Correspondence

Caesarean section deliveries on the rise in Kerala

It is indeed a matter of concern that delivery by caesarean section (CS) is reported to be around 45% in urban Chennai. In Kerala, with an institutional delivery rate of 95.2% in 1994, the CS rates are also reported to be high and over the years this has been increasing. In 1987, a study in rural Kerala showed that the CS rate was 11.9%. The proportion of CS in government hospitals was 12.6% and in private hospitals 16.5%. In the low socio-economic status (SES) group, the proportion was 9.3% and in the high SES group 19.3%. This is in contrast to the findings in a study from Chennai city where they did not find any variation between different SES groups.

In 1995, another study on hospital performance in public and private sector hospitals in Thiruvananthapuram city found that the CS rate was three times higher in private hospitals compared to government hospitals. The mean CS rate was 10% (range 5%-40%) in government hospitals compared to 30% (range 9%-60%) in private hospitals (Fig. 1).

The organization which conducted the survey in 1987 on a sample of 10,000 rural households did another study on a sub-sample (10%) of the same households in 1996 and found that the CS rates had increased from 11.9% to 21.4%. In this study, they also examined the expenditure for CS and normal delivery. The average out-of-pocket expenditure for a CS in the private sector was Rs 4,944, compared to Rs 2,456 for a vaginal delivery. The corresponding figures for the government sector were Rs 2,864 and Rs 1,670, respectively. Even though the amount spent was less in the government sector, it was surprising that even in government hospitals, which are supposed to provide free care, patients had to spend a fair amount of money.

Considering the increased risk for maternal morbidity and mortality from CS compared to vaginal delivery, it is important to reduce the CS rate for health and economic reasons. According to the World Health Organization (WHO), no region in the world is justified in having a CS rate higher than 10%-15%. In 1987, USA had a CS rate of 18% compared to 5% in Czechoslovakia. Strong promotion of vaginal birth after previous CS, circulating CS rates of individual obstetricians to attending physicians and following a protocol have helped reduce CS rates in the USA.

In addition to reducing the CS rates from 27.3% to 16.9%, the above study reported a reduction in the perinatal mortality from 19.5% to 10.3%. It has also been reported that for a repeat CS, non-clinical factors dominated over clinical factors. Efforts for reducing CS rates are urgently required in India.

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Ocular toxicity—A rare side-effect of cyclophosphamide

Cyclophosphamide, an alkylating agent, is one of the most commonly used antineoplastic agents. It is routinely prescribed for lymphoproliferative disorders and carcinomas of the ovary and breast. Common side-effects include nausea, vomiting, alopecia and haemorrhagic cystitis (with high doses).

Rarely, facial discomfort and ocular toxicity have been reported. Recently, we came across a 33-year-old man diagnosed as a case of high-grade non-Hodgkin's lymphoma stage IV B. He received six cycles of CHOP chemotherapy (cyclophosphamide, Adriamycin, Oncovin, prednisolone), which he tolerated well, and achieved near-complete remission.

In view of the high-grade and advanced stage, he was advised high-dose chemotherapy followed by autologous peripheral blood stem cell transplantation. Meanwhile, he received two more cycles of CHOP. During the seventh cycle of CHOP, immediately following infusion of cyclophosphamide (1.2 g), he developed oedema of the left eyelid with left conjunctival chemosis and congestion. He was given injection pheniramine which relieved his symptoms after 3-4 hours. Subsequently, following high-dose cyclophosphamide (2.5 g) infusion, he again developed the same side-effect, which improved after pheniramine injection. His visual acuity and visual field remained normal during these two episodes.

There are two reports of cyclophosphamide-induced facial discomfort described in the literature. Symptoms described in these reports include facial burning, nasal or ocular congestion, opharyngeal tingling, rhinorrhea, sneezing and lacrimation. The symptoms generally occur during or immediately following cyclophosphamide administration. In most cases, these symptoms are bothersome but self-limiting.

Some authors believe that these reactions may be mediated by the parasympathetic nervous system (vagus) and propose the use of anticholinergic medications to mitigate these symptoms. Measures advocated to avoid reactions during subsequent administration of cyclophosphamide include prolonging the duration of administration, diluting the concentration of cyclophosphamide, or administering ipratropium bromide intranasally. Our patient responded well to antihistamines only.

