spectrum anthelminthic mebendazole even when administered in a single small dose against *Ascaris* infection is well established[3]. However, its action against *Trichuris* infection is comparatively less marked[6]. The results of the present study show that a large dose of mebendazole administered as a single dose or in divided doses over a period of three days was able to give 100% cure rates in subjects harbouring only *Ascaris*. These results are similar to those obtained by others.

The results emphasize the efficacy of the multidose regime in single parasite infections as well as multiple parasite infections as shown by the high cure rates and egg reduction rates. This has been shown by others[3 7 8].

Large dose treatment with mebendazole (as in this study) could give lower cure rates in *Trichuris* infections due to two reasons[3]. The share of the drug per parasite may not be sufficient in heavy *Trichuris* infections. This is unlikely to be the cause for lower cure rates with regard to *Trichuris* in the present study. The EPG (232 and 825 — Tables 2 and 3) does not indicate massive *Trichuris* infections. The second and more likely one is that people with trichuriasis often experience diarrhoea, which results in the shortening of the contact time of the parasite with the anthelminthic. Under these circumstances the multiple dose regime over three days may give better results.

With regard to *Necator americanus* infections both regimes give poor results. However, the multiple dose regime was superior to the single dose regime, bringing about higher cure rates and egg reduction rates.

A study carried out in Bangladesh where a single 200 mg dose of mebendazole was used against mixed infections *(Ascaris* and *Trichuris)* showed that this dose was able to yield very high cure rates[9]. The authors recommended the use of this dose (for Bangladesh) as it was very effective, could be administered at any time of the day, had excellent acceptability, low cost and no side effects. They considered the standard three-day treatment with 600 mg mebendazole as not cost effective, and the drugs given on the second and third days a waste[8].

Although our results indicate the effectiveness of the multiple dose regime of membendazole in single or mixed intestinal helminth infections, the advantage of the single dose of mebendazole in mass treatment programmes, remains unchanged. An egg reduction however can be achieved by the single treatment. This may lead to a reduction of the magnitude of soil pollution, resulting in lowered chances of re-infection in a given community but the effect of the single dose treatment is very much lower than that of the 3-day course, thus making the single dose regime a less effective method of mass control.

Our study also shows the need for improving sanitation and sewage disposal in the plantation sector. Despite the provision of sanitary facilities, our study shows the presence of continued soil pollution of the home environment with human faeces in the study areas. The mere provision of sanitary facilities without adequate health education may not fulfil expectations.

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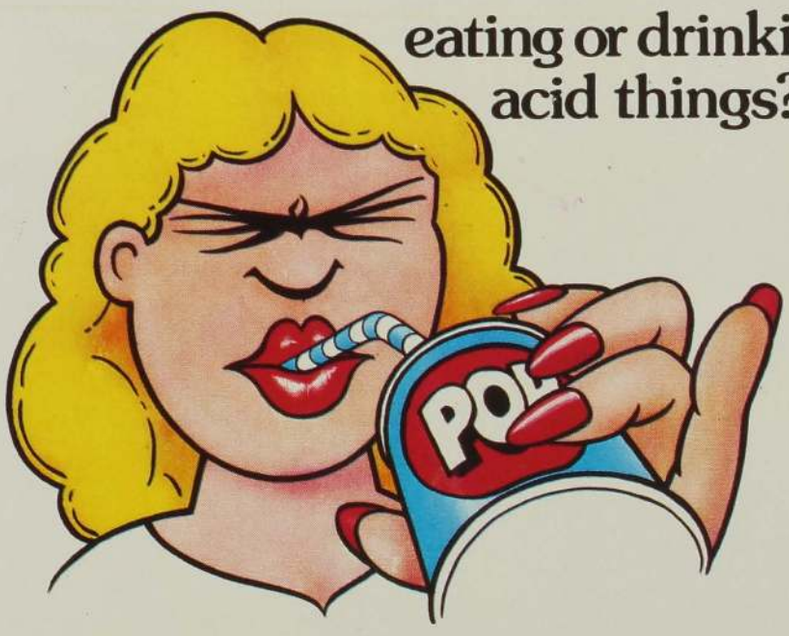

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Glycocalyx Positive Bacteria Isolated from Chronic Osteomyelitis and Septic Arthritis

SYED IQBAL ALAM,[1] KHURSHEED ALI KHAN,[2] AQEEL AHMAD[3]

Ceylon Medical Journal, 1990, **35**, 21-23

Summary

Bacterial cultures isolated from cases of chronic osteomyelitis and septic arthritis were screened for the production of glycocalyx. The presence of glycocalyx was noted in 76.3% of *Staphylococcous aureus*, 57.14% of *Staphylococcus epidermidis*, 50% of *Pseudomonas aeruginosa*, and 75% of *Escherichia coli* isolates.

Introduction

Glycocalyx, a surface exopolysaccharide of bacterial cells plays an important role in the pathogenesis of the organism.[1] Strains of *P. aeruginosa* in cystic fibrosis, *E. coli* in urinary tract infection[2] and *S. mutans* in dental caries[3] were found to be comparatively more virulent due to the presence of glycocalyx. This exopolysaccharide has been reported to mediate bacterial adherence to surfaces, resistance to bacteriophage, specific antibodies, phagocytes and certain antibacterial agents including antibiotics[1,4].

