Correspondence

Single dose ‘ROM’ therapy—Is it really effective?

India accounts for 62% of the global burden of leprosy. The Government of India plans (Leprosy Division, Directorate General of Health Services) to start a new programme in November 1998 to eliminate leprosy which is indeed welcome. As part of this programme, single dose ‘ROM’ (rifampicin, ofloxacin and minocycline) therapy is to be used. However, this should be implemented cautiously because of the following reasons:

1. A majority of patients, particularly of tuberculoid and indeterminate types of leprosy, tend to get cured spontaneously. An earlier study from India has shown that over a period of 20 years, spontaneous regression among children with tuberculoid leprosy was about 90%. A study in Cullion Island in the Philippines showed that among children, self-healing occurred in 77.7%. A long term follow up study from South India on a highly endemic population showed that among newly detected tuberculoid cases of all ages and both sexes, the rate of inactivation was 10.9% per year, the bulk of this being spontaneous. Unless a placebo-controlled study is done, it will be difficult to confirm that patients treated with ‘ROM’ did not get cured spontaneously.

2. Follow up of patients with ‘ROM’ drugs is available for only 18 months. This is insufficient to judge the relapse rate. At least 2-5 years of follow up is necessary as the incubation period of Mycobacterium leprae is very long (few weeks to 30 years; average 2-5 years).

3. ‘ROM’ drugs are beneficial for single lesions only. So, it is vital that all patients should be examined carefully to ensure that there really is only a single lesion, which in field conditions would be very difficult to confirm. Women would be particularly vulnerable because of the purdah system in many parts of India.

I strongly feel that placebo-controlled studies with long term follow up are necessary to prove the efficacy of single-dose ‘ROM’ therapy in all patients with leprosy. The implementation of single-dose ROM at this juncture, though likely to be of value for some patients, is not suitable for Indian field conditions and may not help in eliminating leprosy.

5 October 1998
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Percutaneous biopsy of a solitary kidney

A solitary kidney is generally considered to be an absolute contraindication for percutaneous biopsy. The risk of a major complication such as haemorrhage is no different, whether the patient has two kidneys or one. However, if it occurs in a solitary kidney, an ablation such as nephrectomy or embolization could render the patient dialysis-dependent. In recent years, with the availability of better biopsy instruments and imaging facilities, percutaneous renal biopsy has become a safer procedure. It is time to reassess this contraindication.

At the Christian Medical College and Hospital, Vellore, Tamil Nadu, we prospectively studied, since 1992, all patients requiring biopsy of a solitary kidney. A solitary kidney was defined as either absence of a kidney, or if both kidneys were visualized, the smaller kidney being <7 cm in length, and the larger kidney >9 cm in length. All solitary kidney biopsies were done as inpatient procedures by experienced operators. Bleeding parameters were checked routinely and corrected appropriately. The haematocrit was increased by at least 30% with packed red blood cell transfusions.

With the patient in the prone position, the lower pole of the kidney was localized, marked and its depth measured ultrasonologically. The depth was then confirmed with a probing needle. Since 1994, all solitary kidney biopsies were done using 18-gauge monopry guns (Bard, Covington, USA).

