JEJUNOILEAL ABSORPTION OF SIMPLE NUTRIENTS IN A CANINE MODEL OF SMALL BOWEL AUTOTRANSPLANTATION

by

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GASTROENTEROLOGY RESEARCH UNIT 1988-1990

From left to right :

Seated : Anne M. Walters (author), Sharon M. Herkes

Standing : Dale Witzel, C. Daniel Smith, Del Menske

DECLARATION

The work in this thesis was carried out by myself. This includes all operations on dogs, plus the day to day care of the animals. All experiments were carried out by me, after weighing out all the constituents of each solution, and making them to appropriate volumes and pH. All the radioactivity analyses, glucose and PSP assays were conducted by myself. The sodium, potassium, and chloride measurements were carried out by Dale Witzel, and the morphometrics by Dr. M G Sarr.

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SUMMARY

Since 1988, more than 50 patients world-wide have received small bowel allografts, yet very little is known about the absorptive capabilities of transplanted small bowel.

Background

Transplantation of an organ requires the transection of all nerves and lymphatics connecting that organ to the donor. The effect this has on jejunal and ileal absorptive function is poorly documented and ambiguous. This study specifically addresses this question.

Transplantation

Transference of an organ from donor to recipient involves several steps, each of which may potentially damage the graft; this could result in impaired absorptive function in a small bowel allograft.

(a) Organ procurement : the organ is flushed and cooled with preservation solution, allowing storage.

(b) Ischaemic time : from flushing of the graft with the cold preservation solution until circulation is restored in the recipient.

(c) Reperfusion : when the transplanted organ is revascularised with recipient's blood.

(d) Immunosuppression : pharmacological agents which dampen down the recipient's immune response are required to prevent graft rejection; e.g. cyclosporine A affects absorption.

(e) Rejection : the high content of lymphoid tissue renders small bowel highly immunogenic. Acute rejection targets the mucosa, potentially affecting absorption from it's onset.

Aim of Study

This model of small bowel autotransplantation assesses, in isolation, the effect of denervation and lymphatic transection on small bowel absorption. It excludes the confounding factors of transplantation injury just described. This is crucial for three reasons:

1. To assess any alterations in the physiology of absorption caused by denervation and lymphatic transection by using simple electrolyte and single nutrient solutions, with documented absorptive pathways.

2. Only after the effect of denervation and lymphatic transection has been clearly documented, can meaningful experiments on the absorptive capability of small bowel transplants be carried out, with a view to assessing the effect of transplantation injury.

3. Major absorptive defects in autotransplanted small bowel would imply their existence in transplanted small bowel, which may render it unsuitable to provide adequate nutrition in patients.

This model of small bowel autotransplantation examines the absorption of a member of each of the major nutritional groups, allowing assessment of a broad spectrum of absorptive pathways. Glucose, glycine, phenylalanine, and oleic acid (a long chain fatty acid), were each studied separately, as single nutrient solutions.

Canine Model of Jejunoileal Autotransplantation

This model represents a jejunoileum which is extrinsically denervated, with no connection of the intrinsic neural pathways to proximal or distal gut, and with total lymphatic interruption.

Each dog had an 80cm isolated loop of jejunum or ileum with a perfusion cannula at the proximal end, and a distal stoma.

Two control groups were created to match the two autotransplanted groups; these control animals did not undergo the model of autotransplantation, but simply had the 80cm loop of jejunum or ileum created.

The four groups were :

Group 1 - control jejunum

Group 2 - autotransplanted jejunum

Group 3 - control ileum

Group 4 - autotransplanted ileum

Design and Conduct of Study

The four groups of dogs, each containing a minimum of six animals, were studied at an early phase post-operatively (Week 1 and Week 2), and had the experiments repeated at a later phase (Week 8 and Week 9).

Each of the five isotonic test solutions used polyethylene glycol as a non-absorbable marker to determine steady-state conditions. Each was perfused at a rate of 3ml/min at 38^0C for three hours, being repeated on a further two occasions, resulting in triplicate experiments at both early and late study points.

Loop effluent was analysed for volume, sodium, chloride, potassium, and for the glucose, amino acid or oleic acid content. Transit time was also measured. This provided over 23,000 samples for analysis.

Summary of Results

Denervation and lymphatic transection were found to have little or no adverse effect on absorption of electrolytes or simple nutrients from the jejunum or ileum.

Absorption of volume, sodium, and chloride was not significantly altered after autotransplantation of the jejunum or the ileum, nor was absorption of glucose or oleic acid.

Glycine and phenylalanine absorption were marginally reduced only in autotransplanted ileum at both early and late time points.

Potassium secretion was unaffected, with the solitary exception of the oleic acid solution in the ileum, where it was increased in autotransplants.

Transit time was significantly slower in autotransplanted jejunum, but not in autotransplanted ileum.

Conclusion

This study has provided essential physiological background data on absorption from both normal and denervated small bowel. It forms the solid foundation of basic knowledge required to allow further meaningful investigation of the effect of transplantation on small bowel absorption. Only now, with the basic effects of lymphatic transection and denervation clearly documented, can further studies be conducted to assess the effect which the several different components of transplantation injury may have on absorption.

There is clearly no physiological reason for transplanted small bowel to have a major absorptive defect, which is encouraging for the future of clinical small bowel transplantation. As no specific nutrient out of the wide range assessed showed major impairment of absorption, it should permit small bowel transplant patients to be able to enjoy a normal unrestricted diet. If transplantation injury causes no permanent damage to a small bowel graft, and rejection can be controlled, then absorption from the transplanted bowel should be sufficient to sustain life.

CHAPTER 1

INTRODUCTION

Most patients who require a small bowel resection tolerate it with no adverse effect on their nutritional status due to an apparent natural over-provision of small intestinal length. Dietary manipulation and the process of small bowel adaptation usually allows those who have had more extensive resections to be maintained in a good state of nutrition. There remains a small group of individuals who have no functioning small intestine at all, due to resection or motility disorder, and who must rely on total parenteral nutrition (TPN). For these patients small intestinal transplantation would be the ideal solution. Experience with human small intestinal transplantation to date is limited, and most reports concern patient survival and rejection problems, with little information on the transplanted intestine's ability to absorb nutrients.

Most animal studies have been carried out in rats, a small animal model which may not give results applicable to humans. Dogs have most frequently been used as a large animal model, and these studies have given conflicting results, some showing impaired absorption, while others have not. This may be a reflection of the different time points used, the presence or absence of rejection, and different immunosuppression protocols.

The question of whether transplanted small intestine absorbs nutrients normally or not, is an important one. Normal absorptive capacity would allow shorter lengths of gut to be used, raising the possibility of using living-related donors. Abnormal absorption could mean that dietary supplements or restrictions would be needed, or that the entire jejunoileum would be required, demanding cadaveric donors.

Aim

The purpose of this study is to determine whether absorption of simple single nutrient solutions is altered by the physiological changes imposed on the small intestine by the transection of all lymphatic and neural connections.

Historical Background

Humans and animals who survived the loss of large amounts of small intestine initially lost weight and developed diarrhoea, but over a period of weeks or months they regained weight and their bowel habit tended to revert back to normal. This implied that the

remaining small intestine had adapted sufficiently to compensate for the missing section of bowel. This observation was made by Flint, in 1912[1]. He also noted, in humans, that the villi in the residual bowel increased in height, which resulted in a fourfold increase in the absorptive area. This is part of the process which is now known as adaptation.

His observations were followed up in 1935 when Haymond[2] reviewed 257 cases of massive resection of the small intestine in humans.Mortality was related to the extent of the resection, and he concluded that one third of the small intestine could safely be resected, and that resection of over half of the total jejunoileum was not tolerated.

Ileum is now recognised as having the unique ability to absorb vitamin B12 and bile salts, a function which the jejunum lacks. In 1954[3] experimental studies in dogs noted the importance of the ileum for fat absorption and the maintenance of body weight. They also found that, following resection, dogs with the ileocaecal valve left intact fared better.

Small Bowel Adaptation

Partial resection of significant length of small intestine results in a Type 1 (Physiological) response[4]. This consists of dilatation of the residual small intestine with increase in crypt depth and villus height. This results in a greatly increased surface area for absorption. The rate of this adaptive response varies from species to species, taking about one month in rats, several months in dogs and up to two years in man[5].

Adaptation is so efficient that it is only patients with less than 60cm of residual small intestine who require permanent parenteral nutrition[6].

Not only does the ileum have the specialist properties of vitamin B12 and bile salt absorption, it also has the greatest capacity to undergo adaptive change; ileal adaptation produces an increase in absorptive capacity of 70-100%. In contrast, jejunal adaptation only increases absorption by 20-30%, and jejunum cannot adapt to absorb vitamin B12 or bile salts. These factors give the ileum a distinct importance in studies of small intestinal absorption.

Artificial Nutrition

For those patients who have insufficient small intestine to sustain life on enteral nutrition alone, other methods must be employed which result in nutrients entering the circulation.

(a)Transperitoneal Nutrition

The concept of using peritoneum as a permeable surface is a logical extrapolation of its role in continuous ambulatory peritoneal dialysis in chronic renal failure patients.

In 1983[7], a study in dogs showed that if a solution of glucose, amino acids and fat emulsion was introduced into the peritoneal cavity, these radio-labelled nutrients could be detected in the blood. This finding of peritoneal absorption in dogs was confirmed by other authors who extended the work and found it was also true in rats[8].

Dogs can be kept alive for four weeks solely with intraperitoneal nutrition, but they lose 25% of their body weight and the peritoneum appears to lose its efficiency as an absorptive surface with time[9]. At sacrifice, dense adhesions were found within the peritoneal cavity. Although the number of adhesions were not related to the absorptive ability of the individual dog and were found only on the serosal surface these seem the likeliest cause of the progressive diminution in absorption.

A more recent study in rabbits traced triglyceride absorption and found that it was mainly absorbed via the lymphatics of the visceral peritoneum[10]. This route is obviously compromised as a result of small intestinal resection.

Even if this method of nutrition was found to be applicable in humans several problems would have to be addressed; the main one would be that most patients with short bowel syndrome will have had previous abdominal surgery, this may result in significant adhesions which could reduce the available surface for absorption. Massive intestinal resection will also reduce the amount of visceral peritoneum available for absorption. In addition, previous intra-abdominal sepsis, while contributing to the adhesions, could potentially be reactivated when exposed to feeding solutions which would provide an excellent culture medium. The permanent catheter necessary for feeding by this route would, in itself, provide an entry portal for infection, just as it does for the patients with chronic renal failure. The clinical role for this type of nutrition would be very limited, perhaps restricted to those long-term patients who had run out of venous access for TPN, and in whom no other options were available.

(b)Parenteral nutrition

This involves the delivery of nutrients directly into the venous circulation, administered in sterile form, via an indwelling catheter.

Parenteral nutrition has revolutionised the management of patients with the short bowel syndrome, making survival possible. It's complications, and the restrictions it imposes on patients are acceptable in the short-term, while awaiting small intestinal adaptation, but it is not the perfect solution for the long-term problem of the patient with an absent small bowel with no prospect of adaptation.

Basic dextrose and electrolyte solutions were the forerunners of intravenous feeding solutions, but were obviously inadequate to meet long term nutritional needs. By 1960[11], it had become apparent that a balanced solution of amino acids, carbohydrates, fats, alcohol, vitamins and electrolytes in suitable form for sterile intravenous administration was required to prevent metabolic problems and to maintain body weight.

In 1968 the first report of a positive nitrogen balance, with growth and development was made by Dudrick[12]. He reported on thirty patients, the most dramatic of whom was a baby born with near-total small bowel atresia. He also compared puppies fed orally with their intravenously fed litter-mates, both groups receiving the same amount of calories, and found that the parenterally fed animals gained weight and grew in comparable fashion to their orally fed siblings. This significant advance made clear that not only could people be kept alive by parenteral nutrition, but that children could now be expected to grow normally. By 1972, he had fed 1 400 patients intravenously[13].

The introduction of Broviac's Silastic catheter in 1973[14] resulted in an increase in catheter life span, and by 1976, the first report of a patient being intravenously fed for five years at home was made[15].

Since then parenteral nutrition has been used increasingly, with 2 200 Americans receiving home total parenteral nutrition (TPN) at an annual cost of $80 000-$100 000 each in 1989[16]. In the United Kingdom and Eire over a nine year period ending in 1986, 200 patients were on home TPN at an annual cost of £25 000 each[17]. Of those 200 patients, one third were able to continue in their previous employment and others have shown that this may be possible for up to two thirds[18].

Both the UK study and others[19], have shown that of all patients accepted on to a home TPN programme, probably less than half will require to remain on it. In the UK this is often because a small bowel fistula closes or because of small bowel adaptation, while in the USA a significant number of patients have malignancy.

As experience with TPN has grown, so have the number of reports of complications. One typical report describes 509 complications in 1 647 patients[20]. The myriad of complications reported can be grouped under the three headings of; (a) catheter insertion

(b) sepsis and (c) venous thrombosis[21]. Sepsis was the cause of death of ten of the patients out of the two hundred patients reported by the UK Home Parenteral Nutrition Group in 1986[17]. Superior vena caval thrombosis and thrombus formation within the right atrium have also caused fatalities[22].

Intrahepatic cholestasis[23], may rarely proceed to liver failure and require liver transplantation, especially in children.

Apart from these life-threatening complications, patients have their lifestyles restricted by the need to have daily infusions over many hours and many of them are unable to eat and have diarrhoea secondary to a massive reduction in small intestinal length.

Surgical Strategies for the Short Bowel Syndrome

Considerable ingenuity has been applied in designing procedures which utilise remaining intestine. They fall into two broad categories:

(1)Delaying Transit Time

The transit time is the period of time it takes for bowel content to move a predetermined distance along the length of the bowel. Increasing the transit time implies that the bowel content is exposed to the absorptive surface of the bowel for longer, increasing the amount absorbed. Slowing transit has the disadvantage of allowing bacterial overgrowth to occur, which may result in malabsorption.

(a)Reversed Intestinal Segments.

The principle of reversing a segment of small intestine is that by doing so, peristalsis is reversed within this section of bowel, resulting in delayed transit of intestinal contents. A review in 1975[24], emphasised that the length of the reversed segment is critical, too short a segment does not slow transit sufficiently and too long a segment results in intestinal obstruction. Most case reports have been of only one or two patients and the optimum length of the reversed segment is 7.5-14.0cm.

This procedure therefore requires sufficient small intestine to reverse, allowing for some small bowel to remain peristalsing in the normal direction, and carries the risk that further operative intervention may be required if the length of the reversed segment is misjudged.

(b)Intestinal Valves.

Once again the principle of this procedure is to slow the transit time. A canine study in 1982[25], involved excision of 85% of the jejunoileum with the creation of two valves formed by excising a 1.0-1.5cm width of the seromuscular coat, suturing together the adjacent muscular layers, thereby invaginating a length of mucosa and submucosa. Dogs with these valves lost only 6% of their body weight compared to the 20-40% weight loss of the control animals.

This procedure may have a clinical role in patients with some residual small bowel, although no reports of it being carried out in humans have been made.

(c)Retrograde Pacing.

In dogs, it has been shown[26] that transection of the duodenum separates the jejunoileum from it's pacemaker which reduces the frequency of the pacesetter potential in the intestine distal to the transection. Electrodes placed on the distal bowel set to generate pulsed electrical stimuli at an increased frequency to the pacesetter potentials cause the pacesetter potential to propagate in an orad direction. This slows transit time, allowing increased absorption.

It has proved easier to entrain the pacesetter potentials of canine small intestine, however, than that of humans. Human small intestine refuses to be entrained, this prevents it's use in the clinical setting[27].

(d)Recirculating loops.

This operation reconstructs the residual small bowel with a short reversed segment and remaining bowel loops anastomosed in an arrangement which allows gut content to traverse the same segment several times.

Budding, in 1967[28], carried out an extensive study in fifty four dogs in whom he resected 90% of the small intestine and formed recirculating loops with the remainder. These operations resulted in a high mortality and morbidity rate and did not reduce weight loss or prevent death.

