Fluid and Electrolytes in the Clinical Setting

Dileep N. Lobo

Section of Surgery, University Hospital, Queen's Medical Centre, Nottingham, UK

Introduction

The understanding of fluid and electrolyte balance in the clinical setting is often poor and prescribing is usually left to the most junior member of the team [1, 2]. Fluid prescriptions, especially in the perioperative period, can be very variable, with patients sometimes receiving in excess of 5 liters water and 500 mmol sodium/day [1, 3]. The 1999 UK National Confidential Enquiry into Perioperative Deaths reported that 20% of the patients sampled had either poor documentation of fluid balance or had unrecognized or untreated fluid imbalance [4], leading to increased postoperative morbidity and mortality [4].

In this review some of the pathophysiological aspects of fluid balance will be discussed and some recent and a few classic studies described, particularly in the context of nutritional and metabolic care.

Physiological and Endocrine Responses of Normal Subjects to Crystalloid Infusions

Body water accounts for 60% of body weight in health and is further subdivided into the intracellular and extracellular compartments, the latter being composed of the interstitial fluid and plasma volume (fig. 1). The extracellular fluid (ECF) is separated from the intracellular fluid by the cell membrane which, through the sodium potassium ATPase pump, maintains the equilibrium between the two compartments so that sodium is the main extracellular and potassium the main intracellular cation, the latter balancing the negative charges on protein and other molecules within the cell.

Water deficit or excess results in an increase or decrease in plasma osmolality, with corresponding changes in the secretion of antidiuretic hormone (ADH)
and in urinary volume and concentration. Salt deficiency induces a reduction in the volume of the ECF (which includes plasma volume), stimulation of the renin-angiotensin-aldosterone system (RAAS) and ADH, thereby reducing salt and water excretion in an attempt to preserve intravascular volume (table 1). As hypovolemia also stimulates ADH, hyponatremia may result from a high-water intake or excessive intravenous administration of hypotonic fluid. The efficiency of the physiological response to a salt or water deficit, developed through evolution contrasts with the relatively inefficient mechanism for dealing with salt excess, to which we have had little exposure until modern times. This is illustrated by studies comparing the response to 0.9% saline and to 5% dextrose infusions in normal subjects. 5% dextrose produces prompt diuresis with restoration to normal water balance within 1–2 h of stopping the infusion. On the other hand, 60% of the saline is still retained 6 h later [5]. ADH concentrations fall after infusion of both solutions, reflecting not only the influence of the osmoreceptors but also of the volume receptors on its secretion. Atrial natriuretic peptide rises abruptly during the infusion of both solutions owing to the activation of the stretch receptors, but falls to baseline when the infusion is discontinued, despite a residual ECF overload. Atrial natriuretic peptide seems therefore to be involved in the acute control of intravascular volume but not in the continuing excretion of excess sodium load in the interstitial space. The RAAS, however, is switched off and aldosterone levels remain low after saline, suggesting that normal excretion of a salt load may be largely dependent on the slow permissive effects of reduced RAAS activity [6–8]. This problem is exacerbated in situations
when salt and water overload is combined with a reduction in effective blood volume or cardiac output, as the volume receptors of the cardiovascular system signal activation of the RAAS resulting in further salt retention, despite interstitial overload and edema.

The Cl\(^{-}\) component of saline may also be a problem, since it has a [Na\(^{+}\)]:[Cl\(^{-}\)] ratio of 1:1 compared to plasma with a ratio of 1.25–1.45:1. Saline, therefore, causes a rise in plasma [Cl\(^{-}\)] leading to hyperchloremic acidosis. Hyperchloremia may also cause renal vasoconstriction and reduced glomerular filtration rate contributing further to the retention of a saline load [9]. In contrast, the more physiological Ringer’s lactate or Hartmann’s solution has a [Na\(^{+}\)]:[Cl\(^{-}\)] ratio of 1.18:1 and does not cause hyperchloremia. Sodium excretion following infusion of Hartmann’s solution is also more rapid, reflecting the influence of Cl\(^{-}\) upon renal sodium handling [10]. These observations are of practical importance in the management of patients.

Consequences of Salt and Water Excess

A solution of 0.9% sodium chloride is often misleadingly referred to as ‘normal’ or ‘physiological’ saline [11]. A liter of the solution contains 154 mmol of sodium and chloride, with an osmolality of 308 mosm/kg, exceeding both the sodium (135–145 mmol/l), chloride (94–105 mmol/l) and osmolar concentration in plasma (table 2). The potential problems arising from the high chloride concentrations of 0.9% saline have already been discussed.

