Sclerosing peritonitis (SP) is a well-recognized, uncommon but serious complication of continuous ambulatory peritoneal dialysis (CAPD) of variable reported frequency (1). It is more commonly reported in Europe, rarely in America (2), and never in Hong Kong.

Sclerosing peritonitis (SP) is an uncommon but serious complication of CAPD with various suggested etiologies. We have documented 14 cases of SP in 18 patients who had used chlorhexidine in alcohol (ChA) in the connection procedure for CAPD. Thirteen died. Nine of the 14 patients had been transferred to hemodialysis or renal transplantation, yet all still developed symptoms of SP within a few months after transfer—even the 5 who were originally asymptomatic. The main symptoms of SP were peritoneal ultrafiltration failure, exudative bloody ascites and intestinal obstruction. They presented at around 5 years (30-80 months) after commencement of CAPD. Most deaths were related to intestinal obstruction. Four other patients with a comparable duration of ChA exposure were continued on CAPD with the Travenol Spike System (TSS), without further exposure to ChA. They were all asymptomatic of SP after 9-12 months. Comparing the 2 groups of asymptomatic patients, those transferred to TSS had a much better outcome after 9 months than those transferred to HD or renal transplantation (P=0.0476). We suggest that ChA is the main cause of SP in our patients and that continuing CAPD without further exposure to ChA is a better alternative than stopping CAPD to prevent the progression of SP.

KEY WORDS: Sclerosing peritonitis; connection procedure; chlorhexidine in alcohol; intestinal obstruction; exudative bloody ascites.

SP is characterized pathologically by: 1. hyaline sclerotic thickening of both the visceral and parietal peritoneum, and 2. encapsulating peritonitis, where the bowel is encapsulated by a fibrous neo-membrane of variable thickness into a cocoon form (1,3), keeping apart the visceral serosa from the parietal peritoneum. Mural bowel fibrosclerosis with replacement of the outer longitudinal muscle layer is also reported (4).

The bowel, wrapped in a tight, thick fibrous neo-membrane, becomes kinked, convoluted and obstructed. If the longitudinal muscle layer is seriously invaded, the bowel becomes paralytic.

There are many suggested possible etiologies for SP, including B-blockers, particularly practolol (5), acetate in dialysate (6), recurrent peritonitis (2), plasticizers, bacterial filter (7), intraperitoneal antibiotics, antiseptics, particularly chlorhexidine in alcohol, (8) and even the Tenckhoff catheter.

From January 1988 up until December 31, 1989, we documented 14 cases of sclerosing peritonitis in our CAPD patients employing chlorhexidine in alcohol (ChA) as the antiseptic in the connection procedure.

METHODS

We have a group of patients on a special connection procedure, called the “Hong Kong Connection” in CAPD (9). In this connection procedure, a simple disconnection of the Tenckhoff catheter from the effluent dialysate bag and a reconnection to a new bag is done inside a small transparent polyethylene bag containing a piece of gauze soaked with 0.5% chlorhexidine in 70% alcohol for sterilization purposes. A very low peritonitis rate was achieved with this technique (9). The peritoneal dialysate used was supplied by Japan Medical Supply (JMS). The dialysate contains lactate 35 mmol/L, dextrose 2.273%, Na 132 mmol/L, Ca 1.75 mmol/L, Mg 0.5 mmol/L, Cl1102 mmol/L. Its pH is 5.2-5.5.

Since the discovery of the first case of SP in January 1988, we tried to transfer this group of
CAPD patients one by one to hemodialysis or renal transplantation. From January 1989, the remaining patients were transferred to the Travenol Spike System (TSS) to continue CAPD without further exposure to ChA or, theoretically, any other antiseptics. A few patients died before they could be transferred to other systems. Altogether, there were 18 patients.

The 18 patients can be divided into three groups. Group 1, those who continued to use ChA; CAPD was never stopped. Group 2, those transferred to hemodialysis (HD) or renal transplantation. This latter group can be subdivided into 2 subgroups: Group 2a, those already having symptoms of SP at the time of

| TABLE 1  |
| Patient Data  |

**Group 1 ChA never stopped**

<table>
<thead>
<tr>
<th>patient</th>
<th>Duration of ChA (mos)</th>
<th>Onset of s/s of SP (mos)</th>
<th>s/s of SP</th>
<th>Dx</th>
<th>outcome</th>
<th>sur</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>/</td>
<td>/</td>
<td>A</td>
<td>D-sepsis</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>79</td>
<td>79</td>
<td>gut perf. (io)</td>
<td>L+A</td>
<td>D-gut perf.</td>
<td>79</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>51</td>
<td>uf</td>
<td>A</td>
<td>D-CVS Cx</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>66</td>
<td>64</td>
<td>uf, io</td>
<td>A</td>
<td>D-ps</td>
<td>66</td>
</tr>
<tr>
<td>5</td>
<td>78</td>
<td>77</td>
<td>io</td>
<td>A</td>
<td>D-ps</td>
<td>78</td>
</tr>
</tbody>
</table>