Whilst theoretically attractive, these operative designs all had both an entry and exit point to the loops, hence enteric content did not necessarily have to traverse the loop entirely. The possibility exists that the surface available for absorption is actually reduced

by this procedure, and, since it did not have any benefit in animals, it has not been carried out in man.

(2)Increasing Mucosal Surface Area

All these methods rely on strategies to encourage the normal small bowel mucosa in the residual small intestine to replicate, above and beyond that already provided for by adaptation.

(a)Neomucosa.

Normal mucosa can spread out from incisions in small intestine patched with the serosa of adjacent bowel. This currently remains at the experimental stage.

Binnington, in 1974[29], made a 12-15cm longitudinal incision in the proximal jejunum of rabbits, the resulting defect was 1.5-2.0cm wide and the serosal surface of adjacent colon was sutured around the defect. After 36 weeks jejunal mucosa had covered the colonic serosal surface and resembled the native jejunal mucosa in morphology and brush border enzyme levels. Further rabbit studies in 1985[30] involved the creation of 5cm by 2cm defects patched in similar fashion, in both jejunum and ileum. Bowel diameter was increased by up to 22% and neomucosal growth occurred more rapidly in the ileum. In vitro studies found that ileal neomucosa absorbed more glucose than its jejunal counterpart.

These procedures serve to widen existing small intestine, but have no effect on length; attempts at creating mucosa- lined tunnels utilising colonic serosa as walls have not met with much success[31]. This limits it's application to situations where such adjacent bowel exists, and also limits the amount of neomucosa which can be formed. To achieve a significant increase in absorptive surface would require multiple operations, each one carrying a significant risk of intestinal leakage with it's dire consequences. It is therefore not a clinically useful concept.

(b)Mucosal Expansion.

This is a more recent concept which aims to place functional small intestinal mucosa within a colonic muscular tube. Fenestrating the mucosa allows growth of neomucosa, giving extra length. This has been carried out in pigs[32], with successful growth of neomucosa by 8 weeks; the absorption of fatty acids being equal in neomucosa and control ileal mucosa. Glucose absorption was also normal[33].

This has not been carried out in humans, and carries the obvious disadvantage of losing colonic length.

(c)Enterocyte Growth.

It has been possible to grow enterocytes taken from neonatal rats and grow them for up to one month in vitro[34]. Attempts to graft them in to colonic tubes have not succeeded. This technique is in it's infancy, but may hold some hope for the future.

(d)Intestinal Loop Lengthening.

This elegant method of obtaining extra intestinal length was first described in the pig, by Bianchi[35]. The anatomical basis for this, is the ability to develop a surgical plane within the small bowel mesentery close to the bowel wall which allows the blood vessels to each half of the bowel wall to be separated. Through this gap is passed a surgical stapler, which, when fired, bisects the bowel tube longitudinally, the transected edges being closed by a double row of staples. The original length of bowel is now half the diameter, the twin loops running in parallel. These loops are then anastomosed in series, so doubling the original length. Bianchi carried out this procedure in seven animals and, by 21 weeks post-operatively, the segments which had been halved had regained normal diameter.

A year later, the first report of the Bianchi procedure being carried out successfully in humans was made[36]. This four year old boy had 60cm of residual small intestine, which was dilated to a maximum of 11cm diameter in the distal 30cm. By ten weeks post operatively, he was gaining weight entirely on enteral nutrition. The procedure has subsequently been carried out elsewhere, in two babies, with equal success[37].

This operation, of all those described, is the most useful. It relies on both the existence of some residual small intestine, and the fact that adaptation has resulted in that bowel having a much greater diameter than normal, allowing it to be halved. It has a proven clinical role in suitable patients, and is preferable to TPN.

All the surgical options mentioned rely on there being residual small intestine, and each carries the risk that any complication of the surgery could result in what little gut there is left being lost.

Neomucosal growth remains in an experimental stage and will not have a clinical role until a suitable membrane can be developed to support it interposed along the length of the bowel, thus increasing bowel length, while also increasing the surface area for

absorption. If enterocytes could successfully be grown in culture medium and seeded on to such a membrane, enterocyte-lined tubes could be created in vitro and then inserted in vivo at operation. Ingrowth of capillaries would be required, and the tubes would influence small intestinal motility. It's clinical use remains highly theoretical.

Intestinal Transplantation

Human small bowel transplantation has been a clinical reality for the past 3 decades. Early attempts met with little success: all patients died either perioperatively as the result of major surgery in patients in a poor nutritional state, or within the first few days due to overwhelming rejection.

The Canadians estimate that there are about 40-50 patients country-wide who would be suitable for a small bowel transplant[38], while in Britain it is thought that up to 20 new adults each year become candidates for small bowel grafting[39].

In a letter to The Lancet in 1990, the European Intestinal Transplantation Study Group summarised their experience from 1987 onwards as being 15 small bowel transplants in 12 patients. Of these, only 4 grafts were functioning, allowing complete independence from parenteral nutrition[40].

Transplantation of the small intestine in humans was first carried out in 1964 by Detterling in New York, in two infants who died post-operatively; the details of these cases have never been published. The first reported case was carried out by Richard Lillehei, at the University of Minnesota, in 1967[41]. Two further cases were carried out in Brazil in the following two years[42,43]. By 1972, another three surgeons had reported their individual cases[44-46].

The death of these first eight patients over this five year period resulted in the procedure being abandoned in favour of parenteral nutrition.

The advent of the new immunosuppressant, cyclosporine, in the mid-eighties, reawakened interest and the first report of a small bowel transplant under cyclosporine cover was published in 1986 by Zane Cohen's group in Toronto[47]. This patient had microscopic signs of rejection in biopsies of the transplant mucosa at day 4, and died on day 10, with multiple infarcts of brain, liver and spleen. Her death was suspected of being due to cerebral toxicity of cyclosporine.

The number of reviews published, gives some idea of the high level of interest generated by the concept of small intestinal transplantation, despite these poor results[48-54].

Another hint that cyclosporine may not be as efficacious in small bowel transplantation as had been hoped came from a report in 1984 from Starzl's group in Pittsburgh[55].He described four patients in whom he had carried out a pancreaticoduodenal transplant, in the first two he had included 1-2ft of jejunum along with the graft. These two patients developed abdominal pain and a protein-losing diarrhoea and ultimately required excision of the jejunal portion of their grafts, which showed evidence of severe mucosal damage. Following excision, their symptoms resolved.

Further reports have confirmed that a segment of duodenum is tolerated along with a pancreatic allograft, in patients on cylosporine immunosuppression[56].

The first report of a successful small intestinal transplant was published by David Grant's group in Ontario in 1989[38,57]. This patient had been operated on in November of 1988, but was not fit for discharge home until June of 1989. Her parenteral nutrition had been stopped 8 weeks post-transplant, and she was on normal diet and her nutritional indices were normal. She had received a combined liver and small bowel graft. Post-operatively she developed respiratory insufficiency, and required mechanical ventilation for a period of six months. She had one episode each of intestinal rejection and graft-versus-host disease, plus two episodes of major sepsis. Cyclosporine immunosuppression was used, along with steroids and azathioprine and, in addition, she was given the monoclonal antibody, OKT3 for the first 14 days post-transplant. By 1990, Grant reported a second case, this time an isolated small bowel graft, in an eight-year-old girl whose transplant had to be removed for rejection in the presence of major sepsis[58].

By 1992 Grant's group had carried out 5 transplants, 2 patients dying within the first few post-operative months, the other 3 being well on normal diet 8 months to 3 years after transplant. Grant has abandoned isolated small intestinal grafts in favour of liver/small bowel grafts or multivisceral grafts which also include stomach, duodenum and pancreas.

The Paris group reported their first case in 1988[59], and by 1990 had operated on 5 children, 4 of whom had required graft excision for rejection[60]. The remaining child continues to do well 30 months after receiving her isolated small intestinal graft from an anencephalic baby, and is maintained on cyclosporine and azathioprine. Her parenteral nutrition was discontinued after 10 months[61,62].

Deltz, in Keil, gave 60cm of small bowel from a living related donor, to a 42-year-old woman in 1988 who was alive and well one year later; no comment was made as to graft function[63].

In 1992, a case was reported from Uppsala in which a 13 month old baby received an isolated small intestinal graft, but unfortunately died 8 weeks later of rejection and sepsis[64].

Apart from a single unsuccessful case of a baby given a liver/small bowel graft in Wisconsin[65] in 1988, the largest American series comes from Starzl's group in Pittsburgh.

Having noted the poor outcome of patients receiving small intestinal grafts with cyclosporine and conventional immunosuppression, they used the new agent, FK506, in 9 patients. Only one patient received an isolated small intestinal graft, the rest also received the liver: the patient with just the small bowel had the most episodes of intestinal rejection. The youngest patient in the series, a six-month-old baby, died of graft-versus-host disease. In the remaining 8 patients, it took between 6 weeks and 9 months before enteral nutrition became established, and only 2 patients are completely free of parenteral nutrition. Rejection and sepsis have been the main problems, hepatic rejection being easier to control than intestinal rejection. The latter was severe enough in two cases to cause complete mucosal loss. Each of these transplants has been estimated to cost $500 000[66].

The successful small intestinal transplant patients to date offer hope that this procedure will become the method of choice for the treatment of patients with an absent or non-functioning small intestine.

It must be noted, however, that at present the morbidity and mortality of the operation remains high due to the unique properties of the small intestine with regard to it's high immunological load[67] and the readiness with which bacteria translocate across rejecting mucosa[68]. The success rate of combined liver/small intestinal grafts may be better than that of isolated small intestinal grafts, when using Cyclosporine A immunosuppression, possibly due to immunotolerance produced by the liver. Isolated small bowel grafts appear to be better tolerated when FK506 is used

Pathophysiology of Intestinal Transplantation

Removal of the jejunoileum, and its subsequent placement in a recipient, entails division of the bowel proximally and distally, plus the transection of all vessels and nerves supplying the gut. The organ is then cooled by infusion of a preservation solution, resulting in a short period of warm ischaemia followed by a longer period of cold ischaemia, until the bowel undergoes reperfusion within the recipient.

Unless donor and recipient are an identical match in terms of tissue type, an immune response will result in either rejection of the graft or graft-versus-host disease. In order to prevent this, suppression of the immune system is necessary. Denervation, ischaemia/reperfusion, rejection and immunosuppression may all have an effect on the absorptive ability of the small intestine.

(1)Extrinsic Denervation.

The extrinsic nerve supply to the bowel is composed of a sympathetic and a parasympathetic division.

(a)Sympathetic

The sympathetic nerve supply originates from the spinal cord, from the fifth thoracic segment down to the second or third lumbar segment. These preganglionic fibres synapse within the prevertebral sympathetic ganglia, fibres from the coeliac and superior mesenteric ganglia supplying the small bowel. These postganglionic fibres terminate on enteric ganglia and blood vessels[69].

Experiments on dogs as far back as 1903 showed that removal of the coeliac and superior mesenteric ganglia resulted in watery diarrhoea, with the passage of mucus and blood. This tended to resolve after a few weeks[70]. This was confirmed in a further study in 1941, when it was also noticed that these sympathectomised dogs were prone to peptic ulceration[71]. Carrying out a truncal vagotomy at the same time as the sympathectomy prevented the ulceration, but did not have any effect on the diarrhoea[72].

Ballinger, in 1962, carried out an extrinsic denervation of canine jejunoileum by skeletonising the superior mesenteric artery and vein and dividing the mesentery. This produced a profuse diarrhoea lasting up to four weeks, identical to the ganglionectomised dogs[73].

Surgical sympathectomy in rats results in greatly diminished adrenaline, noradrenaline and dopamine levels within the wall of the small bowel[74]. Splanchnicectomy and lower thoracic ganglionectomy was previously performed in humans with severe hypertension in the days prior to effective medical management and a radiological study carried out in 8 patients in 1947, showed only a delayed small bowel transit time[75]. These patients all complained of anorexia and bloating post-operatively, but no mention is made of diarrhoea. A larger study asked 300 patients about their bowel habit following extensive

sympathectomies, and found 18% had increased frequency of defaecation, while 2% had distressing diarrhoea. These symptoms did not diminish with time[76].

The fact that few humans get diarrhoea following section of the sympathetic supply to the small bowel, whilst all dogs do, may well be a species difference as dogs have five times as many alpha-2 adrenergic receptors in the ileum[77].

(b)Parasympathetic

The small bowel receives its parasympathetic supply from the dorsal motor nucleus of the vagus, in the medulla oblongata. These preganglionic fibres travel within the vagus nerve and terminate on intrinsic neurones.

Parasympathetic denervation of the small bowel has been carried out for many years in the course of surgical management of peptic ulcer disease. Hodges, in 1947[75], in barium examinations, noted gastric dilatation and stasis in patients following vagotomy, and a slowing of small bowel transit, even in patients with post-vagotomy diarrhoea.

A study of 9 patients with post-vagotomy symptoms of diarrhoea or colicky abdominal pain, showed that 8 of the 9 had increased fat excretion on a 60g fat diet[78]. Studies in dogs after selective or total vagotomy showed no abnormality of transit on barium studies, but did show increased nitrogen losses in the stools[79]. Decreased fat and protein absorption was found in another group of dogs after vagotomy and pyloroplasty[80]. Humans on a 100g fat diet were found to have increased fat excretion following truncal or selective vagotomy with a drainage procedure, but not after highly selective vagotomy[81]. Perfusion studies of a 30cm length of jejunum in patients with post-vagotomy diarrhoea showed no defect of absorption of water and electrolytes[82].

(2)Intrinsic Denervation.

The continuity of the enteric nervous system is disrupted by transection of the proximal and distal ends of the small bowel in the course of transplantation. This results in important changes in small bowel motility.

The enteric nervous system is composed of the myenteric plexus (Auerbach's plexus) which lies between the longitudinal and circular muscle layers of the bowel wall, and the submucosal plexus (Meissner's plexus) which lies within the submucosa. Both plexuses contain ganglia and are interconnected, forming a single functional system[69].

At least 10 distinct types of enteric neurone have been identified, some supplying glands, others, smooth muscle, and others blood vessels. Others are interconnecting neurones, both excitatory and inhibitory[83].

The function of the enteric nervous system is to co-ordinate smooth muscle activity, vasculature, epithelial transport, enteroendocrine cells and immune elements[84].

(3)Motility.

The enteric nervous system plays a major role in the initiation and propagation of the migrating myoelectric complex, the absence of which results in a change in the bacterial flora of the gut.

(a)Migrating Myoelectric Complex

In 1969, Szurszewski first described a wave of electrical activity spreading in an orderly fashion from the duodenum to the terminal ileum in fasted dogs. As this migrating electric complex reached the end of the small bowel, another one was starting in the duodenum[85]. This same pattern is found in the fasting state in most non ruminants, including man. Ruminants show this pattern in both the fasted and fed state[86]. Phase three of this migrating myoelectric complex (MMC) is associated with a strong propulsive wave of muscular contraction whose function is to sweep non-digestible foodstuffs and mucosal debris along the small bowel, and in to the colon. It has hence been nicknamed "the intestinal housekeeper".

(b)Extrinsic Denervation

The parasympathetic nervous system appears not to have a major role in control of the MMC. Thoracic vagotomy or cooling the vagus to prevent nerve conduction, does not alter the MMC in dogs[87,88].

Loss of sympathetic nervous input to the small intestine does not prevent MMC cycling, but it does effect coordination and duration of cycling.

Marlett and Code, in 1979, studied 4 dogs after excising the coeliac and superior mesenteric ganglia and found that while Phase three remained unaltered, the other three phases showed greater variability in their duration. In addition, bursts of electrical activity similar to Phase threes, but which did not migrate, were seen[89].

Another study showed a lack of coordination of MMC's between the stomach and small bowel after sympathetic denervation[90]. This observation was also noted in a group of paraplegic patients who had sustained spinal cord transection above T1[91].