Table 1. Indications for renal biopsy and the histological diagnosis

<table>
<thead>
<tr>
<th>No.</th>
<th>Age/Sex</th>
<th>Cause of solitary kidney</th>
<th>Indication for biopsy</th>
<th>Histological diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9/M</td>
<td>Unilateral agenesis</td>
<td>Proteinuria</td>
<td>FSGS</td>
</tr>
<tr>
<td>2</td>
<td>22/F</td>
<td>Unilateral shrunken kidney</td>
<td>Renal failure</td>
<td>Crescentic nephritis</td>
</tr>
<tr>
<td>3</td>
<td>55/M</td>
<td>Nephrectomy</td>
<td>Renal failure</td>
<td>Acute GN</td>
</tr>
<tr>
<td>4</td>
<td>25/F</td>
<td>Unilateral shrunken kidney</td>
<td>Renal failure</td>
<td>End stage histology</td>
</tr>
<tr>
<td>5</td>
<td>18/M</td>
<td>Unilateral agenesis</td>
<td>Renal failure, proteinuria</td>
<td>IGA nephropathy</td>
</tr>
<tr>
<td>6</td>
<td>35/M</td>
<td>Nephrectomy</td>
<td>Renal failure</td>
<td>FSGS, proteinuria</td>
</tr>
<tr>
<td>7</td>
<td>32/M</td>
<td>Unilateral agenesis</td>
<td>Renal failure</td>
<td>FSGS, proteinuria</td>
</tr>
<tr>
<td>8</td>
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<td>Renal failure</td>
<td>Crescentic nephritis</td>
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<td>Proteinuria</td>
<td>Acute GN, haematuria</td>
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<tr>
<td>10</td>
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<td>Renal failure, proteinuria</td>
<td>IGA nephropathy</td>
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<td>11</td>
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<td>Unilateral shrunken kidney</td>
<td>Renal failure, proteinuria</td>
<td>IGA nephropathy</td>
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<tr>
<td>12</td>
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<td>Renal failure</td>
<td>ATN</td>
</tr>
<tr>
<td>13</td>
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<td>Proteinuria</td>
<td>FSGS</td>
</tr>
<tr>
<td>14</td>
<td>42/F</td>
<td>Nephrectomy</td>
<td>Renal failure</td>
<td>FSGS, proteinuria</td>
</tr>
<tr>
<td>15</td>
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<td>Renal failure</td>
<td>CIN</td>
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<tr>
<td>16</td>
<td>28/F</td>
<td>Unilateral shrunken kidney</td>
<td>Renal failure</td>
<td>Oxalosis</td>
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</tbody>
</table>

FSGS focal and segmental glomerulosclerosis  Acute GN acute glomerulonephritis  ATN acute tubular necrosis  CIN chronic interstitial nephritis

With the patient holding his breath in inspiration, the gun was advanced to the surface of the lower pole and then discharged. Two or three cores of the tissue were taken for light microscopic and immunofluorescent studies. The patients were monitored in the ward for 24 hours following biopsy. A post-biopsy ultrasound was done only if required.

Sixteen solitary kidney biopsies were performed between May 1992 and February 1998 in 10 males and 6 females with a mean (SD) age of 33.2 (14.4) years. The causes of solitary kidney included unilateral renal agenesis in 6 and unilateral nephrectomy in 4. In 3 patients, only 1 kidney could be visualized on ultrasound, but further investigations were not done to confirm the absence of the contralateral kidney. Three others had unilateral shrunken kidney (<7 cm in length), with the second kidney of normal size. Thirteen patients had renal failure and 3 required dialysis. The mean (SD) creatinine in the 10 patients was 2.86 (0.98) mg/dl and 9 patients were proteinuric (Table I). Fifteen biopsies were performed using monopry guns and one using a Tru-cut needle. Sufficient tissue was obtained in all cases and there were no complications.

Renal biopsy techniques have improved in the past few years, reducing the risk of major complications. An ultrasound enables direct visualization of the kidney. Automated biopsy instruments and smaller gauge needles have reduced the risk of injury to the kidney. A recent review mentions the risk of renal ablation as 6 per 10 000 and the risk of mortality as 7 per 10 000 following percutaneous renal biopsy. These figures compare favourably with the risk of general anaesthesia. The risk of cardiac arrest associated with general anaesthesia is 7.1 per 10 000 for ASA (American Society of Anaesthesiologists) class 2 patients (mild-to-moderate systemic disturbances, i.e. essential hypertension, mild diabetes or anaemia). For patients with more severe disorders, the risk of...
cardiac arrest is higher; 12.6 per 10 000 for ASA class 3 patients and 25.1 per 10 000 for ASA class 4 patients. Patients with mild renal failure and hypertension are categorized as ASA class 2 and those with dialysis-dependent renal failure ASA class 3. Eleven of our patients were in ASA class 2 and 3 in ASA class 3. These figures indicate that percutaneous renal biopsy was the safer option for these patients.

In conclusion, modern biopsy techniques have made percutaneous renal biopsy a much safer option than open renal biopsy, especially for patients with renal failure, hypertension or anemia, in whom general anaesthesia may be risky. Furthermore, biopsies of renal allografts are routinely performed without major complications. Hence, a solitary kidney should no longer be considered as a contraindication for percutaneous renal biopsy. When done by an experienced operator, using an automated gun under ultrasound guidance, it is likely to be safer than an open biopsy.