In 1913 Trout [12] wrote, ‘(sodium chloride) is a poison to all people when given in large doses, and occasionally very toxic in small doses to a certain class of cases’. Retention of as much as 600 mmol of sodium in the postoperative period, however, is still believed by many to have no deleterious effect in patients without cardiorespiratory or renal disease [13]. Large amounts of fluid are often administered to increase urine output in the postoperative

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**Table 1.** Response to water and sodium depletion in the extracellular fluid

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Pathway</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Sodium deficiency</td>
<td>↓ Baroreceptor activity</td>
<td>↓ Urinary sodium excretion</td>
</tr>
<tr>
<td></td>
<td>↑ Renin-angiotensin-aldosterone-system activity</td>
<td></td>
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<tr>
<td></td>
<td>↓ Natriuretic peptides</td>
<td></td>
</tr>
<tr>
<td>Water deficiency</td>
<td>Stimulation of osmoreceptors</td>
<td>↓ Urinary volume/</td>
</tr>
<tr>
<td></td>
<td>↑ Antiuretic hormone secretion</td>
<td>↑ urinary osmolality</td>
</tr>
<tr>
<td>Sodium and water</td>
<td>↑ Sympathetic nervous system activity</td>
<td>↑ Urinary sodium reabsorption</td>
</tr>
<tr>
<td>deficiency</td>
<td>(via renal blood flow redistribution)</td>
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period even though, in the absence of hypovolemia, there is no evidence of an association between low-urine output and the development of renal failure. Intraoperative urine output did not predict postoperative renal function in 137 consecutive patients undergoing abdominal aortic revascularization [14]. Also, the development of oliguria in critically ill patients is not related to the amount of fluid administered, and can occur in the presence of normal blood urea and creatinine [15].

Critically ill patients are frequently acidotic. These patients may also receive large amounts of sodium chloride containing crystalloids and colloids which may compound the acidosis [9, 16–18]. Acidosis impairs cardiac contractility, reduces responsiveness to inotropes, decreases renal perfusion and can be lethal in combination with hypothermia and coagulopathy [16]. Excess crystalloid also causes cardiorespiratory complications and may compromise both pulmonary gas exchange and tissue oxygenation [19]. Postoperative mobility may also be impaired by edema of the limbs.

Starker et al. [20] found that half their patients receiving preoperative parenteral nutrition had an increase in body weight and a decrease in serum albumin concentration resulting from salt and water retention. These patients had a 50% postoperative complication rate compared to a 4% rate in the remaining patients who were able to excrete a salt and water load with resulting weight loss and increase in serum albumin concentration. Again, in a randomized study in severely malnourished patients receiving preoperative parenteral nutrition, Gil et al. [21] compared a group of patients receiving a standard feed containing 70% of non-protein energy as glucose, 140 mmol of sodium/day and 45 ml water/kg/day with a group receiving a modified feed containing 70% of non-protein energy as fat, no sodium and 30 ml water/kg/day. Weight gain with positive sodium and water balance and lowering of serum albumin concentration

<table>
<thead>
<tr>
<th>Table 2. Properties of commonly prescribed crystalloids</th>
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<tbody>
<tr>
<td>Plasma¹</td>
</tr>
<tr>
<td>Na⁺, mmol/l</td>
</tr>
<tr>
<td>Cl⁻, mmol/l</td>
</tr>
<tr>
<td>[Na⁺]:[Cl⁻] ratio</td>
</tr>
<tr>
<td>K⁺, mmol/l</td>
</tr>
<tr>
<td>HCO₃⁻, mmol/l</td>
</tr>
<tr>
<td>Ca²⁺, mmol/l</td>
</tr>
<tr>
<td>Glucose, mmol/l</td>
</tr>
<tr>
<td>pH</td>
</tr>
<tr>
<td>Osmolality, mosm/l</td>
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</tbody>
</table>

¹Normal laboratory range from Queen’s Medical Centre, Nottingham.
were noted in the standard group while a negative sodium and water balance was noted in the modified group. There was also a significant reduction in overall complications and postoperative stay in the modified group.

Other attempts to limit interstitial edema have also been beneficial. Mitchell et al. [22] randomized 101 patients with pulmonary edema to management based on pulmonary artery wedge pressure (n = 49) or extravascular lung water (n = 52) and found that the latter showed less than half the cumulative positive fluid balance, had reduced interstitial edema and spent fewer days on the ventilator and in the intensive care unit.

The records of 36 patients admitted to the intensive care unit with septic shock, excluding those who needed dialysis, were reviewed and it was found that while all of 11 patients who achieved a negative fluid balance of >500 ml on 1 or more of the first 3 days of admission survived, only 5 of 25 patients who failed to achieve this state of negative fluid balance by the 3rd day of treatment survived [23]. The authors concluded that at least 1 day of net negative fluid balance on the first 3 days of treatment strongly predicted survival.