(c)Intrinsic Denervation

Division of the enteric (intrinsic) nervous system has major effects on the MMC. Smooth muscle cells of distal stomach and small intestine have periodic oscillations of membrane potential known as the pacesetter potential (also known as, electrical control activity, slow wave or basic electrical rhythm). Code transected canine duodenum and mid-small bowel and discovered each region had a different frequency of pacesetter potentials, in a gradient of most frequent proximally to least frequent distally. These frequencies remained unaltered for the 3 month duration of the study[92]. Sarna divided and reanastomosed the small bowel in three separate locations and found the MMC in each of the four segments to be independent of the other[93]. The enteric nerves concerned with propagation of the MMC in dogs appear to be cholinergic, via the nicotinic receptors[94]. Regrowth of these enteric neurones across an anastomosis restores the ability of an MMC to pass an anastomosis[95].

Rats have MMC's both fasting and fed. MMC frequency was reduced in rat ileal isografts in the fasted state but not when fed[96]. Another study in dogs, looked at motility and absorption in a segment of jejunum before and after proximal transection and reanastomosis[97]. The frequency of MMC's decreased distal to the transection line, the transit time for liquids remained the same but increased for solids. Absorption across the segment of jejunum was studied in the fed state for sodium(Na), chloride(Cl), water and glucose and remained unchanged, despite the altered motility.

(d)Bacterial Overgrowth

Normal small intestinal motility is required to prevent bacterial overgrowth within the bowel lumen.

Five patients who had bacterial overgrowth which was resistant to antibiotic treatment had either absent or greatly disordered fasting motility[98]. When the MMC was inhibited in rats for 15 hours, bacterial overgrowth occurred[99].

A study carried out in dogs in 1990, showed that in an end-to-end anastomosis, 91% of MMC's crossed by 20 weeks, compared to only 22% across a side-to-side anastomosis.

2 years later, only 56% of MMC's traversed the side-to-side anastomosis, and there was a tendency towards bacterial overgrowth[100].

(4).Lymphatic Division.

There is clear evidence that, in the absence of rejection, restoration of lymphatic continuity occurs within the first few weeks following small intestinal transplantation. Any changes in absorption, secondary to lymphatic division, should only occur within the first post-operative month.

Fat is normally absorbed from the small intestine, packaged as chylomicrons by enterocytes, and released in to lacteals, which drain via the thoracic duct into the central venous system. Histology of small bowel mucosa, 10 days following small bowel autotransplantation, shows central lacteal dilatation within the villus[101].

Richard Lillehei's group looked at lymphatic regeneration in canine small bowel autografts, using sky blue dye and radiological contrast medium, injected into mesenteric lymph nodes of the graft. By 2 weeks post-operatively, dye and contrast passed in to lymphatic vessels around the portal vein, and in to the thoracic duct[102]. Kocandrle, in 1966, injected Evans blue dye subserosally, and found that it took until the 20th day before passage to the thoracic duct was seen[103]. At 4 weeks, the lymphatic channels within the bowel had regained their normal calibre. These observations were made in autografted dogs, all the allografted dogs died of rejection by the 10th day, with no evidence of lymphatic regeneration.

Two further studies in dogs confirm that there is continuity of previously severed lymphatics by 21 days[104], and 28 days[105].

More recent studies have been carried out in isografted rats; methylene blue injected in a mesenteric lymph node, showed evidence of passage towards the recipient on day 3, but did not clearly pass until day 7, and at day 14 passage was immediate[106]. Contrast medium injected into graft mesenteric lymph nodes did not pass into the recipient's thoracic duct until day 20[107].

(5)Ischaemia/Reperfusion.

Small bowel mucosa is exquisitely sensitive to ischaemia, with microvillus damage to cells at the tips of the villi occurring after only 3-5 minutes of warm ischaemia. After 60 minutes, the upper two thirds of the villi lose all their epithelial cells. Regrowth of epithelium is also rapid, with 60 minutes of ischaemic damage to canine ileum being

almost completely repaired after 24 hours. The mucosal enzymes involved in absorption are the most sensitive to ischaemia-reperfusion, followed by the cells themselves. While cells within the intestinal crypts may replicate and rapidly migrate up the villi repairing the damage as visualised by the microscope, the functional enzyme systems take longer to mature and show diminished absorptive capacity for up to 7 days[108].

Following a period of ischaemia, small bowel develops increased vascular permeability, thought to be a reperfusion injury. The intestinal villi have the highest concentration of xanthine dehydrogenase of any tissue, this enzyme being the major source of superoxide, the free radical implicated in reperfusion injury[109]. It has been shown that administration of naloxone, a superoxide scavenger, before the onset of small bowel ischaemia in the rat, has a protective effect[110]. The longer the ischaemic time, even in preservation fluid, the greater the mucosal damage[111].

A more detailed study looked at ischaemia and reperfusion in canine ileum, and found more damage following reperfusion than simply following an identical period of ischaemia. They looked at mucosal arachidonic acid metabolism, and found reperfusion caused vast increases in mucosal vasoactive eicosanoids, causing a profound drop in blood flow in reperfused tissues[112]. Reperfusion also reduces the glycoprotein levels in canine small bowel mucosa; glycoproteins are believed to have a protective role against enteric bacteria[113]. Mucosal enzymes show a greater fall after reperfusion, than after ischaemia alone[114].

Lipid absorption in rats becomes altered for the first 24 hours following 10 minutes of ischaemia of the small intestine, followed by reperfusion. A significantly greater proportion enters the portal venous system, perhaps as a result of increased mucosal permeability. The net effect is that lipid absorption was unchanged[115].

(6)Cyclosporine A.

This drug may have an adverse effect on absorption. Currently, it is the most widely used immunosuppressant agent in the field of transplant surgery. Its adverse effect on renal function is well known, with elevated serum creatinine and blood pressure secondary to reduced glomerular filtration due to diminished renal plasma flow. This appears to be due to vasoconstriction of the afferent glomerular arteriole, perhaps by cyclosporine's ability to raise thromboxane A2 levels[116].

Less well known, however, are the direct effects of CyA on the small intestine. Rats were found to develop impairment of the microvascular supply to both jejunum and ileum after 7 days of oral or intravenous CyA at the conventional dose of

15mg/Kg/day[117]. It has also been found to increase intestinal permeability via intracellular tight junctions in both normal and isografted rats[118]. In vitro studies show that CyA reduces the active transport rate for glucose in the jejunum but increases it in the ileum, while the passive uptake of long chain fatty acids is reduced in the jejunum, but unaffected in the ileum[119]. An effect on the sodium-glucose cotransporter of the bowel is likely. This is confirmed by an in vitro study on a cell line from proximal renal tubular epithelium, where CyA inhibited the glucose uptake normally facilitated by the sodium-glucose cotransporter, which may be the mechanism of glycosuria in patients on CyA[120].

CyA has even been noted to prolong the regeneration of lymphatics in isografted rats[106].

(7)Rejection/Graft-versus-host-disease.

Histocompatibility has an important role in the immune response mounted following allografting[121,122]. An additional factor, unique to the small intestine, is the large amount of lymphoid tissue it contains. Large numbers of lymphocytes exist in the isolated lymphoid follicles of the jejunum, the aggregated lymphoid follicles (Peyer's patches) of the ileum, and the many lymph nodes within the mesentery. It is therefore not surprising that rejection and graft-versus-host-disease (GVHD) are a major problem in both clinical and experimental small bowel transplantation.

The mucosa is the most sensitive area of the small intestine to the immunological sequelae of transplantation. Rejection in dogs results in decreased glucose absorption, which has been used as a marker of intestinal rejection[123]. Maltase activity has also been used as a marker[124] of rejection, while mice have been noted to develop a protein-losing enteropathy as a result of GVHD[125].

Even with the advent of CyA, initial survival of allografted dogs was only 25 days[126] in 1984, but by 1987 some dogs were surviving 6 months[127], and longer survival is now possible.

Because of the problems with maintaining adequate immunosuppression, several strategies have been employed with varying degrees of success. If donor rats are given pre-treatment with anti-lymphocytic serum, the onset of GVHD is delayed[128]. Irradiating the small intestinal graft prior to transplant does not improve survival in rats[129], but can delay the onset of GVHD, allowing rejection to cause death instead[130]. In dogs, the opposite occurred, the dogs survival increasing from 9 days to 25 days, death being due to suspected GVHD[131]. Using segmental, rather than total small bowel

grafts, increases survival in rats[132]. Ileum contains more immunological tissue than jejunum and, in rats, has been shown to reject more quickly[133], although a later study has refuted this[134].

(8)Venous Drainage

The type of venous reconstruction employed in the recipient may influence both the rejection process and the nutritional state.

Porto-caval anastomosis is the most frequently used drainage route for the small bowel graft, because it is technically more easy to perform and appears to have no adverse metabolic effects despite its similarity to an Eck fistula[135].Other authors, studying rats at 6 months after isografts with either porto-portal or porto-caval venous drainage found elevated serum ammonia levels and moderate liver atrophy in the systemically drained group[136]. Rats with portal venous drainage of their grafts have also been noted to appear healthier, and have better weight gain[137]. In addition, caval drainage may increase the incidence of rejection[138].

Intestinal Function Following Small Intestinal Transplantation.

This has not been extensively studied, mainly due to the problems of rejection, which becomes evident histologically as early as the 6th post-operative day[139], at a stage where most animals are still recovering from the operative procedure. This means that not only are the animals not eating normally this early on, but, if rejection is occurring, the mucosa is actively being destroyed by this immunological process, rendering absorption studies meaningless.

Studies which have been carried out have used a number of different species with differing degrees of similarity to humans. Rats are a small animal model with a different motility pattern than humans and also differ in having broad leaf-like intestinal villi. These differences may make comparisons to humans invalid. Dogs and pigs are a large animal model with similar motility and intestinal structure to humans and may therefore be more relevant.

(1)Rats.

Most of the literature concerns the immunological consequences of small intestinal transplantation, since the rat can be bred to produce strains specific for either rejection, GVHD, or both. This makes it an excellent animal model for immunological studies.

(a)Global Absorptive Function.

Many of the studies which do look at graft function, use body weight as the indicator of absorptive ability of the transplanted gut; this is a rather crude measurement, since the small bowel has such a large reserve capacity, and subtle alterations in graft function could be missed. A large number of studies have shown that after an initial fall in weight over the first post-operative week, rats with isografts or non-rejecting allografts, will gain weight and grow normally[130,140-144]. Several of the studies also looked at serum protein levels, which were normal, and others found that the full length of donor bowel was not needed to achieve these end points.

(b)Intestinal Permeability

Intestinal permeability is closely related to the subject of absorption. Abnormal permeability of the gut wall will alter absorption, as substances "leak through". Permeability of isografted and allografted small intestine is elevated in the first week following transplantation, and whenever rejection is present[145]. Interestingly, small bowel grafts placed in the heterotopic position, have increased permeability, suggesting that small bowel contents play a role in the recovery from transplantation injury[146]. This early abnormal permeability also allows translocation of bacteria from the gut lumen, which will also occur during episodes of rejection, and is probably the reason for the high rate of septic complications seen in the human recipients of small bowel grafts[147]. Abnormal permeability can exist despite normal histological appearances on light microscopy, and its use has been suggested as an early marker of intestinal rejection.

(c)Brush Border Enzymes.

Rather than look at absorptive activity, some authors have looked at the enzymes in the brush border which are normally responsible for digestion. The dissacharidases, neutral a-glucosidase and lactase/beta-glucosidase, as well as alkaline phosphatase and dipeptidylpeptidase-IV, are significantly reduced 6 weeks after transplantation in both isografts and allografts[148]. Maltase, sucrase and lactase levels all fall immediately after

transplantation in isografted rats, but return to normal levels after 4 days. In allografts, the same rise is seen, with the exception of lactase, which remains at low levels. At day 6, the maltase and sucrase levels fell due to the onset of rejection[149].

(d)Maltose Absorption

This has been looked at by several authors, and has been found to be normal at 8 weeks[150], and normal at 1, 3 and 6 months[151]; both studies comparing isografts to normal rats. Allografted and isografted rats were found to have increased absorption of both glucose and maltose at day 25, which returned to normal by day 150[152]. Maltose absorption measured at between 107 and 203 days post-operatively, is normal in allografts[153].

Maltose is split by the disaccharidase, maltase, located in the brush border, and absorbed into the enterocyte as glucose. Both these steps appear to function normally in rats with non-rejecting small intestinal allografts, the early increased absorption may reflect increased mucosal permeability.

(e)Cyclosporine A Absorption

Rats absorb CyA mainly by the lymphatic system[154]. CyA absorption has been found to be normal in isografts at day 7[155], and in isografts and allografts at day 25 and 150[152]. Interestingly, CyA administration enhances the absorption of the fat soluble vitamin, vitamin A, both in normal rats, as well as isografted and allografted animals by day 35[156]. The reason for this is unknown.

(f)Fatty Acids and Vitamins.

Long chain fatty acids, like CyA, are absorbed via the lymphatic system, and oleic acid absorption has been found to be normal in isografted rats at 1, 3 and 6 months following transplantation[151].

Serum levels of the fat soluble vitamins A and E, are normal in allografted and isografted rats at 4-6 and 10-12 months following transplantation despite elevated faecal fat excretion, which was 2-3 times higher than in normal rats on the same diet[157]. In rats which had only the jejunum or ileum transplanted, these vitamins were abnormally reduced at the later time point, suggesting decreased absorption which could no longer be masked due to depletion of body stores. It therefore seems likely that there is a defect in fat absorption, but not sufficient to cause steatorrhoea.

(g)Water, Glucose and Electrolytes

The situation with regard to basic water and electrolyte absorption is not entirely clear, conflicting results having been found.

One group of authors, studying isografts and allografts placed heterotopically and comparing them to Thiry-Vella loop controls, have found water and sodium (Na) absorption to be decreased in both grafts at both 9 and 21 days, and glucose absorption to be decreased only in the allograft at 9 days but in both by 21 days[158,159]. Further experiments showed that water , Na, chloride (Cl) and glycine absorption were all decreased in isografts, allografts and denervated Thiry-Vella loops at the same time points, suggesting that it is the denervation which is responsible[160,161]. Glucose absorption was normal in one of those studies, but was decreased at 21 days in allografts alone, in the other. Work on isografted small intestine by other authors has confirmed this diminished water and glucose absorption, but they do not state at what time the animals were studied, or whether the grafts were orthotopic or heterotopic[162].

By contrast, water, Na and Cl absorption in Thiry-Vella loops and heterotopic isografts have been found to be normal at 14 days[163], and a third group found that isografts at day 35 had decreased water and glucose absorption in the heterotopic position, but had slightly increased absorption if placed orthotopically at day 35 and then studied at day 56[164].

Conclusion.

Rat small intestine quickly undergoes atrophy when deprived of enteral nutrients, which may explain the decreased absorption in heterotopic grafts, while rapid regeneration may explain the increased absorption in the graft which is then placed orthotopically. Decreased absorption within the first week post-transplant could be explained by transplantation injury, but was also seen in loops which had simply been denervated. If atrophy is assumed to occur at equal rates in both innervated and denervated bowel, then atrophy cannot simply be the explanation for the differences seen. The likeliest explanation is the loss of the "sympathetic brake" on intestinal secretion.

(2)Dogs.

Although dogs were the original model for intestinal transplantation, they have proved to be more difficult to immunosuppress than rats, and rejection has been a major problem. The advent of CyA resulted in further attempts at allografting: three out of eleven dogs

survived more than 200 days in 1982[165], three out of forty-two survived more than 200 days, with one dog surviving 432 days, in 1983[166]. Out of forty-two dogs only one survived to 140 days in 1987[167], and a further study in 1987 had one 6 month survivor out of thirty-nine dogs[168]. It has been shown more recently that with major histocompatibility complex matched dogs, survival is markedly increased[169].

(a)Global Absorptive Function

Since most dogs in early series died very rapidly from rejection, comments about nutritional state could only be made about autografted or denervated animals.

The first person to successfully transplant canine small intestine was Richard Lilleihei at the University of Minnesota in 1959[170]. Despite a high perioperative mortality, he found that autografted dogs which survived the initial post-operative course could live for as long as 6 months, allografts dying within the first 2 weeks. He noted the surviving autografted dogs to have diarrhoea for the first 10 days.