28 September 1998 M. Abi Abraham K. N. Arun George T. John Poulose P. Thomas Chakkor korula Jacob Department of Nephrology Christian Medical College and Hospital Vellore Tamil Nadu

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Acute secretory traveller’s diarrhoea caused by *Vibrio cholerae* which does not belong to the O1 or O139 serogroup

About 30%-50% of people travelling from developed to developing countries frequently suffer from traveller’s diarrhoea. Enterotoxigenic *Escherichia coli* (ETEC) is the most common cause of traveller’s diarrhoea worldwide. The unprecedented appearance of a novel epidemic strain of *Vibrio cholerae* non-O1 classified as *Vibrio cholerae* O139 Bengal causing major epidemics of cholera in the Indian subcontinent is of considerable scientific and public health interest. 1,2 Recently, the V. cholerae non-O1, non-O139 serogroups have been implicated in the occurrence of severe cholera-like disease in Calcutta, an area which is endemic for cholera. We encountered a Japanese tourist who developed acute secretory diarrhoea and severe dehydration akin to cholera caused by an organism which did not secrete cholera toxin (CT).

A 30-year-old male from Tokyo, Japan was admitted to the Infectious Diseases Hospital, Calcutta on 3 September 1997 in a semi-conscious state with a history of profuse watery diarrhoea, nausea and severe dehydration. He arrived in Calcutta from Dhaka, Bangladesh on 20 August 1997 and was residing in a hotel. He started having diarrhoea on 2 September 1997 which continued to worsen. In the 1-hour period prior to hospitalization, he had passed 6 loose stools and had not passed urine during the previous 6 hours.

On physical examination, he appeared ill, had a rapid and feeble pulse and his systolic blood pressure was 68 mmHg. He was drowsy and had deeply sunken eyes, dry skin, dry lips and tongue. He was hyperventilating but did not have a history of fever or intake of any antibiotic prior to hospitalization. An intravenous infusion of Ringer’s lactate was started and 2 hours later he was asked to drink oral rehydration salt solution. Subsequently, tetracycline (500 mg 6 hourly) was administered orally. The patient was rehydrated within 6 hours by the intravenous and oral routes. After rehydration, the patient gave a history of intake of sweetened curd (lassi), fried rice, vegetable noodles and tea for dinner prior to the onset of the disease. He was discharged on 4 September 1997.

A fresh stool sample was collected at the time of admission using a sterile rectal catheter and was processed within one hour of arrival at the laboratory for isolation of enteropathogens using standard techniques. 3 A part of the faecal sample was examined microscopically for the presence of ova, cysts and parasites but did not reveal any. No other bacterial enteropathogen including *Salmonella*, *Shigella*, *Campylobacter*, *Vibrio parahaemolyticus*, *V. cholerae* O139, diarrhoeagenic *Escherichia coli* or *Clostridium difficile* were isolated from the stool sample.

The strain was presumptively identified as *Vibrio cholerae* by a multistep medium. Since the strain did not agglutinate with either 01 or O139 antisera, it was categorized as belonging to the non-O1 non-O139 serogroup. The non-O1 non-O139 strain isolated from the traveller, when examined by multiplex polymerase chain reaction (PCR) 4-6 did not possess the ctxA or tcpA genes indicating that the strain did not possess the genetic potential to produce the conventional cholera toxin (CT). The strain was also examined by tissue culture assay 7 using CHO cells to determine if it was capable of increasing intracellular cyclic AMP levels which causes elongation of CHO cells. The isolated strain did not produce the factor which was capable of cell elongation indicating that the strain did not produce CT (confirming the PCR results) or a CT-like toxin.

Antimicrobial susceptibility 8 testing showed that the strain was susceptible to chloramphenicol, gentamicin, streptomycin, ciprofloxacin and norfloxacin but was resistant to, ampicillin, co-trimoxazole, tetracycline, furazolidone, neomycin and nalidixic acid.

Patients suffering from traveller’s diarrhoea, which is usually a mild illness, rarely seek hospital treatment. Serogroups of *V. cholerae* other than O1 and O139 cause a clinical condition which closely resembles cholera and necessitates hospitalization. How this strain potentiates the cholera-like clinical condition is not clear as the PCR revealed that the isolated strain had no virulence genes encoding for CT production and for the surface organelle that is required for intestinal colonization. The clinical state of cholera is principally attributed to the CT which activates adenylate cyclase resulting in increased levels of cyclic AMP leading to hypersecretion of salt and water.