**Group 2A Transferred to hemodialysis**

<table>
<thead>
<tr>
<th>patient</th>
<th>Duration of ChA (mos)</th>
<th>Onset of s/s of SP (mos)</th>
<th>Onset of s/s of SP after ChA stopped (ba mos)</th>
<th>Io(mos)</th>
<th>Dx</th>
<th>outcome</th>
<th>sur</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>53</td>
<td>49(uf)</td>
<td>6</td>
<td>7</td>
<td>B+A</td>
<td>D-i0</td>
<td>60</td>
</tr>
<tr>
<td>7</td>
<td>56</td>
<td>54(io)</td>
<td>4</td>
<td>0</td>
<td>B+A</td>
<td>D-inf.ba</td>
<td>72</td>
</tr>
<tr>
<td>8</td>
<td>60</td>
<td>57(uf)</td>
<td>1</td>
<td>1</td>
<td>B</td>
<td>D-i0</td>
<td>61.5</td>
</tr>
<tr>
<td>9</td>
<td>59</td>
<td>56(uf)</td>
<td>/</td>
<td>0.5</td>
<td>B</td>
<td>D-i0</td>
<td>60</td>
</tr>
</tbody>
</table>

**Group 2b Asymptomatic, transferred to HD/renal transplant**

<table>
<thead>
<tr>
<th>patient</th>
<th>Duration of ChA (mos)</th>
<th>Onset of s/s of SP (mos)</th>
<th>Ds (io(mos))</th>
<th>Dx</th>
<th>outcome</th>
<th>sur</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>39</td>
<td>/</td>
<td>34</td>
<td>A</td>
<td>D-GIB</td>
<td>73</td>
</tr>
<tr>
<td>11</td>
<td>53</td>
<td>2</td>
<td>5</td>
<td>B</td>
<td>D-i0</td>
<td>60</td>
</tr>
<tr>
<td>12</td>
<td>80</td>
<td>3</td>
<td>6</td>
<td>B</td>
<td>D-i0</td>
<td>89</td>
</tr>
<tr>
<td>13</td>
<td>32</td>
<td>5</td>
<td>8</td>
<td>L</td>
<td>S-TPN</td>
<td>&gt;47</td>
</tr>
<tr>
<td>*14</td>
<td>51</td>
<td>9</td>
<td>11</td>
<td>L</td>
<td>D-i0</td>
<td>65</td>
</tr>
</tbody>
</table>

**Group 3 Asymptomatic, transferred to TSS**

<table>
<thead>
<tr>
<th>patient</th>
<th>Duration of ChA (mos)</th>
<th>Onset of s/s of SP after ChA stopped (mos)</th>
<th>s/s of SP</th>
<th>outcome</th>
<th>sur</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>46</td>
<td>&gt;10</td>
<td>/</td>
<td>S</td>
<td>&gt;56</td>
</tr>
<tr>
<td>16</td>
<td>70</td>
<td>&gt;12</td>
<td>/</td>
<td>S</td>
<td>&gt;82</td>
</tr>
<tr>
<td>17</td>
<td>35</td>
<td>&gt;12</td>
<td>/</td>
<td>S</td>
<td>&gt;47</td>
</tr>
<tr>
<td>18</td>
<td>48</td>
<td>&gt;9</td>
<td>/</td>
<td>S</td>
<td>&gt;58</td>
</tr>
</tbody>
</table>

sur = survival from commencement of CAPD (mos)
uf = ultrafiltration failure io = intestinal obstruction
ba = bloody ascites inf = infected ps = peritonitis
A = autopsy B = biopsy L = laparatomy
D = death S = surviving
S/S = signs and symptoms
Dx = diagnosed by
Cx = complication
perf. = perforation
**TABLE 2**  
Patient Group Data