Ballinger, in 1962[72], studied the effect of small intestinal denervation by looking at autotransplanted dogs, and dogs in whom he had stripped the superior mesenteric vessels of their investing sheaths of nerve fibres as well as transecting the small bowel both proximally and distally with immediate reanastomosis. This latter group of animals, therefore, had extrinsic denervation and interruption of the intrinsic nervous system, and, as the entire mesentery with the exception of the superior mesenteric vessels was transected, all lymphatic continuity was lost. He found that both these groups of dogs suffered from profuse diarrhoea afterwards, and this lasted for 3-4 weeks. Fat absorption was decreased and histology of the small bowel was abnormal, with shortening and broadening of the villi, in both groups. In the denervated group both became normal at 4-6 months, but took 6-8 months to return to normal in the full autotransplants.

Diarrhoea in autotransplants, lasting for 2-3 weeks, was noted by another set of investigators[171].

(b)Glucose Absorption

Since rejection of orthotopically allografted small bowel in the abdomen proved so rapidly fatal, several studies were done with small bowel placed ectopically in the neck, with the vascular anastomoses to the carotid artery and the external jugular vein. Some studies simply looked at graft histology[172], but others compared histology with absorption. Autografted and allografted jejunal loops had identical absorption of

radioactively labelled glucose until the onset of rejection, when the allografted loop absorbed less[173,174].

Glucose absorption in Thiry-Vella (T-V) loops and in jejunum transplanted as a T-V loop are equal, as long as the allograft is not rejecting[175,176]. Azathioprine and prednisolone given to the control dogs did not alter glucose absorption. Glucose recovery from allografted loops with rejection present, was greater than that infused, reflecting increased mucosal permeability. As with autografts and allografts placed ectopically, glucose absorption from loops in an abdominal siting, is identical[177]. Oral glucose tolerance tests in the intact animal with an orthotopic jejunoileal allograft, on CyA immunosuppression, show increased blood glucose levels at both 2 and 6 weeks post-transplant[178].

(c)Cyclosporine A Absorption

This has been the subject of several studies by Zane Cohen's group, in Toronto. They found that both autografted and allografted dogs only absorbed 40% of that absorbed by normal dogs at 7 days post-operatively[179]. They also showed, by means of a thoracic duct fistula, that CyA is mainly absorbed via lymphatics[180,181], and that allografted and autografted dogs absorb CyA to the same extent[177]. They found autografted dogs still malabsorbed CyA 10 weeks after transplantation, but noted that the test dose of CyA in olive oil produced severe diarrhoea. They found that regular administration of olive oil enhanced CyA absorption[181].

A study at the University of Minnesota contradicts these findings. Dogs were studied before, and at 1, 4 and 12 weeks following autotransplantation and CyA absorption was found to be the same on all occasions[182].

(d)D-Xylose Absorption

D-xylose absorption has also been the subject of several studies; it has been compared several months after allografting (exact time not stated) with autografts, and found to be identical[165]. Dogs with denervated jejunoileum, in the fashion of Ballinger, had decreased D-xylose absorption for the first 4-6 months[104], however these dogs had been given azathioprine for 5 weeks after surgery, and the same authors had noted azathioprine to decrease D-xylose absorption in normal dogs. Another study looked at D-xylose absorption in allografted dogs on azathioprine and found it reduced at 3 weeks, but improving at 5 weeks[183]. In the CyA era, D-xylose absorption from allografts and autografts in the neck are the same[184], but orthotopic allografts have decreased

absorption at both 3 and 9 months following transplantation, when compared to normal dogs[185].

(e)Fatty Acid Absorption

Oleic acid is first absorbed from grafts in the neck at 10-14 days, coinciding with regrowth of lymphatics[184], it has reduced absorption from autografted jejunum compared to a control T-V loop for 3-4 weeks[105,185], whereas lauric acid (a short chain fatty acid) is absorbed equally from day 2 onwards. Faecal fat excretion remains elevated at 3 and 9 months in allografted dogs[186].

(f)Water and Electrolyte Absorption

Water, glucose, alanine and lauric acid show equal absorption in ileal autografts and allografts, and absorption increases from day 2 to day 8, as the mucosa recovers from the transplantation injury[101].

(g)Long Term Function

Dogs studied at 12 months after autotransplantation all showed impaired D-xylose absorption and increased faecal fat excretion[187-189]. A low serum albumen was noted, and dogs with systemic venous drainage of the gut tended to have a lower body weight and elevated liver enzymes[187]. Increased bacterial counts were found in the autotransplanted small bowel, making bacterial overgrowth a possible cause for the impaired absorption.

Conclusion

The canine studies have produced conflicting results in almost everything studied, the only consistent finding being impaired fat absorption. Few of the studies are directly comparable due to a mixture of autografted and allografted animals, differing immunosuppressants, and the differing time-points post-transplant when the studies were conducted.

(3)Pigs

These animals have not been as extensively studied as rats and dogs. Rejection has once again been a problem[190], but giving CyA intravenously for the first month after

allografting prevented rejection for the full 60 days of one study[191], while using only a segment of 25% of the entire jejunoileum also increases survival[192].

(a)Fat and Cyclosporine A Absorption

Grant, in Ontario, managed to prevent rejection in early studies in 1986, but all the animals died of infections[193]. Two pigs studied post-operatively (time from surgery not stated) had normal faecal fat levels, however pigs are known to have mesenteric lymphovenous connections, which may allow normal fat absorption until the lymphatics reconnect at 30 days[194]. Grant has also found that absorption of CyA, glucose, triglyceride and fat are normal in allografted pigs at 2-3 months after transplantation[195,196].

(b)D-Xylose Absorption

Absorption of D-xylose is abnormal at 5 and 28 days after allografting, and there are an increased number of bacteria within the transplanted gut and also in the mesenteric lymph nodes, as compared to normal animals[197].

Conclusion

Pigs would appear to have essentially normal small bowel absorption post-transplant. Abnormalities of D-xylose absorption are possibly related to bacterial overgrowth.

(4)Humans

The few successful cases of allografting in patients means that data on small intestinal absorption post-transplant is limited.

(a)Global Function

Grant has three patients who have maintained their weight solely on enteral nutrition, however, he makes no mention of specific absorptive functions.

(b)Fat Absorption

Grant's first successful small bowel transplant patient had normal faecal fat output 2 months after operation[57]. The French infant, who was also fed entirely by the enteral route, had 95% absorption of dietary fat and triglyceride[61,62]. Starzl comments that vitamin E absorption was reduced in his seven patients, the time point is not stated[66].

(c)D-Xylose Absorption

Grant's first patient had reduced urinary excretion of D-xylose at both 2 and 6 months post-transplant[57]. Starzl reports that D-xylose was "adequately" absorbed in his seven patients; at what time point these patients were studied is not clear[66].

(d)Specific Absorption

Grant's patient had a normal Schilling test at 8 months[57], while Starzl noted normal absorption of the immunosuppressant FK506[198].

Conclusion

The small number of successful transplants carried out to date appear to have normal global absorption of nutrients, with the exception of vitamin E and , probably, D-xylose. Information on specific absorptive function, such as for glucose and electrolytes, is lacking. Knowledge as to whether the transplanted intestine has similar absorptive ability length for length, when compared to non-transplanted gut, is also missing. It may also be expected that some nutritional deficiencies, such as vitamin A, will not appear until long term follow up has been conducted.

CHAPTER 2

DESIGN AND CONDUCT OF EXPERIMENT

Intestinal transplantation results in a graft with no extrinsic innervation and disrupted intrinsic innervation. It also has no lymphatic drainage. The purpose of this study is to assess the effect this has on small bowel absorption.

Studies were carried out both early and late, to assess any alteration in absorption due to spontaneous reconnection of lymphatic drainage, and also to assess whether any defects in absorption spontaneously correct with time.

Canine Model of Intestinal Autotransplantation

A model of small intestinal autotransplantation was used. This avoids the adverse influences of ischaemia with reperfusion since no vascular clamping or transection of blood vessels is required. Rejection cannot occur and immunosuppression is not required, thus excluding two further confounding factors present in previous absorption studies. It also maintains portal venous drainage of the small intestine.

The dog was chosen as the experimental subject since it is a large animal model with a small intestine which resembles human small bowel both in morphology and motility. In addition, dogs with a small bowel transplant have diarrhoea for several weeks post-operatively, suggesting a defect in absorption. This diarrhoea could be either steatorrhoea due to malabsorption of fat, or else a secretory diarrhoea due to loss of the "sympathetic brake" on intestinal secretion.

The jejunum and ileum were studied separately to determine whether any changes in intestinal absorption were global, or restricted to either segment. This resulted four groups of dogs:

(a)Group 1- jejunal control dogs

(b)Group 2- jejunal autotransplant dogs

(c)Group 3- ileal control dogs

(d)Group 4- ileal autotransplant dogs.

The "control" dogs simply had an 80cm Thiry-Vella loop created, while the "autotransplant" dogs had a similar loop formed after they had undergone the autotransplantation procedure.

All dogs were mongrel bitches, so as to exclude any breed-specific effects.

All dogs were looked after and operated upon according to the regulations of the Animal Care Committee of the Mayo Foundation, and fulfilling the requirements of the National Institutes of Health and the Public Health Service Policy on the humane use and care of laboratory animals.

(1)Operative Procedure

All dogs were fasted for at least 10 hours prior to surgery, having free access to water. Anaesthesia was induced with intravenous methohexital sodium (12.5mg/kg, "Brevital", Eli Lilly&Co., Indianapolis, Indiana) plus atropine sulphate (0.4mg), endotracheal intubation performed, and anaesthesia maintained with inhalational halothane and oxygen. An intramuscular dose of long-acting penicillin was administered ("Flo-cillin", Fort Dodge Laboratories Inc., Fort Dodge, Iowa), and dogs received an intravenous infusion of 1000-2000mls of 0.9% saline, depending on body weight and the length of the procedure.

(a)Autotransplantation Procedure

The abdomen was shaved, and prepared and draped in standard sterile fashion. A long midline incision was made, and the small bowel was mobilised by dividing the ligament of Treitz. The point of transection of the duodenum was chosen to be distal to the inferior pancreatico-duodenal artery, and the mesentery was divided in line between this point and the superior mesenteric artery and vein, the vessels of the intervening arterial arcades and their accompanying veins being ligated and divided. A point is chosen in the terminal ileum, within 4-8cm of the ileo-caecal valve, and the mesentery divided between the bowel wall and the superior mesenteric vessels. The thick investing sheath of neural fibres surrounding the superior mesenteric vessels is then divided, obvious lymphatics being ligated, and all small remaining fibres are gently teased away under optical magnification (x 2) as far proximally as the branch which becomes the inferior pancreatico-duodenal artery. This results in a 2cm length of artery and vein which has been completely stripped of adventitia (Figure 1, page 38). The duodenum is now divided, followed by the terminal ileum, at the points where the mesentery has been transected: this leaves the small bowel attached only by the walls of the superior

mesenteric vessels. Intestinal continuity is restored by end-to-end anastomosis in two layers, using an inner layer of catgut and an outer layer of polyglycolic acid ("Dexon", Davis&Geck), to both duodenum and ileum. To prevent internal hernias, the divided mesentery is apposed with a few sutures, and to prevent torsion of the entire jejunoileum around the narrow pedicle of the superior mesenteric vessels, the ligament of Treitz is resutured. The autotransplantation is now complete.

(b)Construction of Jejunal Thiry-Vella Loop.

This was carried out in the first two groups of dogs. Group 1 (n=9) served as jejunal controls and only had the jejunal Thiry-Vella (T-V) loop constructed. Group 2 (n=8) had the autotransplantation procedure carried out, followed by the construction of the jejunal T-V loop during the same operation.

The construction of the T-V loop is as follows; a point is chosen 20cm distal to the ligament of Treitz, here a 7cm strip of full-thickness bowel wall is excised along the antimesenteric side of the jejunum. The mucosa on the remaining 7cm by 2cm bridge of bowel wall is scraped off, leaving only the seromuscular layer attached to the mesentery (Figure 2, page 39).

A stainless steel cannula (Figure 3, page 40), now has it's flanged end inserted into the distal end of opened bowel, which is closed over the flange with a double purse-string suture of black silk (Figure 4, page 41). The other end of the metal cannula is brought out via a stab incision in the abdominal wall in the animal's left upper quadrant, the circular collar is then placed over the cannula and a screw tightened to hold it in place, a few millimetres away from the skin. A polypropylene plug closes off the external opening of the cannula. Within the abdomen, a "scarf" of omentum is loosely wrapped around the proximal part of the T-V loop, where the cannula enters the bowel, and is sutured in place. The purse-string sutures which close off the proximal end of the loop are used to place a couple of stitches to the inside of the abdominal wall, to further secure the cannula.

From this closed end of bowel, a length of 80cm is measured and the jejunum is completely transected at this point. The bowel on the proximal side of this transection is brought out on the right side of the abdominal wall, in the form of a raised spout; the stoma so produced is sutured in place. Gastrointestinal continuity is restored by anastomosis of the proximal jejunum to the more distal jejunum in standard two layer fashion, the T-V loop remaining attached to the proximal jejunum by the seromuscular bridge (Figure 5, page 42).

The end result is pictured diagrammatically in Figure 6 (page 43).

(c)Construction of Ileal Thiry-Vella Loop

This was carried out in the remaining two groups of dogs. Group 3 (n=6) simply had an ileal T-V loop constructed and served as neurally intact ileal controls, while Group 4 (n=8) dogs had the autotransplantation procedure and formation of an ileal T-V loop.

To form the ileal T-V loop, the terminal ileum is transected 10cm proximal to the ileocaecal valve, 80cm of ileum is measured out proximal to this, and the seromuscular bridge is formed at this point (Figure 7, page 44). In the Group 4 dogs, the ileal transection point for the autotransplantation procedure was also used as the distal point of the T-V loop, this prevented two suture lines in close proximity. Insertion of the cannula and stoma formation, with restoration of gastrointestinal tract continuity is carried out in similar fashion to the jejunal dogs.

The abdomen was closed by mass suture of the fascia with Dexon and subcuticular Dexon to skin.

Validation of the Model

This model of intestinal transplantation has previously been used to study both motility and absorption. The migrating myoelectric complex (MMC) in the autotransplanted intestine becomes more irregular, and cycles independently of the MMC in the non-transplanted proximal duodenum[199]. This continues to be the case for at least 8 weeks, but after 12 weeks there is a gradual return to coordination of the MMC between the two areas[200].

The seromuscular bridge allows the MMC to pass in to the TV loop, keeping it's fasting motility coordinated with the adjacent incontinuity bowel, and preventing the slower cycling rate which would develope in a completely isolated TV loop[201].

Total extrinsic denervation in this model has been proved by the precipitous decrease in the concentrations of norepinephrine and dopamine in the jejunal wall of the autotransplants, compared to controls, for up to 4 months[202]. The only adrenergic innervation to the gut occurs from extrinsic autonomic innervation: thus tissue concentrations of catecholamines serve as markers of extrinsic innervation. This has also been shown in rats, in isografts where the vessels have been transected, and the low levels of dopamine and tyrosine persisted until the study ended at 100 days[203]. Surgical sympathectomy in rats reduces the catecholamine levels in the bowel wall by 90%[74].

Piglets who underwent a jejunal autotransplantation, again with division and reanastomosis of the vessels, were found to have complete absence of adrenergic nerves within the bowel wall for the entire 4 months of the study[204]. This shows that reinnervation of the bowel by the extrinsic nerves does not occur within the time-frame of this study.

Peptidergic nerves of the enteric nervous system remain unchanged after small intestinal transplantation[203-205]. This indicates that the intrinsic nerves themselves are unaltered by the autotransplantation procedure.

Thiry-Vella Loop

A T-V loop was chosen as the method of studying absorption. Use of a T-V loop gives the investigator complete control over the contents of the loop, without the problem of endogenous pancreatico-biliary secretions. It also allows the same exact length of intestine to be perfused repeatedly. It is a simple and easily reproducible method of performing absorption studies.