The pathophysiology of gastroenteritis caused by *V. cholerae* non-O1 non-O139 is still not clear. However, the disease can be severe in rare instances requiring hospital care. In this report, the traveller was infected by a virulent strain of *V. cholerae* non-O1 non-O139 which did not produce the conventional CT but caused cholera-like diarrhoea and dehydration. However, severe cholera-like diarrhoea caused by non-O1 V. cholerae which do not produce cholera-like enterotoxin has been reported previously. 9,10 Hughes et al. 11 also reported an outbreak of *V. parahaemolyticus* in which no enterotoxin could be demonstrated. We are continuing to investigate the virulence factor of the isolated strain responsible for the profound secretory diarrhoea.


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Antiviral chemoprophylaxis after occupational exposure to the human immunodeficiency virus (HIV)

The Acquired Immunodeficiency Syndrome has assumed pandemic proportions with more than 10 million people being currently positive for the human immunodeficiency virus (HIV).\(^1\) India will face a major brunt of this disease by the turn of the century. Health care professionals are at an increased risk of acquiring the virus due to accidental occupational exposure. Prevention of HIV transmission is possible even after exposure and physicians must be aware of the antiviral chemoprophylaxis to be taken. To protect health care workers adequately, the drugs used for antiviral prophylaxis must be made freely available.

The HIV seroconversion rate after accidental occupational inoculation of HIV by a percutaneous injury from a needle or other sharp device is approximately 0.3\%.\(^2,3\) The risk of viral transmission is related to the size of the HIV inoculum and the number of viral particles involved. Factors associated with a higher risk of transmission include an early stage of HIV infection before HIV antibodies have formed, advanced stages of AIDS, high plasma levels of HIV RNA, large-bore hollow needles and deep accidental inoculation.\(^3\)

Until recently, only limited attention has been paid to post-exposure antiviral chemoprophylaxis.\(^4\) Recent reports on the effectiveness of measures to prevent HIV transmission after occupational exposure in health care workers and to prevent vertical transmission of HIV from infected pregnant women to their newborn infants, as well as the development of new, more potent, anti-retroviral agents have led to a renewed focus on HIV post-exposure prophylaxis.\(^5,6\) Both the Centers for Disease Control (CDC) and the International AIDS Society have made recommendations for HIV post-exposure prophylaxis based on recent studies.

The CDC recommends that prophylaxis be initiated ‘within 1 to 2 hours of exposure’ while the International AIDS Society recommends that it be initiated ‘as soon as possible’. Immediate wound management should include soaking the area exposed in povidone-iodine or alcohol.

Combination therapy is more effective than monotherapy for treatment of patients with established HIV infection because viral mutations occur continuously and begin with the first cycles of replication during primary infection.\(^7\) Therefore, combination therapy may also confer more protection than a single drug. The CDC also recommends that zidovudine be considered for all HIV post-exposure prophylaxis regimens because it is the only agent for which there are data supporting its efficacy in the clinical setting. The CDC also recommends the addition of lamivudine (also known as 3TC) for increased anti-retroviral activity against zidovudine-resistant strains, along with the protease inhibitor indinavir (also known as IDV).

The International AIDS Society panel suggests that at least two drugs that have not been used in the source patient should be considered for antiviral chemoprophylaxis.

The optimal duration of the post-exposure prophylaxis is not known. However, the current recommendation is that anti-retroviral medications should be taken for 4–6 weeks.

The combination of zidovudine, lamivudine and indinavir has greater anti-retroviral activity than zidovudine alone and is active against many zidovudine-resistant HIV strains without substantially increasing toxicity. The standard adult regimen recommended by the CDC is: zidovudine 200 mg every 8 hours on an empty stomach, lamivudine 150 mg every 12 hours (without regard to food) and indinavir, 800 mg every 8 hours on an empty stomach.

In India, the National AIDS Control Organization (NACO) recommends zidovudine 200 mg tid for 1 month followed by 100 mg tid for the next 2 months as prophylactic therapy for HIV exposure. If serology (ELISA) is negative at 3 months, the above therapy is stopped; however, if positive it is to be continued life-long. The cost of zidovudine is Rs 25 for a 100 mg capsule and the drug can be procured (free of cost for health care workers with occupational exposure) from the State AIDS Cell.

The best time to begin thinking about HIV post-exposure prophylaxis is before the accidental inoculation occurs. Indian medical institutions must develop a specific regimen to protect health care professionals and have standard prophylaxis kits available for use in occupational and nosocomial exposures in the near future.

3 October 1998

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