<table>
<thead>
<tr>
<th>Group</th>
<th>1</th>
<th>2a</th>
<th>2b</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Median age (range)</td>
<td>55 (45-64)</td>
<td>44.5 (37-54)</td>
<td>35 (20-48)</td>
<td>48 (39-52)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>4:1</td>
<td>3:1</td>
<td>3:2</td>
<td>1:3</td>
</tr>
<tr>
<td>Median duration of ChA exposure (mos) (range)</td>
<td>66 (30-79)</td>
<td>57.5 (53-60)</td>
<td>51 (33-80)</td>
<td>47.5 (35-70)</td>
</tr>
<tr>
<td>Median onset of symptoms after ChA stopped (mos) (range)</td>
<td>/ (0-6)</td>
<td>0.75 (2-34)</td>
<td>5 &gt;11 (9-12)</td>
<td></td>
</tr>
<tr>
<td>Median symptom-free period since CAPD commencement (mos) (range)</td>
<td>64 (30-79)</td>
<td>59.75 (56-61)</td>
<td>60 (37-83)</td>
<td>&gt;57 (47-82)</td>
</tr>
</tbody>
</table>

**TABLE 3**  
Occurrence and Symptoms of Sclerosing Peritonitis

<table>
<thead>
<tr>
<th>Group</th>
<th>1 (100%)</th>
<th>2 (100%)</th>
<th>3 (0%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurrence</td>
<td>5 (100%)</td>
<td>9 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>4 (80%)</td>
<td>9 (100%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Group 2a</th>
<th>Group 2b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrafiltration failure</td>
<td>2 (40%)</td>
<td>3 (75%)</td>
</tr>
<tr>
<td>Bloody ascites</td>
<td>0 (0%)</td>
<td>3 (75%)</td>
</tr>
<tr>
<td>Intestinal obstruction</td>
<td>3 (60%)</td>
<td>4 (100%)</td>
</tr>
<tr>
<td>Surviving</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
transfer, and Group 2b, those who were still asymptomatic at the time of transfer. Group 3, those transferred to TSS, were also asymptomatic at the time of transfer.

SP is diagnosed pathologically by parietal biopsy at the time of Tenckhoff catheter removal, by morphology and biopsy at laparotomy, or by autopsy.

The symptoms of SP and their onset, duration of ChA exposure, outcome, peritonitis episodes, and B-blockers prescribed were compared and analyzed retrospectively until December 31, 1989.

### RESULTS

There were 5 patients in Group 1, 9 patients in Group 2 (4 in Group 2a and 5 in Group 2b) and 4 patients in Group 3. All patients in Group 1 and Group 2 developed SP (total of 14 patients) and only 1 of them (patient 1), who died 30 months after commencement of CAPD, was asymptomatic of SP. Until the end of the observation period on December 31, 1989, no patients in Group 3 developed symptoms of SP or died.

### TABLE 4
Results of the Two Asymptomatic Groups 2b and 3 at 9 Months After Stopping ChA

<table>
<thead>
<tr>
<th></th>
<th>2b</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients symptom free</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>No. of patients symptomatic of SP</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Total no. of patients</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

p=0.0476 by Fisher exact test comparing number of asymptomatic patients of Group 3 against Group 2b.

### TABLE 5
Peritonitis

<table>
<thead>
<tr>
<th>Group</th>
<th>1</th>
<th>2a</th>
<th>2b</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median episodes</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>(range)</td>
<td>(1-6)</td>
<td>(0-5)</td>
<td>(0-5)</td>
<td>(1-8)</td>
</tr>
<tr>
<td>Frequency:</td>
<td>18.18</td>
<td>20.83</td>
<td>15.87</td>
<td>14.08</td>
</tr>
</tbody>
</table>
The duration of ChA exposure, symptoms of SP and their time of onset and outcome for each individual group are shown in Table 1. The age, duration of exposure to ChA, and symptom-free periods of the different groups are compared in terms of median and range in Table 2. The occurrence and symptoms of SP are compared in Table 3.

In Group 1, all patients died. Four deaths were related to SP. Patients 4 and 5 died from peritonitis (*Pseudomonas aeruginosa* and *Staphylococcus aureus*), which was very resistant to treatment. At autopsy, bacteria were found to be harbored in the sclerotic tissue of the serosal surface of the bowel, rendering difficult antibiotic penetration and protection from the host phagocytic activity. Mural bowel fibrosclerosis was also present. Patient 2 died from a small bowel perforation resulting from a kinked and strangulated bowel loop as a consequence of SP. Patient 3 had overwhelming peritoneal ultrafiltration failure causing fluid overload and recurrent heart failure. He had a sudden death while he was receiving supplementary HD to remove his excessive fluid accumulation. Only 1 patient (patient 1) did not have any symptoms of SP. He died of pulmonary sepsis, yet SP was documented in autopsy.