In contrast, absorption studies in humans require either double or triple lumen tubes, which have disadvantages. Endogenous secretions delivered into the test segment at irregular intervals can either be ignored by a simple double lumen tube technique[206], or a proximal balloon used[207]. Fordtran, in 1966, described his triple lumen tube technique in order to take the endogenous secretions in to account[208]. This was used by other authors[209], and gained favour over double lumen tubes[210].

The mixing segment itself produces the problem that some absorption of the test solution will occur there, before reaching the test segment[211]. In addition, reflux proximally from the infusion point will lengthen the available surface for absorption, something which the double lumen tubes cannot take in to account, and which in triple lumen tubes, will effectively lengthen the mixing segment[212,213].

Lastly, the problem that bowel may telescope over a tube has been recognised[211], and one study has shown that this may result in a threefold increase in the length of bowel being perfused[214].

(1)Absorption Studies

A solution is perfused via the proximal end of the loop and effluent collected from the distal end of the loop. This effluent is then analysed and compared to the original infusate. Whatever is missing from the effluent must have been actively or passively

absorbed , or else retained within the loop. Conversely, anything in the effluent which was not in the infusate must have been secreted by the loop.

(2)The Question of Loop Atrophy

It is known that food within the gastrointestinal tract maintains normal mucosal morphology, and intravenous feeding results in the same degree of mucosal atrophy as does fasting[215]. It remains controversial whether it is intraluminal nutrition itself, or it's stimulating effect on the trophic gastrointestinal tract hormones, cholecystokinin and secretin, which is responsible for the maintenance of normal mucosa[216,217].

It would seem logical that a T-V loop, isolated from luminal nutrients may exhibit some mucosal changes over a period of time. This question of atrophy of the mucosa of the loop with time is a vexed one, and appears to be species dependent. Marked changes occur in the rat, with reduced villus height and crypt depth evident as early as 3 weeks following isolation from the intestinal stream[218-221].

Functionally, jejunal loops only showed decreased glucose absorption after 10 weeks, and glucose absorption from ileal loops remained unchanged even after 6 months[222]. Amino acid and peptide absorption are reduced in jejunal loops at 6 weeks, but no further reduction is seen at 12 weeks[223]. This suggests that absorption may decrease slowly with time, but only to a baseline beyond which it will not decline further. The fact that ileal loops show no decline may be due to absorption here being normally at baseline, due to the fact that most ingested nutrients are normally absorbed upstream, by the very efficient absorptive capacity of the jejunum.

Ground squirrels also exhibit atrophy in bypassed segments, although absorption is actually increased when measured in relation to mucosal weight[224]. This finding has also been made in the rat[218]. This is due to the cells in a bypassed segment being more mature, with fully developed enzyme systems, since cell turnover is reduced.

Jejunoileal bypass in baboons results in villus atrophy and slightly decreased absorption of an electrolyte solution at 3 months[225]. In those other primates, humans, the situation appears to be different. Jejunoileal bypass for morbid obesity provides a unique opportunity to study an excluded, but otherwise normal, section of small intestine. In 6 patients, at between 11-39 months following bypass, villus heights in both jejunum and ileum in the bypassed segments remained almost identical to pre-bypass levels, with the specific activities of mucosal disaccharidases being slightly elevated[226]. This finding has been confirmed by others[227,228]. The atrophy which is commonly found in ileal conduits is most likely due to the effects of urine on small bowel mucosa[229].

The situation in dogs is not entirely clear, one group found no histological or functional change in defunctioned loops over 5 years[230]! No histological change was observed in a 6 month period[231], while it has been noted that loops gave reproducible absorption over a 3 month period[105]. This has not been a universal finding; ileal loops were found to have a decrease in villus height and crypt depth only one week after being defunctioned, but this did not progress over the subsequent 10 weeks[232]. Further studies have shown a progressive hypoplasia, when loops have been looked at at 12 and 30 weeks, with a matching decrease in absorption of galactose and leucine[233]. The most recent study looked at brush-border membrane vesicles in a jejunal loop excluded from luminal nutrition for 6 months, but still exposed to pancreatico-biliary secretions. They found that active transport of glutamine, alanine and glucose was decreased[234].

Conclusion

These varied results suggest that major loop atrophy does not occur in the dog, and any changes which do occur are minor and only likely to be evident after 3 months. In this study, dogs were only studied up until 10 weeks after creation of the loop. All the studies were therefore finished before any significant changes in the loop would be expected to occur. Any minor alterations in mucosal function as a consequence of the loop being out of the main gastrointestinal stream, are assumed to occur equally in both the neurally intact (Groups 1 and 3) and the autotransplanted (Groups 2 and 4) dogs. This allows valid comparisons to be made between the groups.

(3)Histological Examination

In order to answer the question of whether atrophy occurred within the Thiry-Vella loops of the dogs participating in this experiment, a histological study was carried out.

Tissue for morphology and morphometrics was taken at the time of creation of the T-V loops in all four groups of dogs. This comprised a full thickness biopsy of bowel wall taken from the site where the seromuscular bridge was made. After sacrifice, a full thickness biopsy was taken from the mid-point of the T-V loop. The bowel wall was immediately pinned out on a board and immersed in formalin. It was later sectioned and stained with haematoxylin and eosin and examined under a light microscope, using an optical micrometer to measure villus height and crypt depth. A further sample was taken at post-mortem from the bowel which had remained in continuity.

Test Solutions

These solutions were chosen to test several different absorption pathways. A 150mM saline solution was used to assess sodium absorption. The addition of glucose was used to assess glucose-facilitated sodium absorption, as well as the active transport of glucose. Amino acid absorption is also an active process, two different amino acids, each absorbed on a different carrier system were evaluated. Lastly, a long chain fatty acid, which is absorbed via the lymphatic system was used, bile salts being added to emulsify it in micellar form for absorption.

A total of five separate test solutions were used:-

(1) 150mM sodium chloride

(2) 135mM sodium chloride and 30mM glucose

(3) 150mM sodium chloride and 2.5mM glycine

(4) 150mM sodium chloride and 2.5mM phenylalanine

(5) 135mM sodium chloride,10mM bile salts and 5mM oleic acid

All of the solutions were adjusted to a pH of 7 and contained 5g/L polyethylene glycol (PEG, Polyethylene Glycol 3350 Powder, Fisher Scientific, New Jersey) plus 3H PEG, 10mCi/L (New England Nuclear, Wilmington, Washington D.C.).

PEG has been shown to be an accurate non-absorbable marker in intestinal perfusion studies[235-237], and radiolabelled PEG gives comparable results to measurement of "cold" PEG by the turbidimetric method[238,239]. PEG recovery allows the demonstration of steady state conditions to be made, a prerequisite of valid absorption studies. The concentration of 5g/L is standard, greater concentrations resulting in an inhibition of absorption[240].

14C-glycine, 14C-phenylalanine and 14C-oleic acid (all obtained from Amersham Corp., Arlington Heights, Illinois) were added as markers to solutions 3, 4 and 5 respectively, at 5mCi/L.

All five solutions were isosmolar, since osmolarity is known to affect absorption[241].

Flow rates also influence absorption[242,243], a rate of 3ml/min delivered at a constant rate by a roller pump, was used. Physiological flow rates in human small intestine are believed to be 5ml/min[213].

The solutions were all heated to, and kept at, a canine body temperature of 38^{0}C.

Conduct of Experiment

The dogs were allowed one week to recover from surgery. This allowed sufficient time for them to be drinking and eating normally so the assumption could be made that they were all in a baseline, normally hydrated state. Studying the dogs any earlier would have caused them distress from wound pain and normal hydration could not be assured since the autotransplanted dogs often required parenteral fluids for the first five or six days post-operatively as they were not inclined to drink sufficiently to compensate for the torrential diarrhoea. The dogs were all fasted for 12 hours prior to the commencement of the day's experiments, but had free access to water.

All experiments were carried out with the dogs standing quietly in a Pavlov sling (Figure 8, page 45). The polypropylene plug was removed from the cannula, and a stainless steel inner cannula with a rubber O-ring to ensure a snug fit, inserted (Figure 9, page 46).

The loop was then flushed with warmed 150mM sodium chloride to clear mucoid debris, prior to commencement of perfusion of the test solution.

Each test solution was infused over a period of three hours, the effluent being collected volumetrically from the stoma (Figure 10, page 47). Effluent was collected in aliquots every 15 minutes, apart from at 60 and 120 mins when transit studies were being carried out.

The transit markers used were phenol red sodium salt (PSP. Fisher Scientific, Fair Lawn, New Jersey) for solutions 3, 4 and 5, and 14C-PEG for solutions 1 and 2. PSP is also a non-absorbable marker[244]. Both were administered as a 0.5ml bolus, and effluent collected every 3 mins for the next 15 mins. The time taken for 50% of the marker to traverse the loop was taken as being the mean transit time. This reflects the flow rate within the loop, which, in turn, influences absorption[245].

At the end of each three hour experiment, the loop was flushed with 100ml of warm saline to clear any residual radioactive perfusate. At least one hour was allowed to elapse before the loop was again flushed prior to starting the next experiment. Each dog had two experiments carried out per day, and experiments were carried out on ten consecutive days, starting at Week 1, and then repeated in the same order at Week 8.

For the first six days, the NaCl, NaCl + glucose, and the two amino acid solutions were each perfused on three occasions, in random order to prevent any potential sequencing

or holdover effects. The NaCl and the fat solutions were each perfused on four occasions, in alternating order, for the last four days. Figure 11 (page 48) illustrates the overall time-scale of the study, and also shows one of the four random perfusion schedules.

Each dog, therefore, had twenty, three hour perfusion experiments carried out starting at Week 1 post-operatively, and repeated at Week 8.

Analysis of Samples

Radioactivity was measured in each sample, after addition of liquid scintillation fluid, in a scintillation counter (Beckman LS 7800, Beckman Instruments, Fullerton, California). Sodium and potassium were measured by flame photometry (Beckman Klina Flame), and chloride concentration by a chloride electrode (Corning 920M Chloride Meter, Corning Scientific Instruments, Medfield, Massachusetts).

Glucose was measured using a quantitative enzyme assay (Glucose[HK], Sigma Diagnostics, St.Louis, Missouri). PSP was measured colorimetrically, after precipitation of protein.

Each three hour experiment was assessed for validity by measuring PEG recovery after a steady state had been achieved. A steady state is reached when all the saline which was used to flush the loop has been replaced with the test solution. At this time the PEG recovery per 15 min period reaches 85% or more. This state was typically reached by 30 mins in the vast majority of dogs, and by 45 mins in the rest. All samples prior to achievement of the steady state were discarded, and the samples taken for the transit time (every 3 mins for 15 mins after hour 1 and 2) were used only to assess transit time, and not used to assess absorption. This resulted in each experiment producing nine samples to be assessed for absorption, the mean of these samples was taken to be the absorption for that study. These mean values for each study and the mean value of these means are shown in the tables which accompany each results chapter. All experiments with a PEG recovery outwith the range 85-115% were discarded.