Lambe and Costerton[2] have shown that glycocalyx producing bacteriodes and *S. aureus* are important in the adherence of this organism to bone surface in experimental osteomyelitis. Similarly, others have reported glycocalyx as a virulence factor which provides a mechanism for adherence of bacteria to damaged bone and tissues[5].

The term osteomyelitis, taken literally, implies inflammation of bone and its marrow regardless of whether it is due to a pyogenic organism, tuberculosis, syphilis, a specific virus or the presence of a foreign body such as shrapnel. However, by universal acceptance the term is applied only to infection by pyogenic bacteria[6]. The aim of the present study was to investigate the percentage of glycocalyx producing etiologic agents of osteomyelitis and septic arthritis.

Materials and methods

The study was done in collaboration with the Orthopaedic Department II, Civil Hospital, and it also includes some cases from Jinnah Hospital, Karachi. Clinical diagnosis was confirmed by the microscopic observations of clinical material, and isolation and identification of the etiologic agent.

(A) Isolation of organisms

Pus, exudate, joint aspirate and blood were obtained under aseptic conditions. The material was stained by Gram's method for microscopic studies and streaked on blood agar (Oxoid, Basingstoke Hants, England), MacConkey Agar (Oxoid), mannitol salt agar (Oxoid), and thioglycollate

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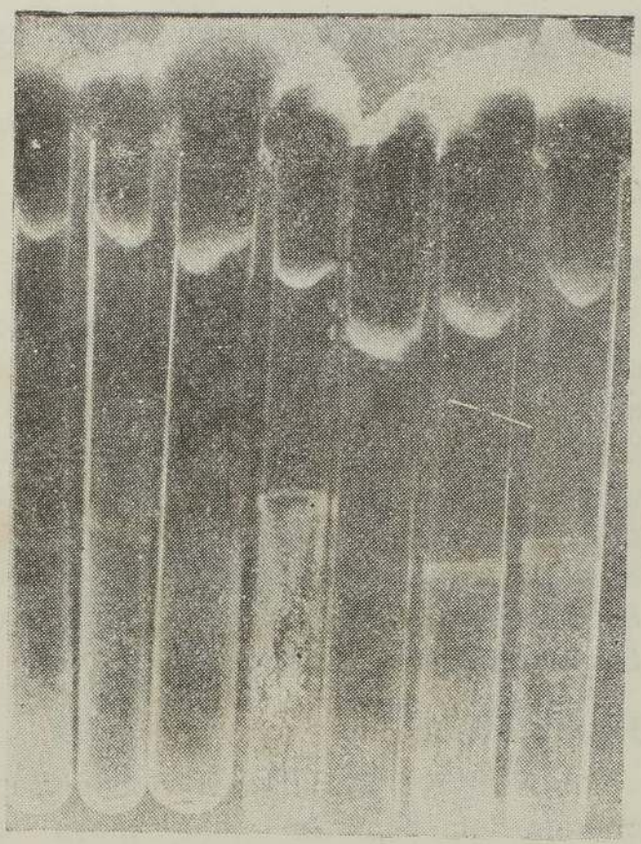
medium (Oxoid). The pure cultures were isolated and identified.

(B) Screening of glycocalyx producing bacteria *in vitro*

For the screening of glycocalyx producing isolates of bone and joint infections, the cultures were inoculated in 20 ml brain–heart infusion broth (Oxoid, Basingstoke Hants, England) in test tube and incubated at 37°C for 24 to 48 hours. The cultures producing glycocalyx were cemented along with glycocalyx to the inner surface of the test tube with the formation of a white layer and glycocalyx negative cultures failed to do so (Fig 1).

Fig. 1



A B C D E F G

In vitro glycocalyx production

A	+++	E	Negative
B	++	F	++++
C	+	G	++++
D	++++		

Results

A total of 111 cultures isolated from cases of osteomyelitis and septic arthritis and included 94 *S. aureus*, 7 *S. epidermidis*, 6 *Ps. aeruginosa* and 4 *E. coli;* 73 out of 94 *S. aureus* (76.3%), 4 out of 7 *S. epidermidis* (57.1%), 3 out of 6 *Ps. aeruginosa* (50%) and 3 out of 4 *E. coli* (75%) were found to produce glycocalyx *in vitro* (Table 1).

Table 1

Frequency of glycocalyx producing bacteria

Name of organism	*Number of isolates*	*Glycocalyx positive*	*% of glycocalyx positive*
Staphylococcus aureus			
(1) From chronic osteomyelitis	90		
(2) From septic arthritis	04	73	76.3
Staphylococcus epidermidis*	7	4	57.1
Pseudomonas aeruginosa*	6	3	50.0
Escherichia coli*	4	3	75.0
Total	111	83	

*From chronic osteomyelitis.

Discussion

The present study deals with the screening of glycocalyx producing bacteria isolated from patients suffering from osteomyelitis and septic arthritis. Out of a total 111 isolates, 83 were found to produce glycocalyx in vitro. Lambe[2] used brain-heart infusion broth for the demonstration of glycocalyx *in vitro*. He also successfully produced osteomyelitis in experimental animals and demonstrated that micrography of the infected catheter revealed gram-posltive cocci surrounded by glycocalyx. His *in vivo* and *in vitro* experiments strongly indicated that glycocalyx of bacteroides and *staphylococci* is an important adherence factor in osteomyelitis.