Another retrospective study has suggested that postoperative pulmonary edema is more likely within the initial 36 h when net fluid retention exceeds 67 ml/kg/day [24]. Increased postoperative morbidity and prolonged hospital stay in patients receiving perioperative salt and water excess have also been reported in a recent audit of a homogeneous group of patients undergoing colorectal resections [25]. A recent study using a standardized multimodal approach that included intraoperative fluid restriction and early extubation on 56 consecutive patients undergoing esophagectomy has suggested that intraoperative fluid restriction may be instrumental in facilitating early extubation and reducing pulmonary complications without compromising renal function [26].

Brandstrup et al. [27] have demonstrated, in a randomized, multicenter study, that patients undergoing colorectal resections fare better if postoperative fluids are restricted to maintain constant body weight throughout the patients’ stay in hospital than if patients are given standard postoperative fluids which may cause a 3- to 7-kg increase in body weight. This was especially apparent when cardiopulmonary complications were looked at (24% in standard group and 7% in restricted group, p = 0.0007). No adverse effects were found in the restricted group and patients in the standard group tended to have decreased oxygen tension and saturation, negative base excess and lower arterial pH in the immediate postoperative period than those in the restricted group.

Although some of these studies are retrospective and some have small numbers of subjects, they show that salt and water excess is not without consequence and suggest that more attention should be paid to sodium and water replacement in postoperative and critically ill patients if clinical outcomes are to be improved.
Salt and Water Overload: A Cause of Acute Intestinal Failure?

There are few studies on the effects of perioperative salt and water balance on gastrointestinal function, but the published evidence tends to suggest that salt and water excess can delay both gastric emptying and small intestinal transit.

Subsequent to their observations of cessation of vomiting after salt and water restriction in hypoproteinemic patients with gastrointestinal anastomoses, Mecray et al. [28] published a series of experiments on dogs relating the serum albumin concentration and salt and water balance status to gastric emptying time. In the first set of experiments, the authors rendered a group of 10 dogs hypoproteinemic by a combination of a low protein diet and repeated plasmapheresis. They infused a volume of 0.9% sodium chloride equal to the amount of blood withdrawn on each occasion. None of these animals underwent surgery and 8 survived more than a month. The mean gastric emptying time in the survivors, as measured by fluoroscopic observation of the transit of a barium meal, was inversely proportional to the serum protein concentration. They concluded that this edema resulting from hypoproteinemia was responsible for the prolongation in gastric emptying time, either by interfering with muscular contraction or by reducing the stoma size. However, the dogs also received significant quantities of 0.9% sodium chloride infusions at varying stages of the studies and it is impossible to determine whether these effects are due to fluid gain, hypoalbuminemia or both, since the two are inseparable.

In 1938, the same group, used a similar model to study the effects of the serum protein concentration on small intestinal motility [29]. They were able to demonstrate an inverse relationship between serum protein concentration and both gastric emptying time and small bowel transit, further strengthening their hypothesis. These findings were subsequently reviewed by Ravdin [30] who recommended that during the period of impaired gastric emptying the administration of fluid and salt must be carefully controlled. He opined, 'It is better to maintain the patient in a state of mild dehydration and hypochloraemia than to push water and salt to the point where tissue oedema is accentuated and prolonged'.

Further studies by Woods and Kelley [31] showed that the serum albumin concentration per se is not the factor responsible for changes in gastrointestinal function, since maintaining its level artificially by infusing albumin did not have any effect, providing further evidence that fluid balance may be the major factor.

Fluid overload is commonly seen in critically ill patients, especially because of the need for large volumes of infusions during resuscitation. Heyland et al. [32], using the paracetamol absorption test, showed that gastric emptying time was significantly prolonged in a group of 72 mechanically ventilated
patients when compared with normal controls. No record of fluid balance was made in this study and the authors attributed the prolongation in gastric emptying to narcotic use.

Hyperchloremic acidosis, as a result of saline infusions, has also been shown to reduce gastric blood flow and decrease gastric intramucosal pH in elderly surgical patients [18], and both respiratory and metabolic acidosis have been associated with impaired gastric motility in pigs [33].

