to all children with kwashiorkor is of doubtful value. A routine antibiotic such as tetracycline might be used, but since half of the children had no infection, and antibiotics may have serious side-effects, and since, moreover, it is difficult to devise a universal "umbrella," the value of routine antibiotic regimens is questionable.

Bacteriological evidence of infection should always be sought before antibiotics are prescribed, and we believe that the routine use of antibiotics in kwashiorkor may lead to a false sense of security and to diagnostic and therapeutic dilemmas.

However, bacteriological services are rarely available where kwashiorkor abounds, and therefore we make the following suggestions. Urine should be examined for pus cells. Pyuria should be confirmed by examination of a suprapubic sample where possible. Antibiotics should be prescribed only if there is some clinical indication of a particular infection—for example, of the skin, chest, throat, or blood stream. Diarrhoea is only occasionally due to a specific organism. Since it is usually impossible to distinguish clinically between infective and non-infective diarrhoea, a working rule might be to give antibiotics to those children with particularly severe diarrhoea (say more than six stools a day) or in whom a complicating septicaemia is suspected because of a high pyrexia or hypothermia, a "soft" spleen, a rapidly falling haemoglobin, or "warm hypotension" in an already very sick child.

Summary

About half the children admitted to this unit with severe malnutrition had an acute bacterial infection.

Gram-negative infections of the urinary tract, or gut, and septicaemia were particularly troublesome, while Gram-positive infections gave less cause for concern. The cause of most of the chest infections remains unknown.

Penicillin would have been appropriate for only a few infections, and if a routine antibiotic is thought to be necessary tetracycline would be better. There are, however, pertinent

arguments against the routine use of antibiotics, and bacteriological evidence of infection should be sought wherever possible before the antibiotics are prescribed.

If bacteriological services are not available antibiotics should be given only if there is clinical indication of a particular infection—for example, of the skin, chest, throat, gut or blood stream.

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Prolonged Peritoneal Dialysis in Patients Awaiting Renal Transplantation

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The value of peritoneal dialysis when used for short periods in the management of patients suffering from acute renal failure is well established (Maxwell *et al.*, 1959; Burns *et al.*, 1962). Peritoneal dialysis carried out for more prolonged periods in patients with chronic irreversible renal failure has been relatively little studied (Boen *et al.*, 1964; Lasker *et al.*, 1965). Compared with haemodialysis, peritoneal dialysis has the advantage that a number of patients can be managed in general medical wards without capital expenditure or the need for a special unit and specially trained nursing and technical staff. For this reason peritoneal dialysis was used in patients awaiting human cadaver renal transplantation, though haemodialysis is preferred for this purpose by most other groups. Because of the difficulties in obtaining suitable donor kidneys some patients have had to wait for months before transplan-

tation, and this is a report of our experience of peritoneal dialysis for periods of two to seven months.

Patients and Methods

Details of the 27 patients who received peritoneal dialysis for more than two months are shown in Table I. They were

TABLE I.—Details of 27 Patients Receiving Prolonged Peritoneal Dialysis

Age	{ Range		8–46 years
	{ Mean		28.6 "
Sex	{ Male		16
	{ Female		11
Underlying renal disease	{ Chronic glomerulonephritis		13
	{ Chronic pyelonephritis		9
	{ Polycystic disease		2
	{ Others*		3
Period on dialysis	{ Range		60–219 days
	{ Mean		104 days
Previous dialysis at other hospitals	{ Range		11
	{ Mean		14–119 days
Period	{ Range		54 days
	{ Mean		54 days

* Acute glomerulonephritis 1, congenital hyperoxaluria 1, and primary hypertensive nephrosclerosis 1.

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selected for transplantation by criteria previously described (Mowbray *et al.*, 1965). In all of them renal function was inadequate to maintain life without dialysis (endogenous creatinine clearance less than 2 ml. per minute).

Patients were managed in two general medical wards and were given a high-protein diet without restriction of fluid or salt. They all received intensive physiotherapy and were encouraged to spend as much time as possible outside hospital. Initially, peritoneal dialysis was performed on alternate nights between 7 p.m. and 6 a.m., with the patient off dialysis during the day and spending free nights at home. Before transplantation patients were started on a low dose of azathioprine (1–1.5 mg./kg./day) and were then dialysed every night to minimize the toxic effects of this therapy. Blood urea and plasma electrolytes were estimated at least twice weekly.