It is also reported that the tangled mass of thin polysaccharide fibres which is produced by many pathogenic bacteria, including *staphylococci*, is very important in attaching bacteria to a wide variety of surfaces including human teeth, small intestine and tissues[7]. Glycocalyx also confers resistance to bacteria from phages, specific antibodies, phagocytes and antibacterial agents including antibiotics[1].

During the study it was particularly observed that the duration of infection in 45 patients yielding glycocalyx positive cultures was considerably longer, even after prolonged treatment with appropriate antibiotics. On the the contrary, in patients infected with glycocalyx negative isolates the duration of infection was shorter. From these observations it could be presumed that the presence of glycocalyx may be one of the factors in the establishment and chronicity of osteomyelitis and arthritis.

Acknowledgment

We gratefully acknowledge the cooperation extended by Professor Ali Mohammed Ansari, Civil Hospital and Dr Ahmed Fawad, Assistant Professor Jinnah Postgraduate Medical Centre, Karachi, Pakistan.

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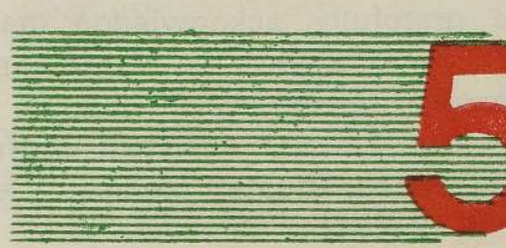

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Brief Report

Serum Protein Binding of Antiepileptic Drugs in Sri Lankans

ERIC H KARUNANAYAKE,[1] P D T M JOICE,[2] J B PEIRIS,[3]
J W A MEIJER,[4] H MEINARDI[5]

Ceylon Medical Journal, 1990, **35**, 25-28

Summary

The percentage protein binding of antiepileptic drugs was investigated in epileptic patients (n=90) undergoing treatment with phenobarbitone, phenytoin and carbamazepine either as a single drug therapy or in different combinations. When administered individually, the percentage (mean ± SEM) protein binding of phenobarbitone, phenytoin and carbamazepine were 50.84 ± 7.03, 87.23 ± 2.98 and 76.80 ± 6.30 respectively. Combination of phenobarbitone and phenytoin resulted in percentage (mean±SEM) protein binding of 51.94 ± 6.09 for phenobarbitone and 83.54 ± 7.01 for phenytoin, while the combination of phenobarbitone and carbamazepine resulted in percentage (mean ± SEM) protein binding of 49.60 ± 2.59 for phenobarbitone and 79.10 ± 3.31 for carbamazepine. When phenytoin was given with carbamazepine percentage (mean ± SEM) protein binding was 87.22 ± 4.48 for phenytoin and 72.50 ± 5.92 for carbamazepine.

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Introduction

Some of the commonly used antiepileptic drugs are bound to plasma proteins and displacement from binding sites represents one possible mechanism of interaction. Since it is the unbound drug concentration that is assumed to be in equilibrium with the drug concentration at the receptor site, information on the degree of binding in the individual patient is essential for interpretation of the drug plasma concentration.

At therapeutic concentrations, phenytoin is approximately 90% bound to plasma proteins, mainly to the albumin fraction.[1,2] Drugs such as salicylate, sulphafurazole, phenylbutazone, acetazolamide and diazoxide have been shown *in vitro* to displace phenytoin from its binding sites, increasing the unbound concentration by as much as threefold [3,4]. Phenytoin has been reported to displace some of the tricyclic antidepressants from their binding sites, doubling the unbound levels[5].

The plasma protein binding of carbamazepine has been investigated both

in vivo and *in vitro*. There is a good agreement between the different studies, and the protein binding of carbamazepine in most studies has been 70% to 80%[6,7]. The protein binding of valproate has been reported to be 95% in man at therapeutic concentrations[8]. Valproate has been found to competitively displace phenytoin from the binding site in the albumin molecule[9].

The relative importance of plasma protein binding of antiepileptic drugs in the interpretation of plasma concentrations, together with absence of any such data on the protein binding of antiepileptic drugs in Sri Lankan population led us to undertake the present studies.

Materials and Methods

The freeze dried control serum (Seronorm™ Pharmaca AED) was purchased from Nyegaard and Co. Oslo, Finland, and the samples were reconstituted according to instructions given by manufacturer. 5-ethyl-5-p-tolylbarbituric acid was purchased from Aldrich chemical company. Stock solution of 5-ethyl-5-p-tolylbarbituric acid (1 mg/ml) was prepared by dissolving the solid material in methanol (1 mg/ml). This solution was diluted 1:20 with phosphate buffer (0.2 M, pH 2.1) and used as the internal standard (5 μg/ml).