Early studies [34–37] demonstrated that patients are intolerant of salt loads in the early postoperative period and that large volumes of 0.9% saline infusions during this period do not produce a corresponding diuresis. We conducted a physiological experiment to study the clinical consequences of modest fluid gains by randomizing patients undergoing uncomplicated colonic surgery to receive postoperative intravenous fluids according to hospital practice at the time, i.e. ≥3 liters water and 154 mmol sodium/day (standard group) or ≤2 liters water and 77 mmol sodium/day (restricted group) [38]. The primary end point was solid and liquid phase gastric emptying time, measured by dual isotope radionuclide scintigraphy on the 4th postoperative day. There was 3 kg greater weight gain in the standard group, reflecting positive salt and water balance, compared with zero balance in the restricted group. There was no significant difference between the groups when urine output, urinary sodium excretion and blood urea concentration were compared. In the standard group solid and liquid phase gastric emptying times (T50) were significantly longer (median 175 vs. 72.5 min, p = 0.028 and 110 vs. 73.5 min, p = 0.017, respectively); passage of flatus was 1 day later (median 4 vs. 3 days, p = 0.001); passage of stool 2.5 days later (median 6.5 vs. 4 days, p = 0.001). Although the study was not designed to look for a difference in complication rate, patients in the restricted group had fewer side effects and complications and were able to be discharged 3 days earlier. These results show that salt and water retention is not a harmless and inevitable epiphenomenon, and should be avoided where possible, by restricting maintenance fluids to the amount necessary to achieve zero balance. This is not to deny the need for adequate replacement of additional losses of intravascular volume or of ECF.

Just as fluid overload causes peripheral edema, it may also cause splanchnic edema resulting in increased abdominal pressure, ascites [39] and even the abdominal compartment syndrome [40]. This, in turn may lead to a decrease in mesenteric blood flow and a further exacerbation of the process, leading to ileus or functional obstruction of anastomoses, increased gut permeability, intestinal failure and even anastomotic dehiscence [41].

**Treatment**

Moore [36] described the sodium retention or early phase of injury, followed by the sodium diuresis or convalescent phase. Salt and water overload
may sometimes be an inevitable consequence of resuscitation, yet it may take up to 3 weeks to excrete this excess [42] and this may be further delayed by complications [36, 41, 43], particularly in the elderly [44], resulting in persistent edema. It is important therefore to avoid unnecessary additional overload caused by prescribing excessive maintenance fluids after the need for resuscitation has passed. All of the salt and water contained in the antibiotic infusions and in maintaining the patency of arterial and venous cannulae should be included in the fluid and electrolyte balance. Many antibiotics are also sodium salts! A low serum albumin concentration may not only be a result of redistribution due to inflammation, but also of dilution from fluid infusions [5, 10, 45, 46]. Prolonged edema in this phase may be associated with an elevated jugular venous pressure, in which case the treatment consists of salt and water restriction, with diuretics in some cases. In some situations, however, with persistent serous losses from wounds or into inflamed areas, there is a gradual fall in blood volume manifest by poor filling of the jugular veins even in the horizontal position. Low blood pressure, tachycardia and oliguria may also be present. In this situation where the transcapillary escape rate of albumin may have returned to normal, it is logical to provide a low salt concentrated colloid with a long half life, i.e. 20% salt poor albumin. It is our experience that 200–400 ml of this solution given over 48 h results in prompt improvement in cardiovascular parameters and a salt and water diuresis, with rarely a need for repeated infusions [47]. Where edema is severe, a diuretic may also be given.

The use of concentrated salt-poor albumin with or without diuretics in the post-acute period is illustrated in figure 2. Such infusions, however, must be monitored carefully by direct measurement of the venous pressure or observation of jugular venous filling, since inappropriate or excessive administration can be dangerous. Indeed at least one study [48] included in the Cochrane report [49] may well have produced excess mortality, not because of the use of albumin per se but of the way it was used and the volume of fluid administered [50]. It should be emphasized that we have used albumin infusions in this situation not to treat hypoalbuminemia but to repair plasma hypovolemia in the presence of an interstitial salt and water overload. Based on the evidence, there is no justification for using such infusions to treat the albumin concentration per se.

**Maintenance**

It is a common error to equate maintenance requirements with those for resuscitation and replacement so that uncomplicated postoperative patients may inadvertently be prescribed an excess of both sodium and water. Oliguria and salt and water retention are almost universal in the early phase after surgery, stress and trauma and most patients require no more than 2–2.5 liters of water and 60–100 mmol of sodium/day for maintenance. This must not be confused with requirements for resuscitation of
the hypovolemic patient in whom the main aim of fluid therapy is repletion of the intravascular volume. Potassium is best avoided on postoperative days 0 and 1, unless serum potassium is low. However, regular potassium supplements should be prescribed from day 2 onwards (table 3). Patients with excessive losses (e.g. nasogastric aspirate, diarrhea, intestinal fistulae, etc.) must be prescribed like-for-like replacements in addition to maintenance requirements (table 4).