Dialysis Procedure

The dialysis procedure was based on that described by Maxwell *et al.* (1959) and Thomson *et al.* (1964). With full aseptic precautions a catheter was introduced into the peritoneal cavity through the midline about 1 in. (2.5 cm.) below the umbilicus. During 1966 the Trocath catheter (McGaw Labs. Inc.) (Weston and Roberts, 1965) was used because the stylet within its lumen requires a much smaller skin incision than catheters introduced through a cannula. The catheter was anchored by a single pursestring suture surrounded by sterile dry gauze swabs and covered with a dressing of Micro-pore Surgical Tape. The swabs and dressing were changed daily. Catheters were changed only when it became impossible to remove obstructing particles by syringing or when they became dislodged. The suture was reinserted as soon as it became displaced. The dialysis solution was a standard commercially available one, Dialaflex (Allen and Hanburys).

Composition.—Solution 141 mEq/l.; chloride 100.8 mEq/l.; calcium 3.6 mEq/l.; magnesium 1.5 mEq/l.; bicarbonate (as lactate) 44.6 mEq/l.; dextrose 1.36% or 6.36%. Mixtures of the two glucose concentrations were used to control fluid balance.

Heparin was added to the solution at a concentration of 1,000 units per litre, and if serum potassium levels fell below 3.5 mEq/l. potassium chloride was also added to the dialysis fluid until the hypokalaemia was corrected. All additions were made immediately before use.

In order to minimize the introduction of viable bacteria every disconnection of or injection into the dialysis system was preceded by five minutes' exposure of the involved surfaces to 0.5% chlorhexidine in 70% alcohol. For all such manipulations attendant staff used an aseptic technique.

The dialysis fluid was introduced through a Dialaflex giving set, with two spearheads, each inserted into a 1-l. plastic bag of dialysis fluid. The drainage tube was secured with its tip in the neck of a Winchester bottle in which the dialysis effluent was collected. Initially, 50 ml. of 0.5% chlorhexidine in 70% alcohol was added to the collection bottle as a disinfectant, but 1 ml. of 40% formaldehyde solution was used instead after it had been discovered that the chlorhexidine tended to be inactivated by the protein in the dialysis effluent. In adults 2 l. and in children 1 l. of dialysis fluid was used for each exchange. The fluid was not warmed and was allowed to run into the peritoneal cavity over a 15-minute period. It was retained for 30 minutes and then allowed to drain out for a further 30 minutes. The volume of dialysis effluent was measured and recorded. Between exchanges the giving set spearheads and, when not in use, the tip of the drainage tube were immersed in 0.5% chlorhexidine in 70% alcohol. Seven exchanges were usually performed during the night, and afterwards the administration set was discarded and the indwelling peritoneal catheter sealed with a sterile disposable plastic spigot in the end of the connecting tube.

Control and Treatment of Infection

A sample of peritoneal dialysis effluent was collected daily, approximately 15 ml. was centrifuged at 1,500 r.p.m. for 15 minutes, and the deposit cultured and examined microscopically. A diagnosis of peritoneal infection was established only when polymorphs and organisms were seen in the deposit and the causative organism was isolated. When Gram-stained films suggested the presence of infection direct sensitivity testing was carried out on the deposit, using impregnated paper discs, and, if possible, the results after an eight-hour incubation were reported the same evening so that appropriate treatment could be initiated if the patient had developed symptoms. If the patient remained asymptomatic treatment was withheld until the following day, when the results of culture were known and a further specimen of dialysis fluid was available for examination. If this confirmed the presence of infection treatment was initiated, regardless of the presence or absence of symptoms. Swabs were taken twice weekly for culture from the skin around the peritoneal catheter and from the nose and throat. Infecting organisms were identified by standard methods, and all strains of *Staphylococcus aureus* were phage-typed and strains of *Pseudomonas aeruginosa* pyocine typed by the method of Gilles and Govan (1966).