Epileptic patients (n=90) from the Institute of Neurology, General Hospital, Colombo, who were being treated with antiepileptic drugs carbamazepine (n=11), phenytoin (n=18) and phenobarbitone (n=21) individually or in combinations of carbamazepine and phenobarbitone (n=4), carbamazepine and phenytoin (n=6), and phenytoin and phenobarbitone (n=30) were recruited for this study. Their age ranged from 16 — 60 years and 30 of them were females. They were admitted to the hospital on the day before the study and were maintained on the dosagee prescribed by the physician. Drugs were administered together with meals and venous blood samples (5 ml) were collected 2 hours later. Serum was separated and stored at —20°C until the total and unbound drug concentrations were measured using High Performance Liquid Chromatography (HPLC).

Liquid chromatography was performed on a Micromeritics 7000 B apparatus with a variable wave length UV detector (Chromonitor 78). The column (25 x 0.46 cm) consisted of Spherisorb-5-ODS. The flow rate was maintained at 1.7 ml/min, recorder sensitivity of 0.01A and 0.10A full scale and a chart speed of 0.25 cm/min. The absorbance of the eluent was measured at 205 nm. The column was eluted with aqueous acetonitrile (20% v/v) which was deaerated by stirring on a magnetic stirrer under vacuum.

Phosphate buffer (pH 2.1) containing internal standard (250 μl) was aoded to serum (500 μl). This mixture was shaken for 10 min on a vortex with 3 ml of ethyl acetate. Two phases were separated by centrifugation and organic phase was transferred to a centrifuge tube and evaporated to dryness. The residue was then taken up in the mobile phase and hexane (0.5 ml), vortexed and centrifuged. Hexane layer was discarded and the aqueous layer (100 μl) was used for the measurement of total drug concentration in serum.

In order to measure the unbound drug concentration, an ultrafiltrate of

serum was obtained by centrifuging serum using Centricon Microconcentrator membrane purchased from Amicon Corporation at 2000 rpm for 15 minutes. The ultrafiltrate was processed for HPLC assay in the same manner as serum.

Results and discussion

The percentage of protein-binding of phenobarbitone, carbamazepine and phenytoin when administered as single medications and the protein binding of combinations of phenobarbitone and phenytoin, phenobarbitone and carbamazepine, and phenytoin and carbamazepine are in Table 1. There were no apparent differences in the protein-binding of antiepileptic drugs related to age or sex. Thus all results were analysed together.

Table 1

The protein-binding of phenobarbitone, phenytion and carbamazepine used alone or in combination in epileptic patients: mean, percentage binding and SEM.

	Used singly	*Phenobarbitone and phenytoin*	*Phenobarbitone and carbamazepine*	*Phenytoin and carbamazepine*
Phenobarbitone	50.84±7.03	51.94±6.09	49.6±2.59	—
Phenytoin	87.23±2.98	83.54±7.01	—	87.22±4.48
Carbamazepine	76.80±6.30	—	79.1±3.31	72.5±5.92

Hooper et al[10] using techniques similar to our studies have reported 73.1% protein-binding for carbamazepine. Their studies also showed that phenobarbitone has no effect on carbamazepine protein-binding. Our studies although of a limited number but from a different geographical area with different dietary habits are in agreement with their results on protein binding of carbamazepine. Similarly, the pattern of protein binding of phenytoin and phenobarbitone observed by us in the present study are in close agreement with those reported by other workers. Saunders and Penry[12] reported approximately 50% protein binding for phenobarbitone, while Finn and Olanow[11] observed 88% to 92% protein binding for phenytoin. Although phenytoin has the highest affinity for protein-binding, our results do not indicate a significant lowering of protein-binding of either phenobarbitone (about 52% binding) or carbamazepine (about 73% binding) as a result of administration of phenytoin along with each drug.

Acknowledgements

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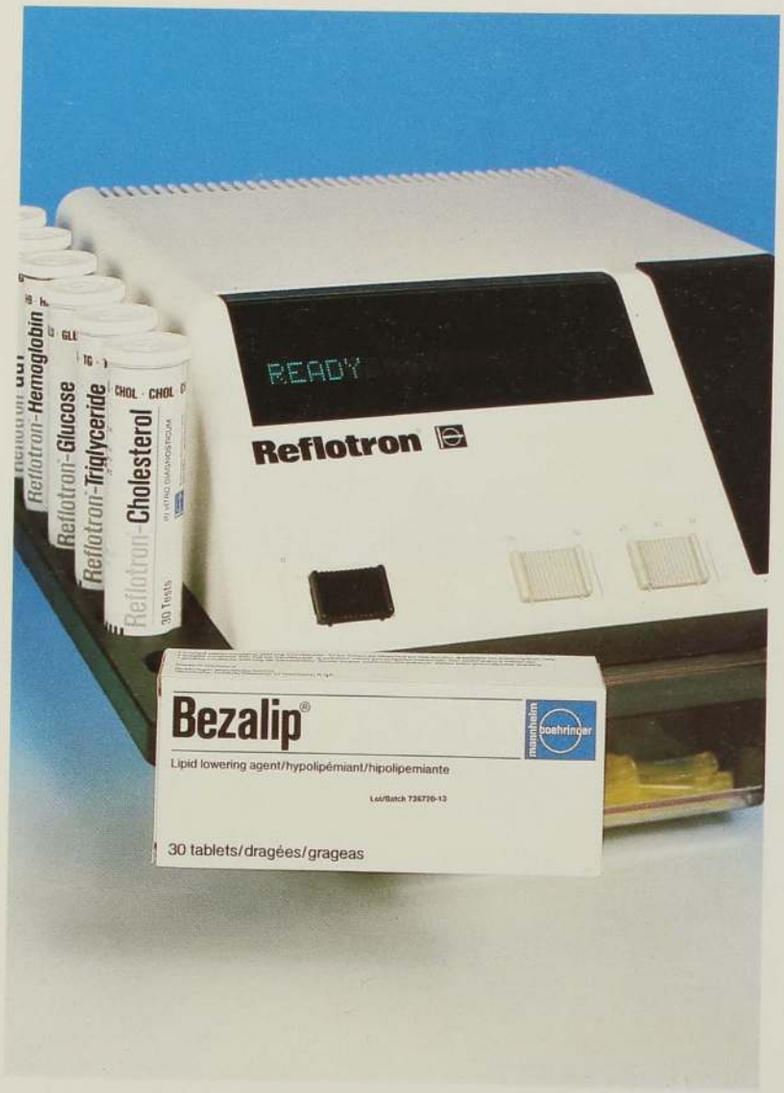