Thus, awareness regarding the ocular toxicity of this commonly used anti-cancer drug would help in its early identification and management.

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1 Silverstein PT, Vercelotti GM. Facial burning from...
Indicators of iodine deficiency disorders

We read the article entitled 'Interpretation of indicators of iodine deficiency disorders: Recent experiences' with great interest and found it informative and useful.

The authors have proposed a new cut-off of indicators for establishing the status of iodine deficiency disorders (IDDs) in a population. In the proposed classification, goitre grade I has been merged with normal-size thyroid gland. Also, the urinary iodine excretion (UIE) levels have been revised.

The prevalence of goitre reflects the past while UIE levels indicate the current status of iodine nutrition in a community. Recent studies conducted in India amongst children 6–12 years of age have revealed the total goitre prevalence to vary from 1% to 20%. Similarly, goitre grade II (visible goitre) prevalence was in the range of 0% to 2%. Merging of grade I with grade 0 would have provided the prevalence rate of visible goitre from 0% to 2% in these studies undertaken. A multicentric study of the Indian Council of Medical Research also reported total goitre prevalence of 5.1%, 4.2%, 2.2% and 0.2% in school children in selected districts of Jammu and Kashmir, Uttar Pradesh, Himachal Pradesh and Maharashtra, respectively.

The prevalence of visible goitre has been reported to be low (range 0% to 2%) by other investigators also. It would be difficult to categorize the small range of visible goitre into those due to mild, moderate and severe iodine deficiency. Before revising the existing classification, there is a need to establish a correlation between the prevalence of visible goitre and UIE levels in mild, moderate and severe iodine-deficient populations. The sample size of these studies should be adequate to make scientifically valid conclusions.

The findings of recent studies in India suggest that the population is in the transition phase from being iodine deficient to iodine sufficient due to a successful universal salt iodization programme. Therefore, a mixed picture of indicators was observed, in which goitre prevalence was more than 5% while median UIE levels were also more than 10 g/dl with less than 20% samples showing values less than 5 g/dl (Table I). We agree with the authors that for interpretation of iodine deficiency, the results of total goitre prevalence, median UIE with iodine content of the salt consumed in the population should be considered in totality.

3 November 1999
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REFERENCES


Table I. Status of iodine deficiency in selected states, India.

<table>
<thead>
<tr>
<th>State</th>
<th>District</th>
<th>Year</th>
<th>Age group (in years)</th>
<th>Prevalence (% of goitre)</th>
<th>Median UIE (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andaman</td>
<td>Andamān</td>
<td>1997</td>
<td>6–12</td>
<td>9.3</td>
<td>2.0</td>
</tr>
<tr>
<td>and Nicobar</td>
<td></td>
<td></td>
<td></td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>Bihar</td>
<td>Champaran</td>
<td>1997</td>
<td>6–12</td>
<td>12.8</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>East</td>
<td></td>
<td></td>
<td>10.4</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>West</td>
<td></td>
<td></td>
<td>10.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Delhi</td>
<td>Entire²</td>
<td>1996</td>
<td>6–12</td>
<td>10.3</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Ernakulam</td>
<td>1998</td>
<td>6–12</td>
<td>0.9</td>
<td>0.1</td>
</tr>
<tr>
<td>Kerala</td>
<td>Kangara²</td>
<td>1996</td>
<td>6–12</td>
<td>14.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Himachal</td>
<td>Hamipur²</td>
<td>1996</td>
<td>6–12</td>
<td>6.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Pradesh</td>
<td>Kinnar²</td>
<td>1996</td>
<td>6–12</td>
<td>5.9</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>Solan²</td>
<td>1997</td>
<td>6–12</td>
<td>11.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Pondicherry</td>
<td>Entire²</td>
<td>1997</td>
<td>6–12</td>
<td>2.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Rajasthan</td>
<td>Bijlaner²</td>
<td>1996</td>
<td>6–12</td>
<td>19.0</td>
<td>1.5</td>
</tr>
<tr>
<td>Uttar</td>
<td>Pithoragarh¹</td>
<td>1998</td>
<td>6–12</td>
<td>1.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Pradesh</td>
<td></td>
<td></td>
<td></td>
<td>1.4</td>
<td>0.2</td>
</tr>
</tbody>
</table>