In the early postoperative period, the 24-hour urine output may be only slightly greater than the ‘volume obligatoire’ but, without any rise in blood urea concentrations, a further fluid challenge is usually unnecessary. In the presence of a normal intravascular or ECF volume, it is inappropriate to give more isotonic sodium-containing fluids.

The aim of maintenance fluid therapy is to prevent an increase in body weight, which is usually a result of accumulation of extracellular water. Body

**Fig. 2.** Urinary responses of a patient in the post-acute phase of critical illness to 20% albumin and frusemide. From Allison et al. [47] with permission from Clinical Nutrition.

**Table 3.** Maintenance: requirements and provision (for a 70-kg man)

<table>
<thead>
<tr>
<th>24-hour requirements</th>
<th>What does 2.5 liters dextrose (4%)/saline (0.18%) provide?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water 25–35 ml/kg (1.7–2.5 liters)</td>
<td>2.5 liters</td>
</tr>
<tr>
<td>Sodium 1–1.2 mmol/kg (70–85 mmol)</td>
<td>75 mmol</td>
</tr>
<tr>
<td>Potassium 0.8–1 mmol/kg (56–70 mmol)</td>
<td>Must be added</td>
</tr>
<tr>
<td>Dextrose 100 g (400 cal) to prevent ketosis</td>
<td>100 g</td>
</tr>
</tbody>
</table>
weight measurement is the most accurate but often underused indicator of fluid balance and an increase in body weight on serial measurement, in the absence of hypovolemia may be treated with a loop diuretic such as frusemide.

The fluid balance of most patients can be easily monitored by daily weighing, the use of fluid balance charts (remembering their inherent inaccuracy and that insensible loss can only be guessed at) and the serum and urinary biochemistry. These must all be interpreted in the light of a clear understanding of the intercompartmental shifts and pathophysiological changes described above.

**Conclusions**

The accurate management of fluid balance is a vital part of the metabolic care of surgical and critically ill patients with important consequences for gastrointestinal function and hence nutrition. It is also an important component of artificial nutritional prescriptions by the parenteral or enteral route and should be given the same careful consideration as other nutritional and pharmacological needs.

**References**

8 Lobo DN, Myhill DJ, Stanga Z, et al: The effect of volume loading with 1 litre intravenous infusions of 0.9% saline and 5% dextrose on the renin angiotensin system (RAS) and volume controlling hormones: A randomised, double blind, crossover study (abstract). Clin Nutr 2002;21(suppl 1):9–10.
11 Wakim KG: ‘Normal’ 0.9 per cent salt solution is neither ‘normal’ nor physiological. JAMA 1970;214:1710.
Discussion

Dr. Wongkietkachorn: I think your data are very interesting. Concerning your standard patients who received standard fluid treatment, you classified them as being fluid overloaded. In terms of physiology, how can you explain the mechanism of the fluid overload? Is there something wrong with the kidney?

Mr. Lobo: No, there is nothing wrong with the kidney, it is just a normal response to stress and injury. My work and the work published in the 1950s have shown that the capacity to excrete sodium on the day of the operation and maybe the 1st and 2nd day after the operation is severely limited. So we go back to the concept of the volume obligatoire. You need about 600 ml of urine to excrete the solute load, but in the early postoperative phase and the early phase after injury, it is very difficult for the body to

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excrete more than a liter of urine in 24 h. We and others have shown that if you increase the fluid input you don't get a corresponding increase in the urine output in the early postoperative phase. It is when the kidney starts recovering, from day 2 or 3 onwards, that excess fluid starts to be excreted. This is a common problem in the wards. For example a patient who has excreted 3.5 liters of urine over the past 24 h is prescribed 4.2 liters of fluid to include insensible losses when actually we should be looking at the serial fluid balance charts and realize that what this patient is doing is excreting the fluid that has accumulated over a few days, and therefore restrict the input.

Dr. Wongkietkachorn: We have seen this problem in our surgical patients as well. Did you have any opportunity to measure the aldosterone level in these patients who have been classified as overload?

Mr. Lobo: No, we didn't do any hormonal assessments for this study because it was a relatively new thing and we didn't really know what results to expect. All our calculations were based on the animal work of Mecray[1] which were first published in 1937, and we wanted to ensure that we didn't cause any problems with restricting fluid.