MODEL OF JEJUNOILEAL AUTOTRANSPLANTATION

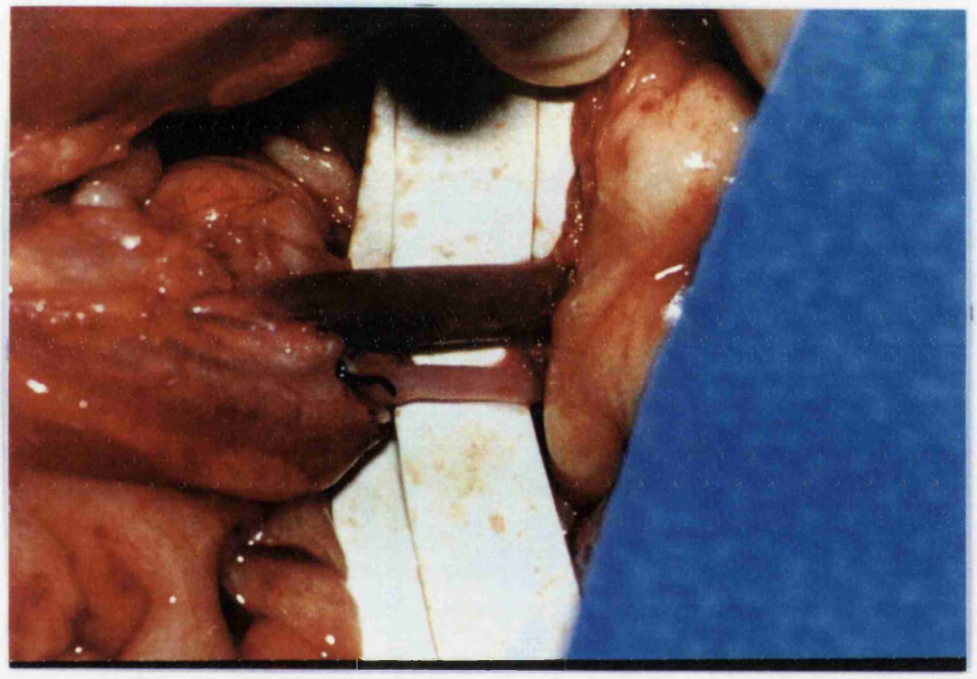


FIGURE 1

SUPERIOR MESENTERIC VEIN AND ARTERY STRIPPED OF ADVENTITIA

MODEL OF JEJUNOILEAL AUTOTRANSPLANTATION

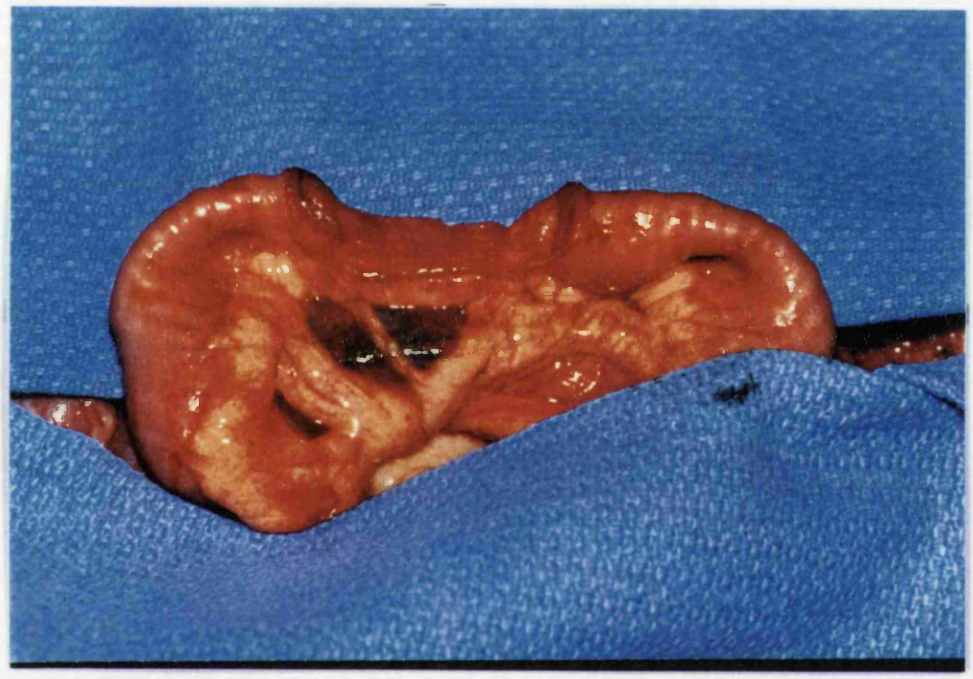


FIGURE 2

THE SEROMUSCULAR BRIDGE JOINING THE MODIFIED THIRY-VELLA LOOP TO THE PROXIMAL SMALL INTESTINE

MODEL OF JEJUNOILEAL AUTOTRANSPLANTATION

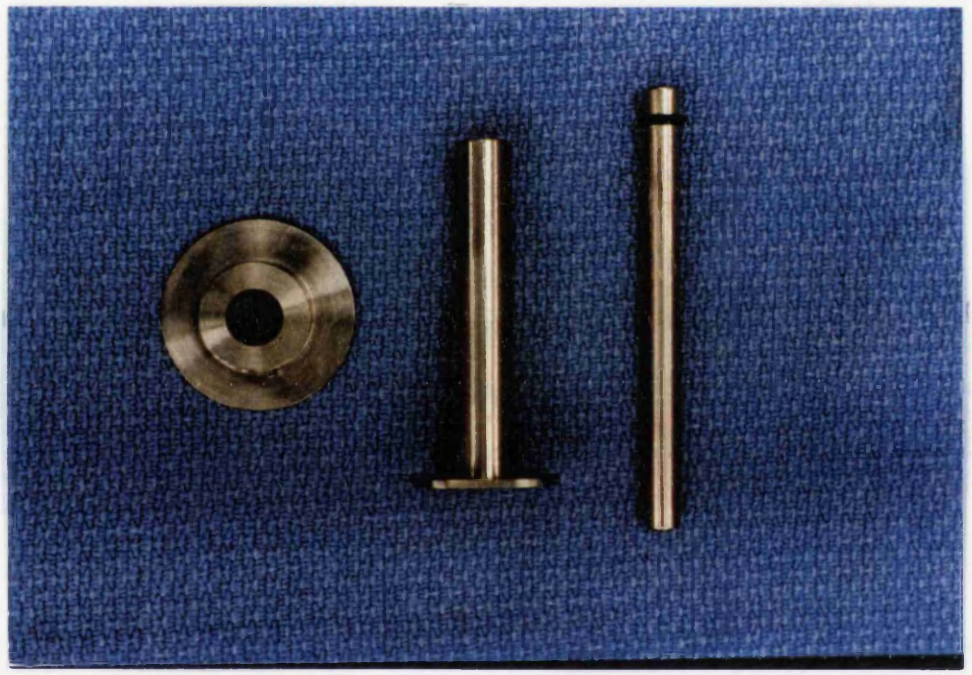


FIGURE 3

STAINLESS STEEL CANNULA FOR INSERTION INTO PROXIMAL END OF THE MODIFIED THIRY-VELLA LOOP

MODEL OF JEJUNOILEAL AUTOTRANSPLANTATION

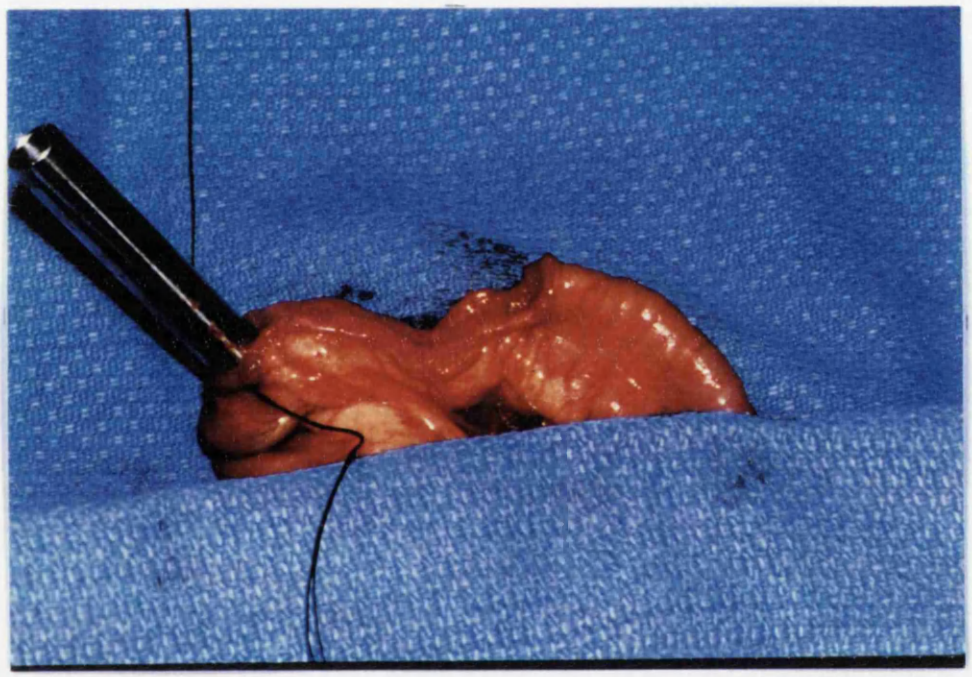
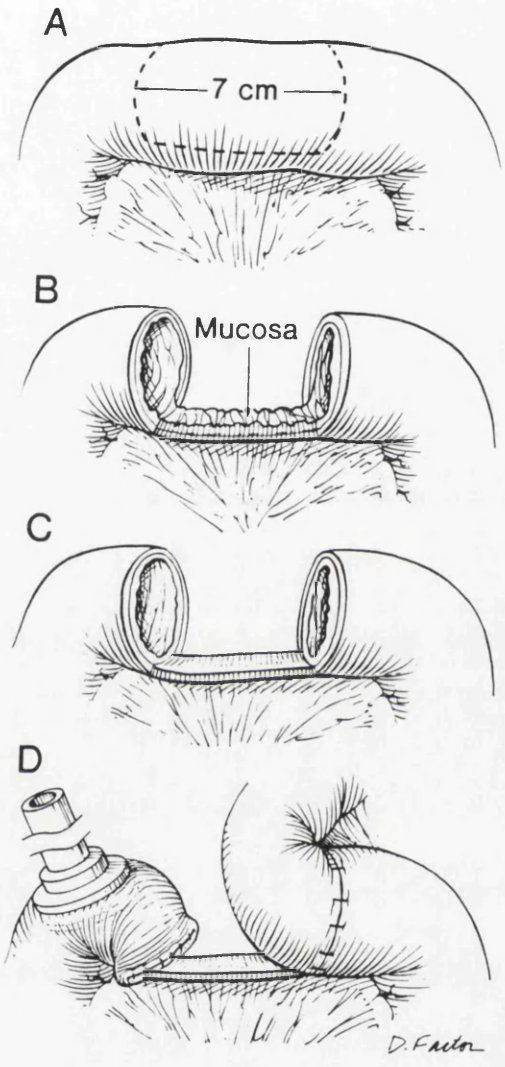


FIGURE 4

CANNULA INSERTED INTO PROXIMAL END OF MODIFIED THIRY-VELLA LOOP

MODEL OF JEJUNOILEAL AUTOTRANSPLANTATION



A : 7cm length of antimesenteric side of small bowel to be excised.

B : area excised, bowel wall on mesenteric side left intact as a bridge.

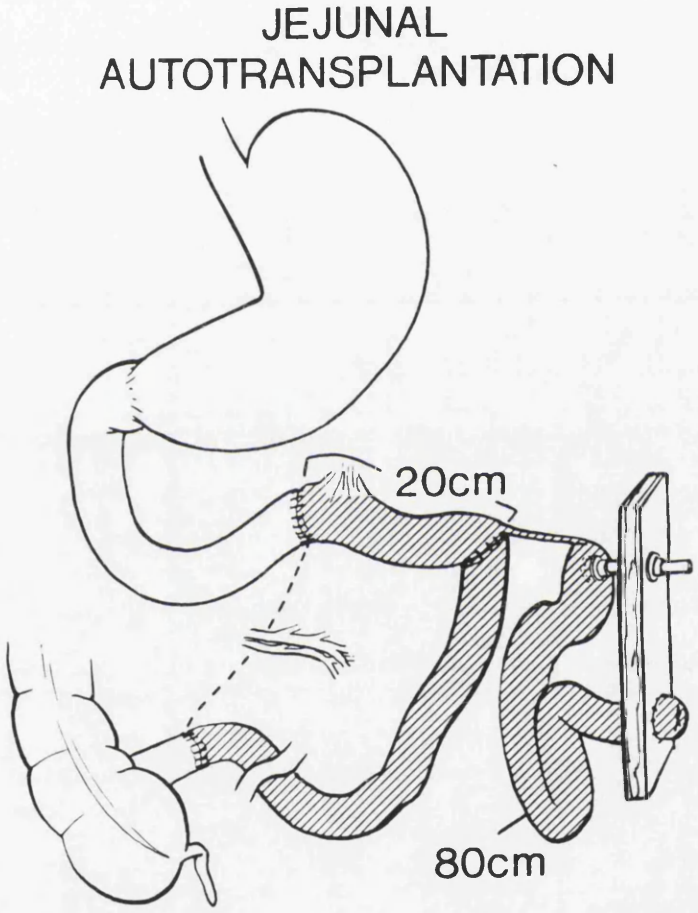
C : mucosa stripped from bridge.

D : bowel continuity restored, cannula in proximal end of loop.

FIGURE 5

FORMATION OF THE SEROMUSCULAR BRIDGE

MODEL OF JEJUNOILEAL AUTOTRANSPLANTATION

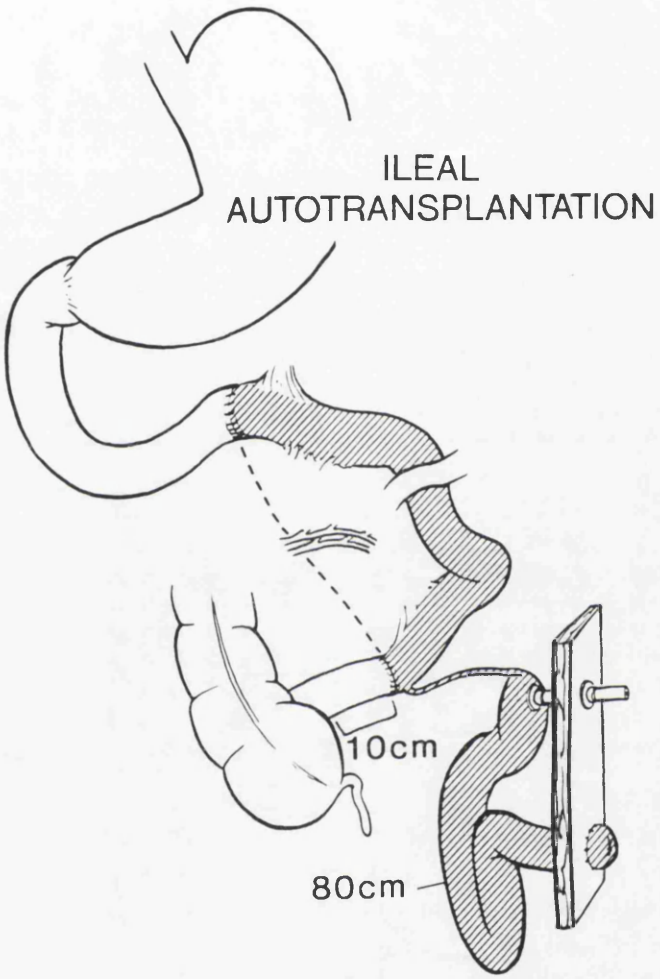


Cross-hatched areas represent bowel which has been denervated.

FIGURE 6

MODIFIED THIRY-VELLA LOOP OF JEJUNUM FOLLOWING "AUTOTRANSPLANTATION"

MODEL OF JEJUNOILEAL AUTOTRANSPLANTATION



Cross-hatched areas represent bowel which has been denervated.

FIGURE 7

MODIFIED THIRY-VELLA LOOP OF ILEUM FOLLOWING "AUTOTRANSPLANTATION"

CONDUCT OF EXPERIMENT

FIGURE 8

SUBJECT UNDERGOING EXPERIMENT

CONDUCT OF EXPERIMENT

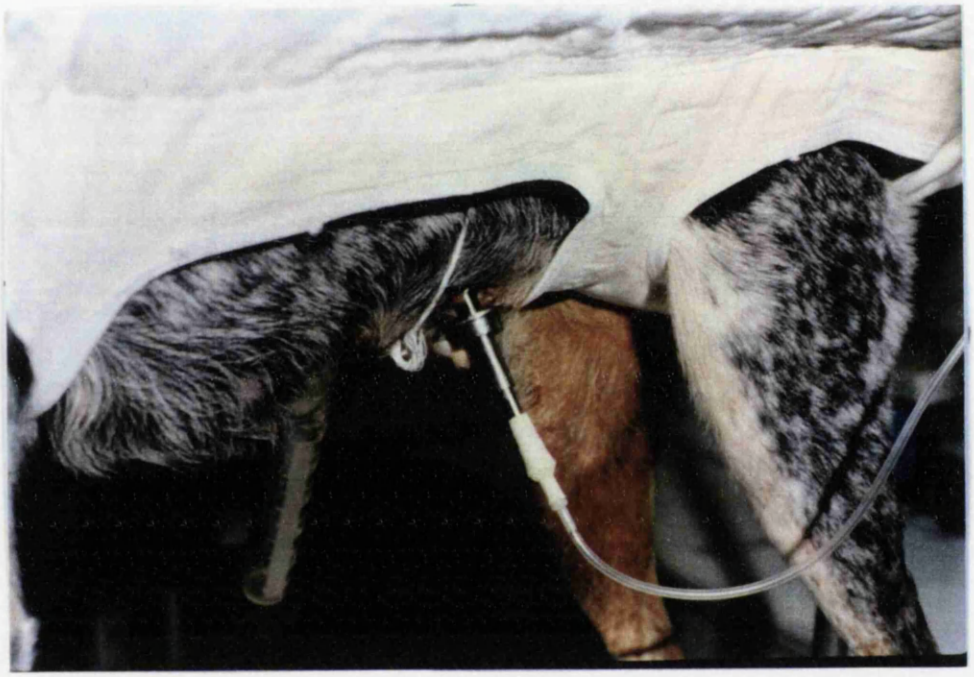


FIGURE 9

PERFUSION CANNULA WITH INFUSION PIECE *IN SITU* DURING EXPERIMENT

CONDUCT OF EXPERIMENT

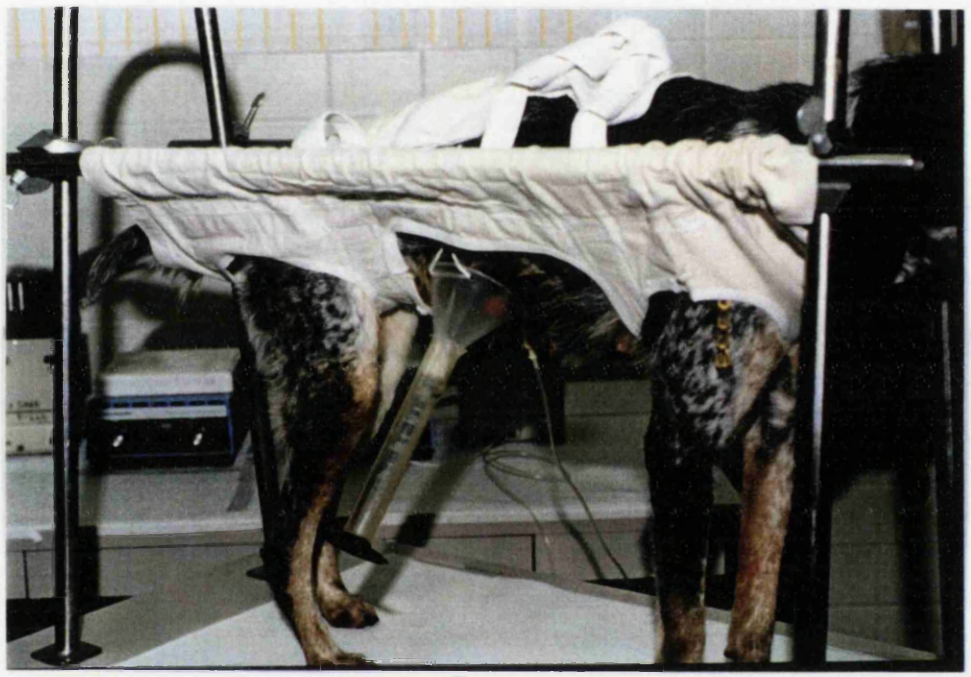
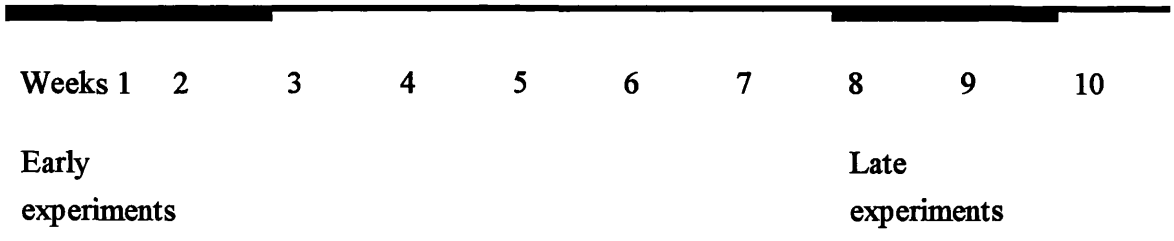


FIGURE 10

COLLECTION OF LOOP EFFLUENT FROM DISTAL STOMA

EXPERIMENTAL DESIGN



Day	Morning	Afternoon
1	NaCl	Glucose
2	NaCl	Phenylalanine
3	Glucose	Glycine
4	Phenylalanine	NaCl
5	Glycine	Glucose
6	Phenylalanine	Glycine
7	NaCl	Fat
8	Fat	NaCl
9	NaCl	Fat
10	Fat	NaCl

FIGURE 11

SCHEDULE OF EXPERIMENTS (EARLY AND LATE)

CHAPTER 3

ANIMAL HEALTH AND COMPLICATIONS

All dogs were allowed a few days to settle in to the kennels prior to their random allocation to control or autotransplant group. A baseline weight was recorded and the dogs had free access to food and water until 12 hours before surgery.