The skin around the peritoneal catheter was treated daily with antimicrobial substances. Initially, nystatin dusting powder (Squibb) and an antibiotic aerosol containing polymyxin B, neomycin, and bacitracin were used, but most peritoneal infections still seemed to be caused by organisms residing in this area. Subsequently, chlorhexidine cream or dusting powder was used and the patients had daily baths with the catheter site exposed; 25 ml. of a 10% solution of hexachlorophane was added to the bath-water. In patients found to be carrying *Staph. aureus* in the nasopharynx a cream containing neomycin and chlorhexidine was applied to the anterior nares twice daily for 10 days. Antibiotics were not routinely incorporated in the peritoneal dialysis fluid.

Bactericidal antibiotics were used for treatment of peritoneal infection and were administered by incorporation in the peritoneal dialysis fluid, usually at an approximate concentration of 25 or 50 µg./ml. for 7 to 14 days, depending on the clinical response and the nature of the infecting organism. Patients with severe infections were also given oral or systemic antibiotic for the first two or three days of treatment, which was then adjusted to produce serum levels of antibiotic that exceeded the minimum inhibitory concentration for the infecting organism (Percival and Cohen, 1967).

Results

The results of prolonged peritoneal dialysis are summarized in Table II. This shows that there was a considerable improvement during the second year of the study. Of the 27 patients 25 were subsequently transplanted. Sixteen were well and active during the entire dialysis period and five did well initially but deteriorated after two to four months. Two of these died—one of peritonitis and one of postoperative haemorrhage after the repair of a catheter-induced bowel

TABLE II.—Response of 27 Patients to Prolonged Peritoneal Dialysis

	No. Studied	Classification of Response			
		Good*	Deteriorated†	Poor‡	Died§
1965	11	4 (36%)	2 (18%)	4 (36%)	1 (9%)
1966	16	12 (75%)	1 (6%)	2 (13%)	1 (6%)
Total	27	16 (59%)	3 (11%)	6 (22%)	2 (7%)

* Active, free from major complications, and spending most of the day out of hospital.

† Initially did well but later became inactive owing to complications.

‡ Never free from complications.

§ One patient died from peritoneal infection and the other from bowel perforation.

perforation. Failure of peritoneal dialysis in another patient necessitated haemodialysis until she was transplanted. Six patients, all subsequently transplanted, were never very well while on peritoneal dialysis.

Fluid and Electrolyte Control

The initial effect of peritoneal dialysis in removing excess fluid in renal failure and in correcting electrolyte imbalance is well known (Boen, 1961). For this reason the changes occurring in the first week are excluded.

The mean change in weight for the entire group over the whole period on dialysis (excluding the first week) was -1.5 kg. (range -20 to $+12$ kg.).

Control of blood urea and electrolytes was achieved in all cases (Table III), but the blood urea level did not correlate with general well-being or frequency of complications. Ten patients had intermittent hyperkalaemia ($K > 6$ mEq/l.), which usually was related to dietary intake and occurred after a few weeks of dialysis. This group were treated with an ion-exchange resin, Resonium-A, orally or rectally when required.

TABLE III.—Effect of Peritoneal Dialysis on Blood Urea

Blood urea (mg./100 ml.)*	..	..	100	101-125	126-150	151-175
Number of patients	..	..	7	8	7	5

* Mean for period on dialysis excluding the first week.

Serum Proteins

The changes in serum proteins were observed during a dialysis period of between 4 and 26 weeks in 17 patients, and are shown in Table IV. Slight ankle oedema apparently due to hypoproteinaemia occurred in only two patients, after four to five months of dialysis, but there were no other manifestations of hypoproteinaemia in any of the patients.

TABLE IV.—Effect of Peritoneal Dialysis on Serum Proteins

	Serum Proteins (g./100 ml.)					
	Initial		Final		Change	
	Range	Mean	Range	Mean	Range	Mean
Total	7.1-3.8	5.5	6.2-3.7	5.1	+1.2 to -1.7	-0.4
Albumin	3.9-1.4	2.7	3.4-1.4	2.4	+1.0 to -1.0	-0.3

Hypertension

Control of hypertension was facilitated within one month of beginning peritoneal dialysis in 21 of the 26 patients who were hypertensive (Table V). Blood pressure returned to normal without the use of hypotensive drugs in four patients. A reduced dosage of hypotensive drugs was sufficient to maintain normal blood pressure in four patients, and to improve control of hypertension considerably in another 13. Blood pressure was unaffected in the remaining five, but two of them were only mildly hypertensive. Hypertension was uncontrollable in one patient until bilateral nephrectomy was performed. After this his blood pressure was controlled by peritoneal dialysis alone. There was a close relation between improved control of hypertension and loss in body weight. An example is shown in Table VI.