Dr. Shenkin: I just wanted to raise the question of how we got to the present situation. It is just amazing that despite knowledge of the metabolic response and fluid and salt requirements, hospitals have standardized to give such a high intake. I wonder if this is because the number of patients who do require more is small: patients who have fistulas, drains or aspirates, and because some of them require more it is better to ensure that those who need it receive it, on the assumption that those who don't require the extra will excrete the surplus. You have shown that this is not the case. I wonder if that is because of the lack of education and training of our junior doctors. The concern might be that if they all use your restricted regimen they start under-providing those patients who actually require more.

Mr. Lobo: I think the whole concept of giving fluid excess has stemmed from the belief that patients will develop renal failure if you restrict the fluid. If you look at the history of how the intravenous fluid regimens developed the initial studies always favored fluid restriction, starting with the work of Wilkinson when he was working in Glasgow [2]. However, during the Korean War it was thought that blood loss ought to be replaced with 3 times the volume of crystalloid, and that sort of picked up and people got confused between maintenance requirements and resuscitation requirements. I fully agree with you, if a patient has got a fistula, or if a patient is losing fluid somewhere in the first place you have to replace that. Those patients cannot be managed by fluid restriction. But if you have a patient who is relatively uncomplicated, you don't need to give that patient an excess of salt and water. Again in surgical practice patients do not develop renal failure because you restrict fluids; they develop renal failure because they are developing complications of surgery such as anastomotic breakdown or sepsis. I am not advocating that we ought to maintain patients in a negative fluid balance state, but we ought to maintain them in a steady state where they do not increase their body weight during their stay in hospital.

Dr. Nimmanwudipong: Have you looked at the end point for the resuscitation in the 2 groups in your study? I think it is very important when you infuse fluid for replacement if the 2 groups have different end points, it might come out in a different way if it is not a fair comparison. It has been shown in trauma patients that if you give the fluids slowly in the first hours of the resuscitation period the outcome will be vastly different from when you adequately resuscitate the patient.

Mr. Lobo: I emphasized earlier that these studies had nothing to do with resuscitation; they were studies on maintenance requirements. This whole resuscitation issue is completely different because when we resuscitate patients we aim to restore the effective blood volume which is the amount of blood in the arterial tree, and you
cannot restrict fluids in these patients. At the same time we should be cautious by not giving them too much fluid, and consider the role for inotropes. There have been studies in the critical care situation which have shown that if you try to prevent excessive salt and water overloading in these patients they do better. In fact there is one study on septic patients in the intensive care unit (ICU) which show that if you achieve a 500-ml negative fluid balance on any one of the first 3 days of the ICU stay those patients do better [3], but that was a retrospective study and I await the results of prospective studies. There has been another study from the United States which shows that if you give patients an excess of 67 ml of fluid/kg/day they are more likely to develop atrial fibrillation and cardiac arrest than those who are given lower amount of fluids [4]. So it is a totally different issue between resuscitation and maintenance and we have to be careful and realize why we are giving the patients the fluid. So if the patient is hypovolemic you cannot restrict fluids because that patient will die. At the same time if the patient has got excessive losses in the form of fistula you have to replace what that patient is losing over and above the maintenance requirements. We chose this model of simple colorectal surgery because it is reasonably straightforward, the complication rate is quite low, and we didn't expect major problems. Our main goal was not at looking at the outcome of the patient, but gastrointestinal function, and we didn't need a very large group of patients to show that difference.

**Ms. Easaw:** I just wanted to ask you if you had this fluid restriction in this kind of patient, how would you actually calculate the enteral or parental feeds for these patients, and how much can we give?

**Mr. Lobo:** It is a very important question because the frequent mistake is to give enteral feeds and intravenous fluid at the same time, and so you are doubling the volume that you are giving to patients. It is the total fluid input that is important. So if you are feeding the patient enterally or parenterally, you have to cut down on the crystalloid input, and that is extremely important because very often we see that patients are getting about a liter to a liter and half of feed and another 2 or 3 liters of crystalloid, and that is disastrous.