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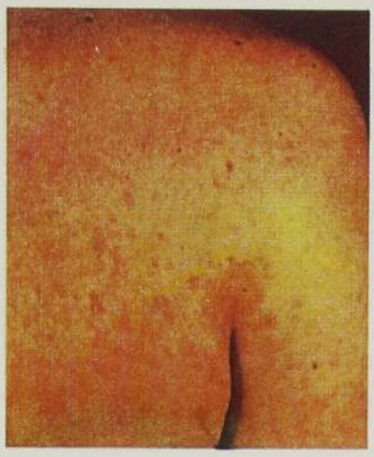

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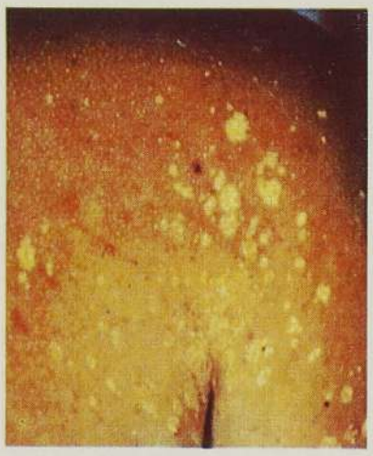

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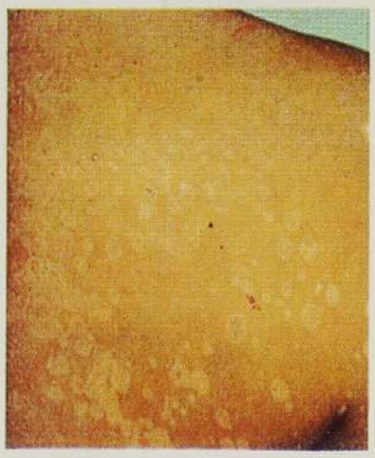

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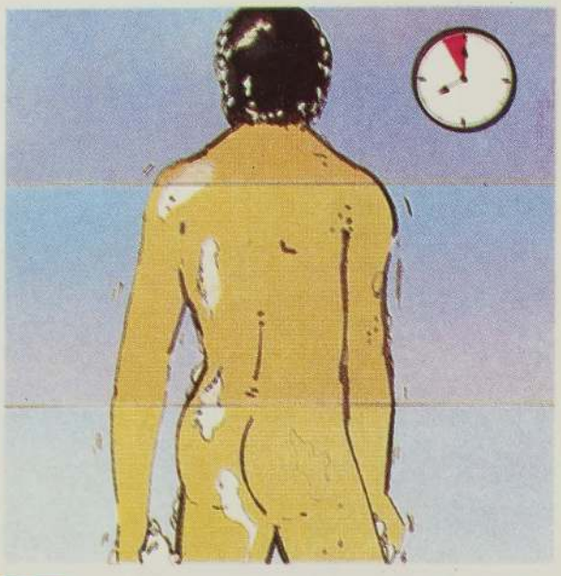

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A Cheap External Fixator Device

D W D COLLURE[1]

Ceylon Medical Journal, 1990, **35**, 29-32

Summary

A cheap external fixator made from readily available materials is described. This device should prove useful in the management of difficult compound fractures of the leg. Multiple staged procedures such as serial debridement, and bone and skin grafts can be carried out while maintaining the fracture fragments in position by means of this fixator.

Introduction

The management of open fractures of the lower extremity, which have resulted in extensive loss of soft tissue and bone, poses a difficult challenge to trauma surgeons. The crushed non-viable soft tissues often require wide debridement. The loss of a segment of the weight-bearing bone (tibia) may tempt the surgeon to perform an immediate amputation, if the distal portion of the limb is flail and crushed. These injuries are not amenable to internal fixation with plates and rods. However, the maintenance of the stability of the limb and management of the soft tissue injuries, can be achieved on an external fixator frame.

The treatment of fractures by means of transfixion pins attached to an external frame was first attributed to Lambotte in 1907. Currently, the more widely used external fixation devices include the Roger Anderson frame, the modified Wagner apparatus, the Hoffman apparatus and AO/ASIF devices. These fixators consist of universal ball joints, adjustable connecting rods and coupling devices, all made of stainless steel.