UIE: urinary iodine excretion

Honour your oath

A few years ago, an American couple visited me in Mumbai stating that they represented the second-largest health insurance company in the USA. They were referred to me by a leading non-resident Indian in their country. They had come to explore the possibility of extending the activities of their private health insurance company to India. Asked if they were interested in assuring health cover to the 85% who lived in rural India and the urban slums, they made it clear that their interest was restricted to the elite and middle class, who though only 15% of the population, nevertheless comprised 150 million potential clients ranging from the ultra elite to the upper and even lower middle class. They were fully aware that this segment of our population was craving for the latest expensive western medical technologies and services. While the rich were reimbursed by their companies for services provided by five-star hospitals, the much larger middle class also desirous of similar services were being pauperized unless insured. Yet they were not willing to utilize the services offered even by the specialized hospitals of the public sector since they were mainly used by the poor. Hence they were dependent on professionals to serve their own profit-oriented end.

The elected representatives of the people with the tacit cooperation of the bureaucracy (and even of our profession) have now agreed to open the doors of our country to this nefarious trade in human suffering. This will further distort the entire health scene. It is also a measure of what our country has been reduced to by those, who like multinationals, have no compunction in diverting the country’s meagre resources for health from basic care of the 85% who are poor, to satisfy the greed and exotic needs of a few. Will someone object to the sell-out of our people by those who worship Mammon under the cloak of democracy? Will they honour the oath taken on joining what was once considered a respectable and even a ‘noble profession’?

9 November 1999

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Polio eradication in India: Are we on the correct path?

Eradication represents the ultimate control of an infectious disease. Smallpox eradication has been one of the most important contributions to public health and preventive medicine in terms of saving millions of lives and money. The other infectious disease which is on the verge of eradication is poliomyelitis. It is a tremendous achievement on the part of the World Health Organization (WHO), which with the active cooperation of Rotary International and governments around the world, has brought polio eradication measures to a final phase. From 35,252 cases reported in 1988 the number has dropped dramatically to 5000 cases in 1998. India, the reported cases of paralytic poliomyelitis decreased from 24,257 cases in 1988 to 3556 in 1998. If the present level of funding and cooperation continues, the world could be free of polio by the year 2003, a moderate re-estimation of the 1998 WHO goal of polio eradication by the year 2000.

The strategies for eradication of wild polio viruses have been defined as: 1) maintaining high oral polio virus immunization coverage by administering three doses of primary immunization to children below 12 months of age; (ii) supplementary immunization campaigns through national immunization days (NIDs) conducted twice a year 4-6 weeks apart; (iii) sampling, door-to-door localized immunization campaigns targeted at high-risk areas where wild polio virus transmission is likely to persist; and (iv) developing effective surveillance systems capable of detecting and investigating every case of acute flaccid paralysis (AFP) which could be due to polio.

According to the WHO, active surveillance for AFP is based on epidemiological and virological information obtained from stool specimens of suspected cases. The sensitivity of surveillance is defined by the rate of non-polio cases among the total paralytic cases reported, and that of adequacy of stool samples collected for wild polio virus culture and identification. The isolates are then classified as polio or non-polio types. This is of critical importance to permit certification of poliomyelitis eradication. In India, nine WHO surveillance centres are accredited to conduct poliovirus isolation from AFP cases and to ultimately certify the country free of polio. Certification depends on: (i) no detection of paralytic polio cases caused by wild virus for a 3-year period; (ii) a satisfactory surveillance system to distinguish polio virus infections from other causes of paralysis; and (iii) environmental surveys (e.g. sewage, stools, etc.) to demonstrate the absence of wild polio viruses.

Embarking upon an eradication programme

Just as eradication of smallpox served as the foundation for eradication of polio, the successes and failures of this campaign would provide lessons for future eradication and elimination initiatives. Elimination of infection has been practised in the case of polio with the aim of reducing the incidence of infection to zero in a defined geographical area. This also requires ongoing measures to prevent re-establishment of viral transmission. The factors that favour eradication of polio are: (i) limitation of the disease to a human host, without an animal reservoir or insect vector; (ii) easily diagnosed clinically; (iii) availability of two safe and potent vaccines which could interrupt wild virus transmission; and (iv) a technological change that has simplified the logistics by introduction of an individual vaccine vial monitor (VVM), a thermo-sensitive marker which changes colour when exposed to heat.