**Dr. Allison:** You talked about surgeons, but physicians are just as bad and we need to remember that conditions like pneumonia or acute inflammatory conditions produce the same metabolic response as that to surgery and that these patients are just as intolerant of salt and water overload. You have shown that each one of us in health is actually intolerant of saline. To retain two thirds of a saline infusion after 6 h is an enormous amount. To extrapolate from your studies back to some of the concerns over chronic conditions, you really have described a method analogous to the glucose tolerance test of testing people's sodium tolerance: in other words a 1-hour infusion of 1 liter and measuring the response. Some people have made measurements during the hours of infusion but they haven't measured what happens subsequently. Measuring 4 h afterwards how much salt they excrete will be a measure of that person's tolerance. Now you and I are interested in looking at this problem in obesity because we are both struck by the fact that these patients have idiopathic fluid retention up to 5 or 6 liters in some cases. The initial studies would suggest that obese patients retain 90% of saline at 4 h, and we are interested in looking at saline tolerance before and after weight loss. That study is in progress. Another extrapolation of some of your work is perhaps for other conditions associated with fluid retention like heart failure. For example, in the absorption of diuretics, the pharmacodynamic data in the literature would accord exactly with the delay in gastric emptying because there actually is no small bowel malabsorption of the drugs and may explain why oral diuretics and maybe other drugs as well are comparatively ineffective in acute heart failure. So there are extrapolations from your work to these other situations which I think are worth studying themselves.
Mr. Lobo: I fully agree with your comments and I also think that patients with renal failure may be in a similar situation, although the prolongation of gastric emptying time may be confounded with uremia in addition to salt and water overload. With obese patients we have the other problem of inflammation; we know now that central obesity is an inflammatory disease and these patients may also have an increase in capillary permeability and that may be one of the reasons why they retain so much more fluid than you or I.

Dr. James: How easy is it to get a system for measuring body weight in your hospital set up? As I look at your very elegant and clean analysis I get the impression that it implies that your end point is this very boring measurement, and I guess it is easier to get an X-ray or a plasma measurement than getting body weight. How do you go about it? The implication is that you need to change the whole system of medical practice in hospitals.

Mr. Lobo: It is very difficult, but education of the nurses is very important and once they realize how important fluid management is, they cooperate. In fact one of my colleagues has just been appointed as a consultant in a district general hospital in the UK, and he found that there was a poor understanding of fluid balance management, so he organized a talk and presented my work. Now he says when he comes into the ward the first thing the nurses say is: ‘we haven’t overloaded your patients’. In fact they are very impressed because these patients go home about 2 days before the other consultants’ patients, and so the others are being converted as well.

Dr. Kopelman: To comment on Dr. Allison’s point. Arginine vasopressin release is altered in obesity and this may be the reason. It is actually well described that there is a delay in the diuresis of a water load in a fit normal obese individual. But the other point is the effect of diuretics because we have always had the custom of giving frusemide intravenously in severe congestive cardiac failure on the basis that it is not absorbed. The counter to that is if you give metolazone which is a distal loop diuretic that works orally, and I could never explain why is metolazone absorbed if there is congestion of the bowel.

Mr. Lobo: I can’t comment on that.

Dr. Allison: I am not aware of any pharmacodynamic data on metolazone, but there is quite a lot of literature on, for example, bumetanide and frusemide blood levels after an oral load. The data do suggest that absorption from the small bowel, if it is put directly into the small bowel, is normal suggesting a gastric effect. Why it should be different from one drug to another, I don’t know. It may be a dose-related effect. If a sufficient amount is given orally, it will get through somehow.

Dr. Endres: My question is related to potassium. Do you restrict potassium during the first 4 or 6 h, for example, while waiting for the first diuresis or is it only true for diabetic ketoacidosis?

Mr. Lobo: We know that in acute injury, although the urinary excretion of potassium is increased, cellular injury causes if potassium to leach out from the intracellular compartment to the extracellular compartment. So as long as the potassium concentrations are in the normal range we do not supplement potassium on the first day after the operation. We usually start potassium supplements from day 2 onwards. However, if the serum potassium concentration is low, potassium ought to be supplemented, and it is very important to start potassium supplements at least on day 2 because otherwise these patients become hypokalaemic later on during the hospital stay.

Dr. Shenkin: Can I ask another question about the fluids that you actually use on the wards? Hartmann’s solution was something which was used by anesthetists, whereas saline was something that was used in wards because it was simple and people knew what was in it. Do you use Hartmann’s solution on your wards, and have you given up using saline?
Mr. Lobo: No, because even with Hartmann’s solution you would be providing the patients with 130 mmol sodium/day. So what I have used for my studies is 2 liters of 4% dextrose and 0.18% saline which provides the patients with about 60 mmol sodium/day. Potassium can be added to that as necessary. Two liters of that also provides 80 g glucose, so ketosis is prevented from developing as well. However, for resuscitation purposes, if you look at the ATLS manual for trauma, the recommendation is Ringer’s lactate or Hartmann’s solution should be used for resuscitation. But if you look at most hospitals in the UK they are using saline. There was a very nice review article published in the *Journal of Trauma* a couple of years ago which has highlighted the problem of hyperchloremic acidosis after resuscitation.