TABLE V.—Effect of Peritoneal Dialysis on Hypertension

	No. of Patients
Blood pressure returned to normal	8
Without hypotensive drugs	4
With hypotensive drugs at reduced dosage	4
Improved control with reduced dosage of hypotensive drugs	13
Unaffected	5

TABLE VI.—Relation Between Weight Loss and Hypertension in a Patient on Peritoneal Dialysis

Period on Dialysis	Weight (kg.)	Weight Lost (kg.)	Mean* B.P. (mm./Hg)	Dosage per Day
Initially	60	—	190/125	Reserpine 1 mg., spironolactone 300 mg., chlorothiazide 1 g.
1 week	59	1	140/80	Bethanidine 30 mg., spironolactone 300 mg., chlorothiazide 0.5 g.
2 weeks	57	3	180/105	Methyldopa 750 mg.
3 "	53	7	175/100	" 1 g.
4 "	47	13	140/80	" 1 g.
5 "	43	17	115/70	None

* Blood pressure is the weekly mean of all observations, both standing and lying.

Neurological

Peripheral neuropathy was present in 12 patients on admission. In two dialysis resulted in marked improvement in their sensory changes. There was no progression of neuropathy in eight of the other 10, but in two the condition became progressively worse during 11 and 16 weeks of dialysis.

Psychiatric

Psychiatric complications occurred in six patients. Four became depressed, but two of these were known to have had depressive personalities before they became uraemic. In another patient depression followed an episode of cardiac arrest, and in the remaining patient depression was associated with a breakdown in her marriage. An acute anxiety state developed after six months on dialysis in one patient, and a boy of 14 became withdrawn and regressed to an infantile pattern of behaviour after one month on dialysis.

Mechanical

The average life of the catheter was eight weeks and of the catheter anchoring suture one month. In one case the catheter lasted seven months. Previously described mechanical complications, such as catheter blockage, intermittent problems with fluid drainage, leakage of fluid, and extraperitoneal subcutaneous extravasation, occurred rarely. In no instance was there any difficulty in correcting these complications. Four patients complained of persistent nausea, which was not relieved by antiemetics. Respiratory embarrassment occurred in only one patient, and that during the first exchange (Berlyne *et al.*, 1966). Pain sufficient to prevent the patients from sleeping during the dialysis or to warrant the administration of analgesics occurred in association with some episodes of peritoneal infection, but rarely at other times.

One patient suffered from haemorrhage from the abdominal wall when the catheter was first inserted, and had to be transfused with 4 pints (2.3 l.) of blood. In two patients who had suffered repeated episodes of peritoneal infection bowel perforation occurred during reinsertion of a peritoneal catheter. This led to the death of one and to maintenance by haemodialysis in the other.

Cardiovascular

Postural hypotension was troublesome in eight patients, including three who were not receiving hypotensive therapy. It was most pronounced in the morning soon after the end of the dialysis period. Both pericarditis and congestive cardiac failure, present on admission in many patients, rapidly resolved within a few days of starting peritoneal dialysis. Two patients developed pericarditis after two months' dialysis, but this resolved within a week without specific treatment.

Anaemia

All patients were anaemic initially. Transfusions were given when progressive symptoms of anaemia appeared, or if the haemoglobin fell below 5.6 g./100 ml. The mean haemoglobin level for the whole group during the period on dialysis was 8.7 g./100 ml. On average, patients received 9 pints (5 l.) of blood during every 100 days on dialysis. Patients were always dialysed throughout the blood transfusion to prevent precipitation of cardiac failure.