They use multiple transfixion pins above and below the fracture site. The device once assembled with the transfixion pins in position, provides very rigid fixation of the fracture fragments. The main drawback of these sophisticated fixators is their cost, which is in the range of a thousand dollars each.

We have devised a frame made out of PVC "S-lon" tubing which although not as rigid as the stainless steel frames, provided sufficient stability of the fracture fragments in the patient described, allowing management of the soft tissue injuries and eventual bone grafting of the missing fragment.

Description of the fixator

The framework is assembled from a five-foot length of 1 inch PVC heavy duty pipe (S-lon) which is obtained from plumbing suppliers. Two 35 cm lengths and six 11 cm lengths are assembled together using eight right-angle elbow bends (Fig. 1), and the whole apparatus is glued together with PVC adhesive. Holes are drilled in the two long limbs of the frame at 4 cm intervals to accomodate the transfixion pins. Once assembled, this frame is 45 cm long and will fit the leg of an average Sri Lankan adult. The height

[1] *Head, Department of Surgery, Faculty of Medicine, University of Peradeniya, Peradeniya.*

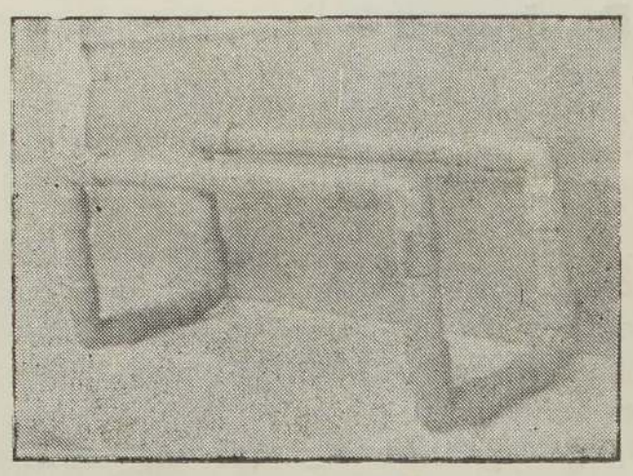

Fig. 1

The external fixator device showing details of construction

of the frame is 18 cm and will allow the limb to be maintained in elevation with the knee in approximately 15 degrees flexion. The dimensions of this frame can be altered to suit individual needs. In our patient, we used four transfixion pins of 3 mm Kirschner wire, and once the frame was assembled, it provided adequate stability. The pins were inserted two in each segment using a hand-drill. They were positioned at 4 cm intervals so that they could be accommodated in the pre-drilled holes of the frame.

Once the pins were inserted through the holes in the frame, they were bent at right angles outside the long limbs of the apparatus and anchored in position with adhesive tape. The spring like nature of the frame in the transverse direction, once the fixation pins wete bent snug against it, adds to the stability of the whole apparatus.

The entire device weighs less than a kilogram, and allows the patient to start quadriceps and knee-bending exercises, because he can easily lift the leg and the fixator, once the initial pain of the Injury subsides. The frame itself can be kept clean by washing with soap and water or an antiseptic solution. One can add a heel-sling or a foot-piece to the bottom of the frame to start the patient on foot exercises. The cost of materials for this frame is about one hundred and seventy five rupees.

Case report

A 27 year old motorcyclist sustained a compound fracture of the right leg with complete separation of a 7 cm fragment of the tibial shaft. The distal portion of the extremity was mobile, but the foot was viable and the dorsalis pedis pulse was present. In the operating theatre wide debridement of the wound was carried out, and the limb cradled in a plaster backslab. He was administered tetanus immunisation and intravenous antibiotics. The wounds were serially debrided over the next week and it was decided to treat the fracture in the external fixator device.

Twelve days after the injury, under general anaesthesia, four 3 mm Kirschner wires were inserted, two each in the proximal and distal segments. The pins were inserted 4 cm apart and were fed into the drilled holes in the fixator. It was noted that the leg length was equal to that of the normal limb at the end of the procedure. The wounds were debrided and slough excised while the leg was maintained in the fixator (Fig. 2) over the next few weeks. Later, under general anaesthesia, the granulating wound over the midshaft of the tibia was opened and the bone fragments which were approximately 6 cm apart, were freshened. Cancellous bone chips were harvested from the right iliac crest and the space between the

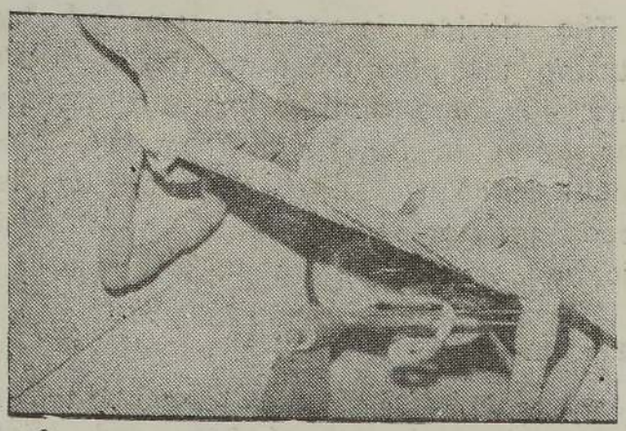

Fig. 2
The fixator in use.

tibial fragments was packed with these chips. The muscle and granulation tissue were closed over the bone grafts. Three weeks later the granulating wound was grafted with split thickness skin from the right thigh, while the limb was maintained in the flxator. Afte the skin grafts had taken well, the pins were removed along with the fixator device. There was still some mobility at the fracture site, and an above-knee plaster caster was applied with the knee in 15 degrees flexion and the foot plantgrade. He was walking on crutches and discharged home two months after being placed on the fixator.