In Group 2a, there were 4 patients. Three had ultrafiltration failure a few months before they were transferred to HD. One (patient 7) had intestinal obstruction rendering CAPD impossible and was changed to HD as well. She was maintained on total parenteral nutrition (TPN) until she died, 16 months later, from infected bloody ascites after repeated therapeutic aspiration. Bloody ascites after cessation of CAPD was also noticed in 2 other patients (6 and 8). All developed intestinal obstruction within 1-6 months after cessation of CAPD, and died.

In Group 2b, there were 5 patients. Four were electively transferred to HD, and one received a living related renal transplantation from her brother. However, all 5 patients still developed symptoms of SP. Four patients (patients 11-14) developed bloody ascites a few months after cessation of CAPD (2-9 months), which was followed by intestinal obstruction around 23 months afterwards. Two patients (patients 13 and 14) received surgical intervention, including the stripping away of the encapsulating fibrous sheath, enterolysis and a gastrojejunostomy to bypass a high obstruction at the duodenojejunal junction. Surgery failed in both patients. One died and 1 still survives on TPN. Two other patients died before surgery was arranged. Patient 10 was electively transferred to HD before January 1988 for recurrent peritonitis (6 episodes in 39 months). He was well until 34 months later, when he developed intestinal obstruction and died from massive gastrointestinal bleeding. No definite source of bleeding could be identified, even after autopsy. SP was also documented in this patient.

The median symptom-free period after cessation of CAPD was 5 months (2-34 months) and the median total symptom-free period from the commencement of CAPD was 60 months (37-80 months), comparable to that of Group 1 and Group 2a.

The bloody ascites occurring in Groups 2a and 2b occurred a few months after cessation of CAPD and was typically exudative (protein content 40-45 g/L). An infective cause, including tuberculosis, could not be identified, even at autopsy.

In Group 3, all 4 patients were symptomatic at the time of transfer. The median duration of ChA exposure was 47.5 months (37-70 months), comparable to that of Group 2b. One patient (patient 18) had a
Various etiologies of sclerosing peritonitis have been suggested. We have a very high incidence of sclerosing peritonitis: 14 out of 18 patients using ChA in the connection procedure of CAPD developed sclerosing peritonitis. Thirteen of them died; only 1 survives on TPN (10). In searching for an underlying etiology for our high incidence, we analyzed the medication prescribed, peritonitis, and the nature and method of CAPD in our patients. None were prescribed practolol, though propranolol and metoprolol were commonly prescribed, as in any other renal center. The prescription pattern is similar in each patient group. The number of peritonitis (infective and chemical) episodes in our patients has a median of 3 (range 0-6) only. Two of them had no recorded peritonitis history. The peritonitis rate of 1 episode/14.1-20.8 patient months is low compared to many dialysis centers (11, 12). In contrast to Slingeneyer’s analysis of 68 cases of sclerosing peritonitis from various centers where he noticed an excessively high peritonitis rate (1 episode in 5.5 patient months) and suggested recurrent peritonitis as the main cause for sclerosing peritonitis (2), we have a much lower peritonitis rate. We do not think peritonitis is the main cause for our high incidence of sclerosing peritonitis.

The dialysate of JMS contains lactate but not acetate, which has been reported to have a relationship to sclerosing peritonitis. The concentration of glucose and other electrolytes does not differ from most other systems. Sclerosing peritonitis is not known to be reported in other centers using JMS dialysate.

The most notable element in our patients is the use of 0.5% chlorhexidine in 70% alcohol in the connection procedure. A small amount of ChA is able to enter the tubings during disconnection and reconnection, and subsequently the peritoneal cavity. In fact, some patients experienced accidental entrance of ChA into the peritoneal cavity, leading to chemical peritonitis with severe abdominal pain. Our high incidence of a culture-negative rate (44%) reflects that some of this peritonitis may be due to chemical peritonitis.

Junor et al. reported 11 cases of sclerosing peritonitis in their series (8). All of them used ChA as the antiseptic spray for the Fresenius system. Sclerosing peritonitis was not found in 2 other groups using the Travenol and Fresenius system employing povidine iodine and povidine respectively as the antiseptic spray. They also demonstrated that daily intraperitoneal injection of dialysate containing 5 mL/L of ChA into rats induces varying degrees of oedema of the immediate submesothelial tissue with chronic inflammatory infiltrate, but not in those injected with dialysate alone or a lower concentration of ChA.

Our finding of a very high incidence of sclerosing peritonitis with the use of ChA is consistent with that of Junor et al. The evidence strongly suggests that chlorhexidine in alcohol is the culprit for sclerosing peritonitis in our patients.