Since December 1995, India with active support from the WHO and international funding agencies has conducted massive polio immunization drives called ‘pulse polio’ campaigns. Despite this, there has been an increase in AFP cases. From the available information it is evident that:

1. In 1998, a total of 1281 confirmed cases of poliomyelitis associated with wild polio virus isolation were reported (Table 1). There has been a rise in cases of AFP, from 1005 in 1996 to 3556 in 1998.
2. Despite high immunization coverage, there is widespread circulation and upsurge of poliovirus type 1 and type 3 with focal circulation of polio virus type 2 in various states of India.
3. The continued circulation of wild polio virus in places which have conducted 4 or more NIDs is an indicator of the failure to immunize a large enough population.

These could be due to:

1. continued under-reporting of cases,
2. poor sanitation, and unhygienic and poor standards of living especially, in crowded urban slums,
3. failure of the vaccine to induce appropriate neutralizing antibody levels,
4. insufficient field studies with regard to determination of vaccine efficacy and seroprotection, and
5. frequent failures in cold chain (~20°C) maintenance.

Persisting with the OPV and NIDs till polio is eradicated

In view of WHO’s worldwide success with OPV and the logistics and ease of OPV administration, it is probably best to continue with the current strategy. With OPV, eradication measures primarily aim to achieve an interruption in the wild virus circulation with a Sabin vaccine strain in the population. The vaccine strains persist with the population forever. This option accepts that the present number of poliomyelitis cases are a temporary setback to the programme due to breaks in the cold chain during vaccine distribution and administration, subsequent inadequate quality control measures and incomplete vaccine coverage. In India, even a 10% missed target population (i.e. an estimated 13 million children), especially in areas with high endemicity, and crowded slum conditions is a major obstacle to eradicating the disease. A targeted large-scale house-to-house mapping-up immunization campaign in crowded areas with persistent virus transmission is required to achieve the goal of polio eradication in India.

Use of injectable polio vaccine (IPV) along with OPV and NIDs

The use of IPV after OPV as a ‘mop-up’ has been done in Israel (West Bank and Gaza strip) and Denmark. This offers the advantage of high levels of humoral antibody production in addition to sustained gut immunity established by OPV. There are fears that with the use of IPV–OPV combinations the OPV vaccines will frequently excrete inter-typic recombinants. There is then the possibility of excretion of IPV–OPV recombinants where an attenuated strain of the OPV component and a virulent strain of the IPV component may result. However, these fears have not been substantiated. The complete eradication of both wild and vaccine strains can be achieved only when OPV is discontinued after a certain time and replaced by IPV. IPV should then be continued till such time as surveillance proves to be negative for both the wild and vaccine strains. The Advisory Committee on Immunization Practices (ACIP-USA) has also recommended the use of a combined IPV–OPV schedule in order to minimize the occurrence of vaccine-associated paralytic polio (VAPP).

While success is not yet assured and with just over a year remaining to reach the target for global polio eradication, the lessons learnt during the ‘pulse polio’ programme are:

1. The best strategy would be mopping-up immunization: house-to-house immunization campaigns, to saturate high-risk areas. To identify such pockets of polio, an extra round of NIDs was conducted in March 1999, in the states of Bihar, Uttar Pradesh, Madhya Pradesh and Rajasthan.
2. To continue with OPV till eradication of the wild virus is achieved and documented worldwide. Otherwise, this virus may be imported.