Discussion

External fixation is the preferred method of stabilisation of severe open fractures of the tibia.[1 2] There is still controversy whether the fixator should be of low or high rigidity. The low rigidity frames are likely to induce a large callus across the fracture site, and this may of advantage when there has been loss of bone substance. The high rigidity frames such as the AO/ASIF devices are more adaptable to hold unstable fractures, heavier limbs and permit early weight bearing, but they too are not without complications. The profusion of transfixion pins needed to maintain this degree of rigidity can lead to compartment syndromes, injury to neurovascular structures, and pin track infection.

The basic principles in the use of fixator devices[1] are:

1. There should be no damage to vital anatomical structures.
2. They, should provide sufficient access for debridement and secondary procedures.
3. They should fulfil the mechanical demands required for the management of the injury.

The least interference with the anatomical structures is likely with the use of transfixion pins, and these should be inserted away from the site of bone injury, consistent with maintenance of rigidity. Biomechanical studies indicate that greater rigidity of the tibial fracture is achieved if the transfixion pins and frame are oriented in the anteroposterior or sagittal plane rather than in the coronal plane. However, pins inserted in this plane are more likely to damage vital anatomical structures in the calf.

The multiplicity of transfixion pins in the more rigid frames, also interferes with access to sites of injury.

In our patient, who had loss of a tibial segment, we were able to obtain sufficient mechanical rigidity with the use of four transfixion pins. The natural spring of the PVC frame coupled with that of the Kirschner wires maintained the limb in a stable position when the whole assembly was in place under tension. Ready access

to the site of injury was available as the frame was completely open at the front and back. Other advantages of this frame were that it did not interfere with knee and ankle movements and that it maintained the limb in a position of elevation with slight flexion at the knee.

The light weight of the fixator allowed the patient to elevate the whole assembly in carrying out quadriceps exercises quite early in the post-operative period unlike in a closed fracture encased in an above-knee plaster cast.

The device is easily removed by cutting the pins close to the skin on one side, and pulling them out through the holes in the frame from the opposite side. The fixator device is ready for re-use once it has been cleaned with a detergent solution.

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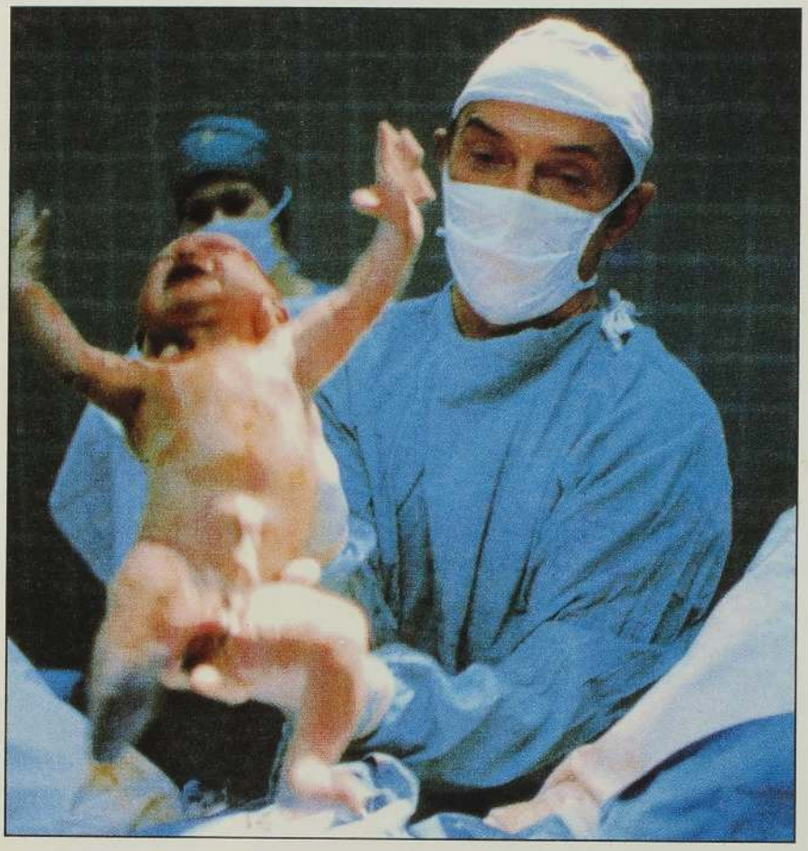

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15.11.88

Book Review

Physiology and Biochemistry in Clinical Medicine

by I Thabrew and Colvin Goonaratna, 1989.
Pp 106. Rs 127/50. Gunasena, Colombo.

Ceylon Medical Journal, 1990, **35**, 33

The fruitless old argumet whether medicine is an art or a science is now seldom heard, probably because it is generally realised to be both, the study of the body and how disease affects it being a precise science, whereas the practice of clinical medicine is an art requiring years of training and experience. In the west students often neglect the art of medicine and concentrate on the science, not realising that the skills of clinical management cannot be replaced by scientific knowledge — detailed awareness of the pathogenesis of pleural effusion, for instance, being of little value if one cannot diagnose the condition when confronted by a patient.