The operative procedure took approximately one hour for the control animals, and three hours for those having the model of small intestinal autotransplantation. No animal died intraoperatively.

Mortality

A total of five dogs died in the early post-operative period, before they could be allocated a study number; all were autotransplants. One had an anastomotic leak at the site of the duodenal transection, one had a small bowel obstruction at multiple sites and another died of pneumonia. These three dogs had had jejunal loops fashioned. The other two dogs were to have been ileal autotransplants, one infarcted the terminal ileum between the transection line and the caecum, and the other ripped at the stoma with her teeth and succeeded in avulsing the entire T-V loop and had to be sacrificed.

Post-operative Care

The control dogs (Groups 1 and 3) recovered very quickly from their operation, usually requiring parenteral fluid given by the subcutaneous route only on the first post-operative day. Thereafter normal oral fluids and food was readily consumed.

The autotransplanted dogs (Groups 2 and 4), by contrast usually required subcutaneous fluid to be administered for three to four days, after which they were inclined to drink but were disinclined to eat for an additional 48 hours.

All dogs had free access to water at all times and were fed standard dry dog food except during the two week study period. Whilst being studied, to ensure a 12 hour overnight fast, the dogs were given canned dog food (Hill's Prescription Diet Canine i/d, Hill's Pet Products, Topeka, Kansas) immediately after the day's studies were completed. This was

usually instantly eaten, but on the few occasions when it was not, the food was removed from the dog's cage after two hours.

All autotransplanted dogs developed a profuse watery diarrhoea, often explosive in nature, within 48 hours of surgery. Neither mucus nor blood was noted in the diarrhoea. This diarrhoea was a constant feature in all autotransplanted dogs for the first two weeks after surgery, with no solid stools being passed. After this time the diarrhoea became less watery, and some dogs occasionally passed formed stools. After four weeks most autotransplanted dogs had soft but formed stools, but would still have daily episodes of diarrhoea, particularly after being fed. This diarrhoea did not distress the dogs, nor did it affect their eating habits after they had recovered from their initial surgery. These dogs spontaneously drank more water than the control dogs, in compensation for their increased fluid loss.

Weight

All dogs were weighed before operation, and on a weekly basis throughout the study. The two dogs who were found to be pregnant at the time of surgery had a hysterectomy carried out and hence their weight loss appears greatest. All the dogs, with the exception of one animal in each of Groups 3 and 4, initially lost weight over the first two post-operative weeks. Average weight loss was around 1-1.5kg, which represents approximately 8% of the total body weight. There was then a tendency to regain weight, but the original weight was only regained in two of five jejunal control dogs, one out of seven jejunal autotransplants, four of six ileal control dogs, and three of six ileal autotransplants. None of the jejunal dogs overshot their original weight, but several of the ileal dogs did so. Dog weights are shown in Table 3.1 (page 54).

Stomal Problems

The stoma was a major problems with these dogs. Self-induced trauma occurred on several occasions; Dog 1F tore at the stoma with her teeth and ripped out the entire T-V loop after Day 8 of the early experiments, and was sacrificed as a result. Dog 4F scratched the stoma flush with the skin and, at a laparotomy to assess the extent of the damage, was found to have only 10cm of the original 80cm loop remaining. She was therefore sacrificed, and no late experiments performed. Dogs 1A and 4H both bit their stomas flush with the skin, where they healed satisfactorily, allowing experiments to continue. The only prolapsed stoma occurred in Dog 1A: she developed a 10cm prolapse of the jejunostomy, which was irreducible and had to be sacrificed.

In order to attempt to prevent this self-induced injury, all dogs were fitted with an "Elizabethan collar" (Saf-T-Shield, EJay international Inc., Glendora, California), which consisted of a large polyethylene collar placed around the neck and secured with stud-fasteners. These collars were notoriously difficult to keep in place and were used only for the first two weeks after the stoma had been fashioned, since most dogs tolerated the stoma by then. Dogs who exhibited an interest in damaging their stoma with their teeth, once a collar was fitted, succeeded in traumatising it by vigorous scratching with a hind paw. This behaviour applied to Dogs 1H, 2G and 3F, and was unable to be stopped.

Another problem was stomal stenosis, at the level of the fascia; this was easily dealt with by local incision under a short general anaesthetic, and occurred in nine of the dogs (2G, 2H, 3A, 3D, 3F, 4C, 4D, 4E, and 4G). Prior to the stenosis developing, two of these dogs had a small peristomal abscess which required draining.

Cannula Problems

The other main problem with the model was the stainless steel cannula. A total of six dogs had the cannula extrude from the loop; this resulted in 1C missing the early studies and 2G missing the last half of the late study. Dog 4C missed the entire late study when laparotomy to replace the cannula revealed an abdomen so solid with adhesions that the dog had to be sacrificed. In addition, 2F died of aspiration pneumonia following an operation to replace the cannula which came out within the first few days of the early studies. Dogs 3E and 4B both had their cannulas uneventfully replaced. The cannula extrusion was associated with an abscess at the skin exit site in three dogs, while another three dogs had cannula site abscesses which required local drainage.

Dogs 1C and 2F were technical failures since the flanged end of the cannula slipped out of the proximal end of the loop within the first few experiments, this was detected by perfusate entering the loop but failing to emerge from the stoma. In the other four dogs the cannula coming out was secondary to local abscess formation, with weakening of the abdominal wall.

One further dog, 1D, managed to work the external collar off the cannula during the night, peristalsis moved the flanged end along the entire loop and it impacted just deep to the abdominal wall at the stomal end. An enterotomy was required to extract it from the loop, and the dog missed the early experiments.

Fistula Formation

Three dogs developed a fistula via the seromuscular bridge; this was readily detected by bile-stained fluid emerging from the stoma. Dog 1B had the mucosa of the bridge stripped again, and the defects in the walls of the bowel oversewn. This fistula rapidly recurred and the dog was sacrificed, missing the late experiments. When Dog 1D developed a similar fistula, it was sacrificed and also missed the late experiments. Until this point in the study a 5cm seromuscular bridge was used; after these fistulas, it was elongated to 7cm and only one more fistula occurred, in 2G, which was successfully treated by reoperation.

The only other morbidity was an anastomotic leak from the duodenal suture line in Dog 2C which required relaparotomy, this dog was ill for several days after the second operation, and missed the early experiments.

Jejunal Dogs

The jejunal experiments which were carried out are listed in Table 3.2 (page 55). NaCl/AA/Glu refers to the first six days of the study period, while NaCl/Fat refers to the last four days. Dogs 1A and 2A had a fat solution containing 10mM oleic acid perfused in their early studies, this induced a profuse net secretion of fluid and mucus. The concentration of oleic acid was thereafter reduced to 5mM for the remainder of the study. Those experiments with the higher concentration of oleic acid were deleted from the analysis of results.

Only four of the jejunal control dogs (Group 1) completed all their studies, a further four completed part or all of the early studies but missed all the late studies, and one missed all the early studies but completed all of the late studies.

The jejunal autotransplanted dogs (Group 2) similarly had four dogs which completed all the studies, another two which completed part or all of the early studies, and a further three who completed part or all of the late studies.

Ileal Dogs

The ileal experiments are listed in Table 3.3 (page 56). The ileal control dogs (Group 3) have the distinction of being the only group to have all six dogs complete all early and late experiments.

The ileal autotransplant dogs (Group 4) had five dogs which completed all experiments, another two who completed the early experiments, and a final dog who completed only the late experiments.

Summary

A total of thirty-six dogs were operated on, with five dying within the first post-operative week, two from technical complications (anastomotic leak, infarcted terminal ileum), two from post-operative problems (small bowel obstruction, pneumonia) and one from a self-induced injury (avulsed the T-V loop).

Only eleven of thirty-one dogs (1E, 1G, 1H, 1I, 2A, 2B, 2D, 2E, 3B, 3C, 4A) succeeded in having only the original surgical procedure carried out; all the others required further procedures either on the stoma, the cannula site, or for complications.

All dogs were sacrificed within a week of completion of the late experiments, eleven weeks after the original operation.

ANIMAL HEALTH AND COMPLICATIONS

Dog	Pre-op Weight (Kg)	Lowest Weight (Kg)	Final Weight (Kg)
1A	15.0	14.2	-----
1B	15.6	13.5	-----
1C	16.5	14.2	14.5
1D	15.8(pregnant)	13.0	-----
1E	12.0	11.0	11.5
1F	16.5	14.0	-----
1G	10.0	9.0	10.0
1H	14.0	13.0	14.2
1I	16.6	14.5	14.5
2A	16.0	14.0	15.0
2B	15.0	12.0	13.5
2C	14.6(pregnant)	9.5	11.0
2D	15.0	12.5	15.0
2E	9.0	7.5	8.0
2F	11.0	-----	-----
2G	10.8	8.5	8.5
2H	14.7	11.4	12.5
3A	9.8	9.0	9.0
3B	11.2	11.0	12.0
3C	14.8	13.0	13.5
3D	11.8	11.0	12.0
3E	12.2	12.0	14.5
3F	9.0	9.0	12.0
4A	9.0	8.0	8.5
4B	12.0	10.0	10.0
4C	13.0	11.0	-----
4D	13.4	13.4	14.0
4E	15.0	13.0	16.5
4F	13.8	12.5	-----
4G	14.5	13.0	17.0
4H	16.0	13.0	14.5

TABLE 3.1 : DOG WEIGHTS

JEJUNAL EXPERIMENTS

CONTROLS				
	WEEK 1		WEEK 8	
DOG	NaCl/AA/Glu	NaCl/Fat	NaCl/AA/Glu	NaCl/Fat
1A	yes	no	no	no
1B	yes	yes	no	no
1C	no	no	yes	yes
1D	yes	no	no	no
1E	yes	yes	yes	yes
1F	yes	no	no	no
1G	yes	yes	yes	yes
1H	yes	yes	yes	yes
1I	yes	yes	yes	yes
AUTOTRANSPLANTS				
2A	yes	no	yes	yes
2B	yes	yes	yes	yes
2C	no	no	yes	yes
2D	yes	yes	yes	yes
2E	yes	yes	yes	yes
2F	no	no	no	no
2G	yes	yes	yes	no
2H	yes	yes	yes	yes

NaCl = sodium chloride
AA = amino acids
Glu = glucose
Fat = oleic acid

TABLE 3.2 : EXPERIMENTS SUCCESSFULLY COMPLETED

ILEAL EXPERIMENTS

CONTROLS				
	WEEK 1		WEEK 8	
DOG	NaCl/AA/Glu	NaCl/Fat	NaCl/AA/Glu	NaCl/Fat
3A	yes	yes	yes	yes
3B	yes	yes	yes	yes
3C	yes	yes	yes	yes
3D	yes	yes	yes	yes
3E	yes	yes	yes	yes
3F	yes	yes	yes	yes
AUTOTRANSPLANTS				
4A	yes	yes	yes	yes
4B	yes	yes	yes	yes
4C	yes	yes	no	no
4D	yes	yes	yes	yes
4E	yes	yes	yes	yes
4F	yes	yes	no	no
4G	yes	yes	yes	yes
4H	no	no	yes	yes

NaCl = sodium chloride
AA = amino acids
Glu = glucose
Fat = oleic acid

TABLE 3.3 : EXPERIMENTS SUCCESSFULLY COMPLETED

CHAPTER 4

STATISTICS

BACKGROUND

The null hypothesis which has been tested by this study is: "autotransplantation of the small bowel produces no change in absorption of simple nutrient solutions".

This global statement was explored in greater depth by assessing several different aspects of absorption in further detail:

1. Does this model of small bowel autotransplantation produce any change in absorption of any of the 5 test solutions?

2. Does any change in absorption occur in both jejunum and ileum?

3. Do any absorptive changes which occur vary with time after autotransplantation?

The data produced by this study is complex and of considerable volume. The large number of experiments performed generated over 23 000 samples of stomal effluent for analysis. The complexity exists not only due to the substantial number of variables assessed, but also due to the death of some dogs prior to completion of their experiments, and the deletion of some experiments from further analysis because of poor PEG recovery.

The missing values and the studying of the same animal at different time points precluded the use of standard analysis of variance methods and required expert handling of the results and interpretation of the statistical data.

Advice was sought from the Department of Statistics at the University of Leeds and the statistical analysis has been carried out in conjunction with them.

THE EXPERIMENTAL DATA

The data produced by these experiments falls in to several categories:

Intestinal Site

Two different sites of absorption were studied; jejunum and ileum. This results in two comparisons being made: firstly, the comparison of a control jejunal group (Group 1) against an autotransplanted jejunal group (Group 2) and, secondly, the comparison of a control ileal group (Group 3) against an autotransplanted ileal group (Group 4). As previously described, these four groups each contain up to nine dogs.

Time

Two separate time points were looked at. The early experiments were conducted at Week 1 and Week 2 post-operatively and the late experiments were a repeat of the earlier experiments conducted six weeks later, at Week 8 and Week 9 post-operatively.

Solutions

The series of experiments carried out involved five different test solutions. For each solution each experiment was repeated in random order on up to four occasions at Week 1 and/or Week 2, and then again at Week 8 and/or Week 9. Hence up to twenty experiments were conducted on each dog at the early time point, and repeated again at the late time point.

Experimental Samples

Each 3 hour experiment produced twenty samples. The first two samples, taken 15 and 30 minutes after the start of infusion of the test solution were discarded, as the experiment had not achieved a steady state at that point (as shown by PEG recovery). The five samples taken at 3 minute intervals at 60 and 120 minutes, respectively, were used solely for determining transit time. This leaves eight measurements of volume, sodium, chloride, and potassium per experiment plus either glucose, glycine, phenylalanine or oleic acid for their respective solutions. These eight measurements out of each 3 hour experiment were averaged, giving a single mean value per experiment. These mean values are shown in the tables at the end of each of the results chapters.

Statistical Structure of Experimental Data

The structure of the data consists of dogs within each treatment group (nested cases), experiments conducted at different weeks (a repeated measure), and multiple values for each Dog x Week combination (nested replicates).

The number of dogs in each study group is different, and may differ within the same group between the early and late experiments, due to the loss of a few dogs. For the same reason, plus the loss of some experiments due to poor PEG recovery, there are also a variable number of experiments in each Dog x Week combination and some totally absent values for some Dog x Week combinations. The uneven numbers of experiments within and between experimental groups results in this study being described in statistical terms as having an extremely non-orthogonal data structure.