Are there any other antiseptics safe from inducing sclerosing peritonitis if they enter the peritoneal cavity? Mackow et al. documented that 10% povidine iodine, chlorhexidine acetate and formaldehyde in dialysate are also capable of inducing a similar change of sclerosing peritonitis in rats (13, 14). We suggest that we should avoid any possibility of an antiseptic entering the peritoneal cavity.

The extremely high incidence of sclerosing peritonitis in our series suggested that sclerosing peritonitis occurs almost invariably in CAPD patients with prolonged use of ChA. It usually presents at around 5 years (30-80 months) of ChA exposure. The 3 main features of SP in our series is ultrafiltration failure, bloody ascites and intestinal obstruction. Patients who developed ultrafiltration failure ultimately required a transfer to HD. However, the transfer to HD did not save our patients, as all of them developed intestinal obstruction within a few months after cessation of CAPD and died.

Similarly, we electively stopped CAPD in 5 asymptomatic patients, hoping that they might be saved from sclerosing peritonitis, yet most of them still developed intestinal obstruction within a few months. Surgery is known to be difficult and carries a high mortality. Theoretically, the encapsulating fibrous sheath can be stripped to release the bowel obstruction (3). We find this difficult, as it usually produces areas of raw surface and leads to subsequent adhesion and reobstruction. Moreover, it is very easy to perforate the bowel during enterolysis. The intraluminal pressure can be very high (3), rendering persistent leakage from the perforation. The result of surgery is often unsatisfactory (1, 15).

Collection of exudative fluid inside the peritoneal
cavity or within the fibrous sheath has been reported (1, 3). But we noticed that heavily blood-stained exudative ascites occurring commonly in patients after CAPD had been stopped. This is not found in those continuing CAPD. The exact cause could not be identified even after autopsy, though in a few patients there were some areas of bruised peritoneum. The ascites are often massive and tense, causing a lot of distention symptoms, nausea, anorexia and wasting. Reaccumulation occurs very quickly after therapeutic aspiration, making management difficult. Occurrence is noticed to be preceding intestinal obstruction by 23 months. The time sequence observed suggests a relation to intestinal obstruction in terms of reflecting the severity of sclerosing peritonitis or even an etiological contribution to intestinal obstruction. The exudative bloody ascites are likely a result of the continuous inflammatory process. As this cannot be drained out after cessation of CAPD, the accumulation may induce the fibrosing activity further (2, 16).

When we compare the management of the 2 asymptomatic groups (2b and 3), both have a comparable median exposure of ChA (51 and 47.5 months), yet the group that continued on CAPD with TSS did significantly better. All in Group 3 were still asymptomatic after a follow-up of 9-12 months, while for the same observation period of 9 months, only 5 of 5 patients who stopped CAPD (Group 2b) was asymptomatic. Similar observation is found in Slingeneyer's report (2). He noticed that 66% of all cases of SP had been transferred to another treatment modality a few months before sclerosing peritonitis was diagnosed. We postulate that though patients in Group 2b were no longer exposed to ChA, the inflammation and fibroblastic activity was not halted immediately. With the cessation of CAPD, the lack of free fluid inbetween the bowel loops makes the inflamed bowel surfaces approximated together to form adhesion to hasten the onset of intestinal obstruction. If CAPD is continued without the stimulant for the fibrosing activity, it allows time for the inflammation at the raw surfaces to subside and less adhesion will be formed.

Though there are reports that sclerosing peritonitis may regress after CAPD has been stopped (17), particularly in the early phase, more reports suggest that it is a progressive disease and does not regress with cessation of CAPD (2, 8). One of our patients still developed intestinal problems from sclerosing peritonitis 34 months after cessation of CAPD. Whether the 4 patients in Group 3 can be prevented from the progression of SP by continuing CAPD with TSS without further exposure to ChA still awaits further observation.

In conclusion, sclerosing peritonitis is a serious and lethal complication of CAPD. Prevention is more important than treatment. It appears that chlorhexidine in alcohol is one of the causing agents. We have to be very alert to identify any possible risk factors. If risk factors are known to be present for a long period, it is of prime importance to find a way to prevent the progression to save the patient's life.

ADDENTUM

Upon subsequent follow-up of Group 3 patients till March 31, 1991, patient 15 died at 14 months after ChA stopped with symptoms of intestinal obstruction. The other 3 patients were still surviving and asymptomatic rendering a symptom free period of >24-27 months after ChA stopped, and a total duration of survival of greater than 97, 62 and 73 months for patients 16; 17 and 18 respectively.

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