Peritoneal Infection

During the study period the frequency of peritoneal infection was considerably reduced, the average rate of infection being once in every 32 days of dialysis during the first year but only once in 77 days of dialysis during the second year. Three patients remained free from peritoneal infection during periods of 62, 158, and 180 days of dialysis. Fifty-seven episodes of infection occurred in the other 24 patients: 10 had one episode, 6 had two, 3 had three, 2 had four, and one each of three patients had five, six, and seven episodes respectively. The majority of infections were caused by *Staph. albus* or *Staph. aureus* (Table VII), and in 70% of all infections the same organism was isolated from the skin around the peritoneal catheter within a few days before the onset of infection. Symptoms were minimal or absent in many of the infections caused by less pathogenic organisms such as *Staph. albus*, but infection by *Staph. aureus* and the Gram-negative organisms was usually associated with abdominal pain and fever above 100° F. (37.8° C.), and blood culture was positive in 15%.

TABLE VII.—Organisms Causing Peritoneal Infections in Patients Receiving Prolonged Peritoneal Dialysis

Organism	Number of Infections		
	First Episode	Subsequent Episodes	Total
<i>Staphylococcus albus</i>	14 (58%)	12 (36%)	26 (46%)
<i>Staph. aureus</i>	6 (25%)	4 (12%)	10 (17%)
<i>Acinetobacter anitratum</i>	0	5	5
<i>Escherichia coli</i>	1	2	3
<i>Proteus mirabilis</i>	1	2	3
<i>Streptococcus faecalis</i>	1	2	3
<i>Ps. aeruginosa</i>	0	2	2
Others*	1	4	5
Total	24	33	57

* One each of *Str. pyogenes*, *Str. viridans*, *Bacillus cereus*, *Klebsiella aerogenes*, and *Candida albicans*.

Thirty-six infections were eradicated by a single 7-to-14-day course of an appropriate antimicrobial agent. In 20 episodes infection by the same organism occurred within two weeks of stopping treatment, but, because of the persistence of the infecting organism on the skin around the peritoneal catheter it was not possible in some instances to determine whether this was failure of treatment or reinfection. In five staphylococcal infections which failed to respond to treatment with cloxacillin or cephaloridine further investigation showed that the organisms were "cloxacillin-resistant" staphylococci, though initial sensitivity testing by the paper disc method had indicated that the organisms were sensitive (Percival and Cohen, 1967). Despite treatment one patient died from peritonitis and bacteraemia due to *Ps. aeruginosa* after 62 days of dialysis.

Discussion

At present the major limiting factor in treating patients with irreversible renal failure by cadaveric transplantation is the difficulty in obtaining suitable donor kidneys. Patients may have to be maintained for many months in a condition suitable

for transplantation at any time, and for this purpose haemodialysis is usually preferred to peritoneal dialysis, mainly because of the high incidence of peritonitis associated with peritoneal dialysis (Bower and Hume, 1965). In the cases described here the rate of peritoneal infection was reduced by more than 50% during the study period to once in every 77 days of peritoneal dialysis. Three patients were dialysed for between two and seven months without developing peritoneal infection, and a further 10 suffered only one episode of infection. Many of the infections were associated with minimal symptoms and responded readily to antimicrobial treatment without cessation of peritoneal dialysis. Only one patient died from peritonitis, but in two patients recurrent infection eventually caused peritoneal adhesions with subsequent bowel perforation during reinsertion of the peritoneal catheter. Bowel perforation is probably an indication for transferral of the patient to haemodialysis. The two perforations which occurred were repaired immediately.

The majority of peritoneal infections were caused by staphylococci (Table VII), and in 70% of all infections the same organism was isolated from the skin around the catheter site during the few days before the onset of the infection. There have also been four peritoneal infections, including one in a case described here, due to *B. cereus*, which was found to be a contaminant in the nystatin dusting powder applied to the skin around the peritoneal catheter. Though it has been supposed that the endogenous intestinal flora is the main source of peritoneal infection (Schwartz *et al.*, 1967), these findings suggest that in our patients infecting organisms usually gained entry to the peritoneal cavity by passing through the abdominal wall around the peritoneal catheter. Organisms could also have been introduced along the lumen of the peritoneal catheter, particularly during syringing to relieve obstruction, but care to maintain sterility of the dialysis connexions may have reduced the incidence of exogenous infection. It is unlikely that the skin around the peritoneal catheter can be rendered sterile for long periods. Nevertheless, we attempted to minimize the number of organisms residing in this area.