Table 1. Polio surveillance in India (1995–98)

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<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Number of confirmed AFP cases</td>
<td>3263</td>
<td>1005</td>
<td>2278</td>
<td>3556</td>
</tr>
<tr>
<td>Number of wild poliovirus cases</td>
<td>313</td>
<td>17</td>
<td>234</td>
<td>1281</td>
</tr>
<tr>
<td>Indicators of surveillance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate of non-polio cases*</td>
<td>&lt;0.1%</td>
<td>&lt;0.1%</td>
<td>&lt;0.2%</td>
<td>1.39%</td>
</tr>
<tr>
<td>Adequacy of samples for AFP†</td>
<td>not reported</td>
<td>11%</td>
<td>34%</td>
<td>60%</td>
</tr>
<tr>
<td>Number of surveillance centres</td>
<td>5</td>
<td>5</td>
<td>7</td>
<td>9</td>
</tr>
</tbody>
</table>

AFP: acute flaccid paralysis • Non-polio AFP (such as Guillain–Barre syndrome and transverse myelitis) rate at 1 case per 100 000 population aged under 15 years indicates WHO-specified sensitivity of surveillance • WHO-recommended target of 2 stool specimens collected at 24–48 hour intervals within 14 days of onset of paralysis from at least 80% of AFP cases.

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and may spread widely in the absence of continued or inadequately immunized sub-populations.

3. Immunization with IPV should be considered. This will avoid any OPV-induced AFP, once eradication is achieved.

Having come this far, it would be tragic if the goals are not met and polio remains a risk for children beyond the year 2000.

6 November 1999
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REFERENCES

Mortality due to adverse drug reactions in a large general hospital

The World Health Organization defines an adverse drug reaction (ADR) as any noxious, unintended, undesired effect of a drug that occurs at doses used in man for diagnosis, prophylaxis or modification of physiological function. A serious ADR is defined as one that requires hospitalization, is permanently disabling, or results in death (serious ADRs thus include fatal ADRs). ADRs account for 2%–6% of hospital admissions, are encountered in 30% of hospitalized patients and, in addition, .5% of admitted patients have their hospital stay prolonged by ADRs. In the USA, it is estimated that ADRs could account for more than 100,000 deaths each year, making them the fourth most common cause of death after heart disease, cancer and stroke. Studies of ADR incidence in the hospital setting have been carried out since the 1960s. We report here a retrospective analysis of hospital records at the King Edward Memorial VII Hospital, a large Indian general hospital and our findings about the nature and proportion of deaths due to ADRs.

This study was carried out as part of the ADR monitoring activities of the Drugs Controller General’s ADR centre at the Department of Clinical Pharmacology, which is also a WHO special centre.

Hospital admission registers (all admissions to all wards) of the year 1996 were systematically screened and data on deaths were noted. From these, based on the cause of death written in the register, deaths attributed to ADRs were separated. Once a death was identified as being ADR-related, the case notes of the patient were obtained and following the details noted: age and sex of the patient, diagnosis, management, total number of drugs received, whether the patient was hospitalized with the ADR or developed it during his/her stay in the hospital, and the suspected drug to which the ADR was attributed.

There were 62,647 admissions in 1996 and 4,840 deaths, giving a mortality rate of 7.7%. Of these, 23 (14 women, 9 men) deaths were classified as due to ADRs (0.48% of all deaths). There were 18 adult, 2 geriatric and 3 paediatric deaths. Fifteen of these were attributed to antituberculare drugs, 2 each to NSAIDs (both ibuprofen), anti-biotics (tetracycline and penicillin), anticancer drugs (cytoxanthem and cisplatin) and 1 each to diagnostic media and prednisolone. The primary organ systems involved were: gastrointestinal (16), skin and musculoskeletal systems (2 each) and genitourinary and cardiovascular systems (1 each). One death was due to anaphylaxis. Twelve of the 23 patients were admitted with ADR while 11 developed them in the hospital.

Thus, serious ADRs accounted for 0.48% of the total deaths and antituberculosis drug-induced hepatotoxicity was the most common cause of death. ADRs as a cause of death were ranked eleventh in our study. Other meta-analyses have shown that serious ADRs account for 6.7% and fatal ADRs for 0.32% of the total ADRs occurring in the hospital setting. In this study, we have not computed the fatal ADRs as a percentage of the total ADRs due to the lack of a true incidence.

Our study could be biased towards under-detection of ADR-related deaths, since it was retrospective and based on the cause of death written in the hospital registers as against actual verification or spontaneous reporting of cases. It is also possible that physicians may not have recognized or attributed the cause of death to a particular drug in some cases. Under-reporting of ADRs is a worldwide phenomenon. Reporting of serious and fatal adverse reactions, particularly to within-hospital ADR monitoring centres will help provide the true incidence in the Indian setting.

15 November 1999
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REFERENCES