In this little book Professors Thabrew and Goonaratna point out that in Sri Lanka the opposite problem exists — the science of medicine tending to be neglected, and in particular the help that laboratory science can provide to the clinician is often disregarded. To some extent the present poverty of training in laboratory personnel, referred to by Dr. Nihal Perera in his presidential address in the journal in September 1988, is resdonsible for this deficiency. Laboraiory disciplines are often unattractive ftnancially, presenting little opportunity for private practice, and suffering from government investment because of the expenses of modern methodology. The problems is not confined to Sri Lanka, but is usual in the poor countries of the world, and is likely to get worse if clinicians are not aware of these deficiencies and are not constantly pressing for greater government support in this field.

The authors do what they can to correct this problem, by emphasizing the vital assistance provided by biochemical and physiological laboratories in diagnosis. Their book contains a synopsis of 35 case histories, each of which provides clues which should lead to key investigations and hence to correct diagnosis and appropriate treatment. They read like detective stories and can be studied by medical students or doctors of all ages with benefit. The book concludes with brief relevent sections on the meaning of an abnormal report, by Dr H. R. Wickremesinghe, and on SI Units, by Professor Goonaratna.

Two words of caution: first, readers must realise that some of the diseases presented are uncommon, for rarities like Wilson's disease and acute porphyria are often better illustrations of the importance of the laboratory than are the humble stroke or myocardial infarct, and second, it is no use doctors having all this information at their finger tips if they have no clinical skills. Otherwise they do not ask for the correct tests and will misinterpret the results provided.

Oliver Wrong
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Letter to the Editor

The Glycaemic Index of Foods

Ceylon Medical Journal, 1990, **35**, 35

The glycaemic index of a food has been defined as the ratio of the post-prandial blood glucose area of a test food to the post-prandial blood glucose area of a reference food, expressed as a percentage.[1,2]

If two foods contain identical quantities of digestible carbohydrate (amyloses and amylopectins), the total blood glucose area will be the same for both. If one contained more dietary fibre or protein or fat than the other, its digestion and subsequent absorption will be delayed, the rate at which blood glucose rises will be slower and the peak value less than in the case of the other food. But the total area under the curve will still be same for both.

Legume grains have a lower glycaemic index than cereals, if fed in isocaloric amounts. The energy content of the legume grain is due mainly to its fat and protein content. There is little digestible cerbohydrate in it.

Therefore, the glycaemic index, as defined above, will be of little use in the management of a diabetic. Food exchange lists will be more useful[1].

A rapid rise in blood glucose level, resulting in a high peak value, taxes the pancreas by requiring a rapid secretion of insulin. The diabetic should obtain about 60% of his energy from carbohydrate. It will be to his advantage to be able to absorb this energy slowly, without a rapid rise in blood glucose level, so as to lower the burden on the pancreas. The glycaemic index should therefore be able to compare foods that provide equivalent amounts of glucose, not total energy. Such an index will take into account the height of the peak in the blood glucose curve.

The glycaemic index should therefore be defined as the ratio of the height of the peak of the blood glucose curve obtained after a test food or meal to the height of the peak of the curve obtained after an equivalent amount of glucose, expressed as a percentage.

The determination of such an index, as the one in common use, involves drawing several samples of blood from each subject after feeding different foods and food mixtures. The procedure could be simplified if the index is taken as the ratio of the post-prandial rise in the blood glucose level one hour after the test food or meal to the rise of blood glucose one hour after an equivalent amount of glucose.

Such an index will compare the "diabetogenic" property of a food or food mixture. It helps in distinguishing diets which, while providing identical quantities of glucose, will tax the pancreas less. The index coulde be used along with food exchange lists in the effective management of diabets mellitus.

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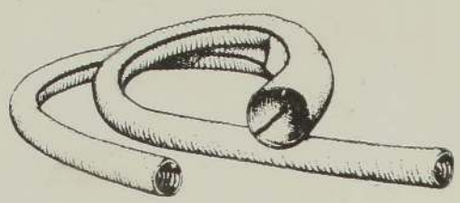

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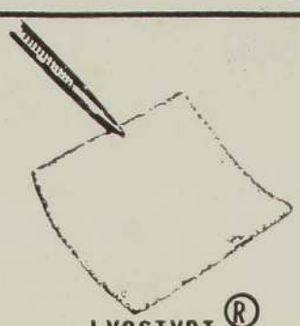

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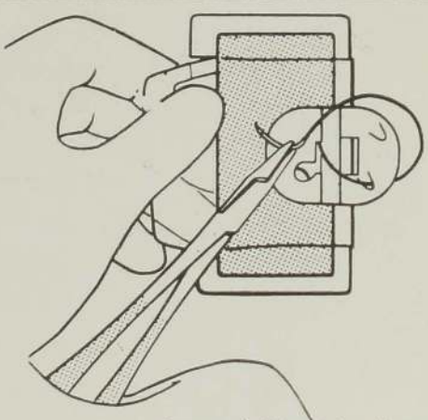

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