Dr. Sitges-Serra: I have a comment on your talk concerning albumin. Shouldn’t we start to replace the term ‘dilution’ with ‘distribution’? For example, I agree with you with regard to hemoglobin because hemoglobin really dilutes in the plasma whereas for albumin we don’t just have dilution in a higher plasma water volume but we also have a distributional component with flowing of albumin to the interstitial space. So probably I would use ‘dilution’ more for hemoglobin for example, whereas for albumin I think we should start to use the word ‘distribution’ because it graphically explains the dynamics of albumin when you infuse a volume.

Mr. Lobo: I think you are 100% correct because in the studies in volunteers we calculated the predicted fall in serum albumin concentration based on the drop in hematocrit and hemoglobin. The actual fall in serum albumin concentration was much greater than the predicted fall, and that again represents some albumin going out into the interstitial compartment. I am not entirely sure how that happens, whether it is by a process of convection or whether a saline load increases capillary permeability. Dilution is involved, but with the distributional component.

Dr. Sitges-Serra: I think it is worth going back to that because I would deal with that difference between normal permeability and disease capillary permeability. Anyway there is a lot of basic research done on convective transport, and Dr. Allison was asking whether somebody had already done this test of infusing volume to patients to see how they respond. There is a very nice study by Mullins and Garrison [2] who in fact did these 2-liter infusion tests to see whether the patients would develop problems when entering the circulation. They very clearly showed that patients who were able to excrete the test infusion were the ones who had the better outcome after heart surgery. So I think there is already one past attempt at qualifying the ability in heart disease to dilute or to excrete these volume loads.

Mr. Lobo: The important difference between the Mullins and Garrison paper [5] and ours is that they looked at patients whose physiology was not entirely normal. We have looked at normal volunteers; they were medical students with a normal body weight range and the expected physiology was normal. I fully agree with the results of Mullins and Garrison, and they have done a lot of work on animal models as well, looking at the albumin escape in mice. It is extremely interesting work, unfortunately we don’t have a full understanding of the whole process at the moment.

Dr. Allison: As Dr. Sitges-Serra pointed out surgery produces increased capillary permeability, and a response to trauma is to increase the distribution of albumin which leaks out of the circulation. As far as we know, nobody has looked at how long it takes to come back to normal. Would you like to tell us about your data on albumin transfer out of the circulation and its return to normal?

Mr. Lobo: The initial work was actually done by Fleck et al. [6] when they showed that, in patients undergoing cardiac surgery, the transcapillary escape of albumin went up by 300%. Normally about 5% of the albumin escapes from the circulation every hour and returns into the circulation by the lymphatics. However, Fleck et al. showed that in patients undergoing major cardiac surgery the albumin escape rate rose from 5%/h to somewhere between 12 and 15%/h on the day of the operation. But we
reviewed the literature and there was nothing published on when this albumin escape rate returns to normal. We conducted a study on patients undergoing major surgery without complications [7]. Again on the 1st postoperative day our results were very similar to those of Fleck et al., where the transcapillary escape rate of albumin rose from 5%/h preoperatively to about 13%/h on the 1st day of the operation, and by day 10 it had returned to about 6%/h. So these are patients who undergo major surgery without complications. I suspect that on the ICU and in patients who are septic, the transcapillary escape rate of albumin remains elevated for much longer periods and that is why it is so difficult to get rid of this fluid excess in these patients, and they also demand more fluid because whatever crystalloid you give them leaks out of the circulation, goes and fills the interstitial compartment rather than the intravascular compartment.

Dr. Wongkietkachorn: I am convinced by your speculation about the impact of the hyperchloremic acidosis on gastric emptying time. In some clinical situations, such as some patients requiring total parenteral nutrition for specific reasons, we know that total parenteral nutrition can cause hyperchloremic acidosis by the property of the cationic amino acids from the amino acid solution. So if this is correct, do you think that total parenteral nutrition can cause a delay in these critical patients?

Mr. Lobo: I don't have an answer to that because I don't have the evidence. However, it is not the acidosis itself, it is the hyperchloremia. If you look at most of the previously published papers they focused on the acidosis, but in my opinion it is the hyperchloremia that is the problem. I have tried to look at the literature, there is much written on how the kidney handles sodium, but little on how the kidney handles chloride. This is an area where much work needs to be done: how the kidney handles chloride and how the kidney excretes chloride.

Dr. Allison: You were implying that Mr. Lobo's results show an effect of hyperchloremic acidosis on gastric emptying. That is not what he was saying. He was looking at salt and water overload on gastric emptying although accepting that hyperchloremic acidosis may be a factor. Is that all right, Mr. Lobo?

Mr. Lobo: Yes, but because this is my own hypothesis, I don't know whether it is true or not. I hope to prove or disprove it with an animal model in the near future, but until that is done I can't give you an honest answer to that question.

References