The changes in procedure associated with the reduction in peritoneal infection during the study period were the use of chlorhexidine cream around the peritoneal catheter instead of antibiotic spray, allowing the patients to have frequent baths, and the substitution of formaldehyde for chlorhexidine as the disinfectant in the container of the dialysis effluent. Unfortunately, cream rendered the skin around the peritoneal catheter soggy and was discarded in favour of chlorhexidine powder.

In this study peritoneal infection was always associated with increased turbidity of the peritoneal dialysate (Lasker *et al.*, 1965), but turbidity due to increase in the number of white cells commonly occurred without bacterial infection. Because daily microscopy and culture of peritoneal dialysate creates additional work for the laboratory, it might be thought sufficient to examine the dialysate only when this is observed to be turbid. However, before beginning the study we had seen two patients with peritonitis due to resistant Gram-negative organisms who died before isolation and sensitivity testing of the causative organism enabled the appropriate antibiotic to be selected and given. To prevent this happening it would be necessary to begin treatment of all symptomatic infections with wide-spectrum antibiotics, which have toxic side-effects (Lasker *et al.*, 1965). We found that daily examination of the dialysate allowed specific treatment to be initiated at an early stage, which was thought advisable in order to minimize the risks of fatal complications and the development of peritoneal adhesions. On a number of occasions bacteria were isolated from asymptomatic patients, but the next day's specimen was sterile, and no antibacterial treatment was given.

Loss of protein in the peritoneal dialysate has been reported to cause complications due to hypoproteinaemia in patients undergoing prolonged peritoneal dialysis (Berlyne *et al.*, 1964), but the fall in serum proteins in our patients was slight (Table IV), in part because the patients were given a high-protein diet.

In 21 of the 26 patients who were hypertensive the control of hypertension was facilitated by peritoneal dialysis, without dietary salt-and-water restriction (Kolff *et al.*, 1964) or hyponatraemic dialysis (Moriarty and Parsons, 1966; Palmer *et al.*, 1966). The mechanism of this effect is uncertain, though a close relation between changes in body weight and in blood pressure (Hegstrom *et al.*, 1962) was found in our patients (Table VI). Even in the absence of oedema or cardiac failure hypertensive patients with chronic renal failure have excess total body sodium with expanded total body water and extracellular fluid. It would have been difficult to restrict salt and water without reducing protein intake, but fortunately such unpleasant measures were not found necessary.

Because of different selection criteria and varying periods of observation it is difficult to obtain comparative figures for haemodialysis and peritoneal dialysis. The mortality rate of a group of 68 patients maintained by haemodialysis before transplantation was 11% in one study (Bower and Hume, 1965), and in another study (Abella *et al.*, 1967) 43% of patients maintained for prolonged periods, mainly by haemodialysis, were thought to be well controlled. Sixteen of our patients (59%) were well controlled, but two (7.4%) died before transplantation. Though peritoneal dialysis is widely recognized as the treatment of choice for short-term use in acute renal failure (Cameron, 1966), opinions vary regarding its value over prolonged periods (Scribner *et al.*, 1965; Moriarty and Parsons, 1966; Palmer *et al.*, 1966). Our results show that many patients can be well controlled by peritoneal dialysis for periods of up to seven months. With the same techniques smooth and efficient control of the dialysis of patients with acute renal failure in our hospital is also obtained. At any one time at least eight patients were managed in two general medical wards. We estimate that this required one-third of a medical registrar's and one-half of a laboratory technician's time. During the nights on dialysis in the two 22-bedded wards the nursing coverage of each ward consisted of either one State-registered nurse who had recently qualified, one student nurse, and one nursing auxiliary, or two student nurses and one nursing auxiliary.

Summary

Twenty-seven patients with irreversible renal failure and awaiting renal transplantation were maintained by peritoneal dialysis for periods of between two and seven months. Six-

teen (59%) were well and active during the entire dialysis period. Five did well initially but deteriorated because of complications, which proved fatal in two patients. Six patients were never well while on peritoneal dialysis, but all were subsequently transplanted.

Control of blood urea and electrolytes was achieved in all patients, and control of hypertension was facilitated in 21 of the 26 hypertensive patients without restriction of salt or water. A high-protein diet was given and the fall in serum proteins during the dialysis period was only slight.

During the study the average rate of peritoneal infection was reduced from once in every 32 to once in every 77 days of dialysis. Measures were taken to minimize peritoneal infection.

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