THE STATISTICAL ANALYSIS

ANALYSIS OF VARIANCE

A one-way analysis of variance of dog against replicates for each experiment, week, test solution and criterion (e.g. volume, sodium etc.) showed the residual error variances were similar throughout treatment groups and weeks within each experiment. This means that experimental variability on a day to day basis remained fairly evenly spread in all four groups at all time points.

Both ileal groups of dogs had larger residual error variances than the jejunal dogs, indicating a greater experimental variability in experiments carried out in the ileum.

Frequently the variation among cases within a treatment was significantly greater than the residual error variance. This is due to experimental variability in some groups being greater than the baseline variability seen in all the experiments (the ERROR) and this had to be taken in to account statistically, as will be explained further in the following description of analysis of variance tables.

A nonorthogonal analysis of variance of the data for each experiment, solution, and criterion using the GLM (General Linear Model) command of the statistical software package SAS (SAS Institute Inc., Box 8000, Cary, North Carolina, U.S.A.) was carried out. This results in a type 3 analysis of variance for each set of data, produced in table

format, these are found at the end of each results chapter. In all sections of the statistical analysis the level of significance is taken as $p < 0.05$. The total variability of each set of data has 6 components, laid out in the analysis of variance tables as follows :

1.**ERROR** - (Also called RESIDUAL) this estimates the variability among repeat experiments within each dog x week combination (experiments repeated in the same dog within the same study week) and combines them over all such combinations. As described earlier, this reflects the "average" experimental variability across all dog groups throughout all weeks of study.

2. **WEEK x CASE(TREATMENT)** [WK x CASE(TR)] - this estimates the random variability among dog x week combinations, combining control and autotransplant groups, and compares it against the residual ERROR variance. When significant, it illustrates that the experimental variability which occurs in the dogs when studied from week to week exceeds the baseline experimental variability, as described by ERROR. This requires that the other components of variance must be assessed against this variance rather than against the ERROR variance.

3. **WEEK x TREATMENT** [WK x TR] - this is compared against the ERROR variance, or the WK x CASE(TR) variance if the latter reached significance.

This looks at the control dogs and the autotransplanted dogs separately, keeping the different weeks of the study separate also. When significant it illustrates the occurrence of a different trend over the weeks in the autotransplants as compared to the controls.

4. **WEEK** [WK] - this looks at control and autotransplant groups together, looking at each week of study separately. It detects any overall trend in absorption which occurs over the weeks of the study.

5. **CASE(TREATMENT)** [CASE(TR)] - this reflects the experimental variability among all dogs. It combines both control and autotransplanted dogs and reflects variability among dogs for the same experiment. When significant this was taken to be an

additional random variance component operating from case to case, and the effect of treatment must be assessed against its variance.

6. **TREATMENT** [TR] - this compares the control and autotransplant groups. It is assessed against the ERROR or WK x CASE(TR) or CASE(TR), as appropriate. When significant it is interpreted as there being a difference in absorption following autotransplantation.

An analysis of variance table is produced for each parameter assessed for each solution in the jejunal dogs and also in the ileal dogs. There is a table for each of : volume, sodium, chloride, potassium and transit time. There is also a table for glucose, glycine, phenylalanine and oleic acid, for the appropriate solution. The sodium chloride solution therefore has ten analysis of variance tables associated with it, five for the jejunal dogs and five for the ileal dogs. The other four solutions each have twelve tables.

The column headings are :

DF - degrees of freedom

SS - sum of squares

MS - mean square (variance)

F - F statistic

p - significance level

CONFIDENCE INTERVAL

The confidence interval describes a range of data produced by a study. This study has a lot of inherent variability which results in a broader spread of results and therefore a relatively wide range of values within the confidence interval.

A confidence interval for the difference in means between the control group and the autotransplant group was determined. This was done separately for each week if WK or WK x TR was significant. It was determined as follows :

(a) If WK x CASE(TR) and CASE(TR) were not significant, confidence intervals were determined from the individual measurements, ignoring weeks if non-significant.

(b) If WK x CASE(TR) was not significant but CASE(TR) was, then the confidence interval was determined from the individual dog means from both control and autotransplant groups, ignoring weeks if non-significant.

(c) If WK x CASE(TR) was significant while CASE(TR) was not, the confidence interval was determined from the means of each week and dog combination in the controls and in the autotransplants, ignoring weeks if non-significant.

(d) If WK x CASE(TR) and CASE(TR) were both significant the confidence intervals were determined from the means of each week and dog combination in the controls and in the autotransplants, further averaged over weeks if the effect of weeks was non-significant.

A 95% confidence interval has been generated. This indicates with 95% confidence that the results which fall within the range described by the confidence interval are true results. The confidence interval is composed of two numbers which in this study are both percentages, the same nomenclature as the mean values for absorption. These reflect the range of differences in the mean value of absorption between the two groups of dogs being compared. Using the volume criterion for the sodium chloride solution in the jejunum (Table 5.17, page 92) the mean absorption for the controls is 14.3%/15min, while in the autotransplants it is 15.6%/15min. The difference between the means is therefore 1.3%/15mins. The 95% confidence interval for this set of experiments is -5.2, 7.8. The difference in the means of 1.3%/15min lies in the middle of this range which is expected since the range of the confidence interval covers the normal distribution of results obtained by these experiments on multiple repetition.. A narrow confidence interval reflects an experiment which shows little variability.

In order for the confidence interval to indicate a statistically significant difference between the two groups being compared, the difference in the mean value between both groups must exceed the mean value of the confidence interval. In the preceding example the mid-point of the confidence interval lies between -5.2 and 7.8 and is therefore 6.5%/15min. This indicates that the difference in the means would have to exceed 6.5%/15min in order to achieve significance. The second method by which a confidence interval may indicate statistical significance is when it does not span zero. This reveals that the difference between the means on multiple repetition of an experiment is consistently in the same direction e.g. autotransplants absorbing more, or less, sodium.

SUMMARY

This dog model is complex in view of several potential sources of variability; the first is experimental error associated with testing a dog on any one occasion, then the week to week variability in testing a dog, and the dog to dog variability within a treatment group. The statistical analysis is also complicated by the non-orthogonality of the data structures. The analysis of variance methodology used and the methodology used for the construction of confidence intervals takes account of these complexities.

CHAPTER 5

RESULTS : SODIUM CHLORIDE

This is the first of five results chapters. Each test solution will have the results pertaining to both jejunum and ileum described in a single chapter with two sets of accompanying tables. The first set of tables contain the mean values for each valid experiment; there being between one and four experiments, plus the overall mean value of that set of experiments in each dog. The second set of tables are the statistical tables of analysis of variance.

The mean values obtained for absorption in each experiment with the sodium chloride solution are shown in Tables 5.1-5.16 (pages 76-91) at the end of this chapter. A total of 316 experiments were carried out in all four groups of dogs and 39 (12.3%) of these were excluded from further analysis because of poor polyethylene glycol (PEG) recovery. This was defined as less than 85% or more than 115% PEG recovery (as previously discussed in Chapter 2). The number of experiments performed in each group over the four weeks studied are as follows:

Number of experiments

	Total	**Discarded (%)**
Group 1(jejunal control)	86	6 (7%)
Group 2 (jejunal autotransplant)	82	15 (18.3%)
Group 3 (ileal control)	74	10 (13.5%)
Group 4 (ileal autotransplants)	74	8 (10.8%)

The discarded experiments are randomly distributed (chisquare test, p=0.15) between control and autotransplant groups implying that this is random experimental error rather than a factor produced by autotransplantation.

VARIABILITY

As discussed in Chapter 4, several types of variability co-exist in this study.

Variability Between Dogs and Study Weeks

The same experiment carried out in different dogs of the same group may result in variability. An example of this is Dog 1C who, at Week 8 (Table 5.3, page 78), absorbs 4.8, 9.6, and 2.4% of volume infused/ 15 mins while her neighbour, Dog 1H (Table 5.3, page 78), absorbs 18.0, 22.6 and 29.8 respectively. Similar examples can be found in all four groups of dogs.

Another example of variability exists when the relative absorption among dogs differs at the different time points, and this is statistically quantified as WEEK x CASE(TREATMENT).

Both types of variability are detected, quantified, and taken account of in data interpretation by the analysis of variance as shown in the statistical tables at the end of this chapter (Tables 5.17-5.22, pages 92-97) and are depicted as CASE(TR) [variability from dog to dog, within treatment groups, and averaged over weeks] and WKxCASE(TR) [variability amongst dogs of all groups between the weeks of study].

With the sodium chloride solution, variability between dogs [as expressed by CASE(TR)] is significant ($p<0.05$) for all parameters looked at in all four groups of dogs with the single exception of transit time in both jejunal groups of dogs. Variability between dogs over the weeks of study [as expressed by WKxCASE(TR)] is also significant for all the parameters measured at Week 1, 2, 8 and 9 in the two groups of jejunal dogs. It is only significant for transit time in the two ileal groups of dogs, at all four study weeks.

This significant variability is taken into account by the analysis of variance, which therefore allows the effect of transplantation to be assessed.

ABSORPTION

The ability of the study to detect a difference in absorption between control and autotransplanted dogs is calculated from the 95% confidence intervals, as discussed in

Chapter 4. For example, looking at volume absorbed in the jejunal dogs (Table 5.17, page 92) the mean volume absorbed by Group 1 (jejunal controls) is 14.3%/15 min, while for Group 2 (jejunal autotransplants) it is 15.6%/15 min. The difference in means between the groups is 1.3%/15 min. The 95% confidence interval is -5.2 to 7.8%/15 mins. This indicates with 95% confidence that a difference in the means of greater than 6.5%/15min will be detected. This may represent an increase or a decrease in absorption following autotransplantation.

VOLUME

Jejunum

Autotransplantation : no effect (p=0.603).

Week of study : no effect (p=0.182).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the Difference
	14.3	15.6	-5.2, 7.8

Since the effect of week of study was insignificant, all data from the four time points was aggregated and a single confidence interval was produced.

The confidence interval span is from -5.2 to 7.8 = 13%/15min. The mid-point of this range is therefore 6.5%/15min. This indicates that for this series of experiments, a difference in mean absorption between the groups of greater than 6.5%/15min would have been detected. The difference in the mean between the two groups is 1.3%/15min.

No change in volume absorbed was detected at any of the four weeks studied. Autotransplanted jejunum shows no impairment of water absorption.

Ileum

Autotransplantation : no effect (p=0.386).

Week of study : is significant (p=0.034).

Absorption :	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
Week 1	33.3	37.8	-8.3, 17.3
Week 2	29.6	35.0	-3.2, 13.8
Week 8	29.4	30.6	-10.1, 12.5
Week 9	25.9	32.2	-6.4, 19.0

Since the effect of week of study is significant in the ileum, with absorption decreasing at the later weeks, a separate confidence interval was generated for each study week.

At Week 1 these experiments would have detected as significant an increase or decrease in absorption of 12.8%/15min. For Week 2, it was 8.5%/15min, for Week 8 it was 11.3%/15min, and for Week 9 the experiments would have detected an increase or a decrease of 12.7%/15min as significant.

Autotransplantation results in no change in volume absorbed from the ileum. Unlike jejunum, the ileum shows a decrease in volume absorbed over time. This decrease over the nine weeks of the study is similar in both groups of dogs, being 7.4%/15min in the controls and 5.6%/15min in the autotransplants. This time-dependent reduction in absorption may be explained by isolation of the loop, resulting in a decrease in its functional ability. As mentioned in Chapter 1, mucosa deprived of luminal nutrients may undergo atrophy and a decrease in enzyme activity. This will be discussed more fully in relation to the results of the morphometrics data (Chapter 10).

SODIUM

Jejunum

Autotransplantation : no effect (p=0.476).

Week of study : no effect (p=0.303).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	16.0	17.9	-5.0, 8.9

A single confidence interval has been generated since the effect of week of study is not significant.

These experiments would have detected an increase or a decrease in absorption of 6.9%/15min.

Autotransplanted jejunum shows no impairment sodium absorption with this saline solution.

Ileum

Autotransplantation : no effect (p=0.316).

Week of study : is significant (p=0.029).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
Week 1	37.6	42.2	-8.8, 18.0
Week 2	33.4	40.1	-1.8, 15.2
Week 8	33.4	34.2	-11.3, 13.0
Week 9	30.3	37.5	-5.9, 20.3

Four separate confidence intervals have been generated since the effect of week of study is significant.

At Week 1 these experiments would have detected an increase or a decrease in absorption between the two groups of 13.4%/15min. For Week 2, a difference of 8.5%/15min would have been detected, while for Week 8 it was 12.1%/15min, and for Week 9, an increase or decrease of 13.1%/15min would have been detected.

Autotransplanted ileum shows no difference in sodium absorption when compared to control ileum. The decrease in sodium absorption with time parallels the findings for volume and is seen in both groups, presumably due to defunctioning of the loop.

CHLORIDE

Jejunum

Autotransplantation : no effect (p=0.545).

Week of study : no effect (p=0.213).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	15.6	16.9	-5.3, 7.9

A single confidence interval was generated since week of study has no significant effect on absorption.

These experiments would have detected an increase or a decrease in absorption of greater than 6.6%/15min.

Chloride absorption is not significantly altered by autotransplantation. This is expected since sodium absorption is unaffected and absorption of these two elements parallel each other.

Ileum

Autotransplantation : no effect (p=0.462).

Week of study : is significant (p=0.032).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I. of the difference
Week 1	39.0	43.4	-10.4, 19.2
Week 2	34.2	38.4	-5.0, 13.5
Week 8	35.1	35.1	-12.4, 12.3
Week 9	30.2	38.1	-7.0, 22.7

Four confidence intervals have been generated since chloride absorption decreases with time.

At Week 1, an increase or a decrease in absorption of over 14.8%/15min would have been detected. At Week 2, an increase or decrease of over 9.2%/15min would have been detected, and at Week 8, it was 12.3%/15min while for Week 9 it was 14.8%/15min.

Chloride absorption is unaltered by autotransplantation of the ileum. As with sodium and volume, chloride absorption decreases in both groups over the nine weeks of the study.

Ileum appears to be more sensitive to the effect of being isolated from the intestinal stream than jejunum. The reason for this is not apparent.

POTASSIUM

No potassium was added to any of the test solutions, therefore any potassium in the effluent has been secreted by the loop. Hence it functions as a marker of secretion.

Jejunum

Autotransplantation : no effect (p=0.093).

Week of study : is significant (p=0.015).

Secretion	Control Mean (μM/15min)	AutoTx Mean (μM/15min)	95% C.I.of the difference
Week 1	70.6	62.6	-21.1, 5.0
Week 2	71.7	65.9	-17.0, 5.6
Week 8	62.8	57.2	-18.1, 6.9
Week 9	63.3	58.1	-13.8, 3.4

Each week had a separate confidence interval generated because the effect of week of study is significant; less potassium is secreted in the later weeks of the study.

This study would have detected a decrease or an increase in secretion of 13.0μM/15min at Week 1, 11.3μM/15min at Week 2, 12.5μM/15min at Week 8, and 8.6μM/15min at Week 9

Potassium secretion by autotransplanted jejunum was similar to control jejunum. This implies that no increase in secretion has resulted from extrinsic denervation and the loss of the "sympathetic brake" on intestinal secretion.

Jejunum showed a decrease in secretion of potassium at Weeks 8 and 9 when compared to Weeks 1 and 2. This decrease occurred to the same extent in both the control and autotransplant groups. This is probably due to the enzyme systems of the mucosa of the defunctioned loop being reduced in number and function as a result of deprivation of luminal nutrients.

Ileum

Autotransplantation : no effect (p=0.065).

Week of study : is significant (p=0.047).

Secretion	Control Mean (μM/15min)	AutoTx Mean (μM/15min)	95% C.I.of the difference
Week 1	76.1	129.0	-20.0, 126.2
Week 2	76.5	128.5	3.0, 101.4
Week 8	65.7	65.8	-16.8, 16.9
Week 9	61.4	86.9	-8.0, 58.9

Four separate confidence intervals exist since the diminished potassium secretion in the later weeks of study is significant.

This study was capable of detecting an increase or a decrease in potassium secretion of 73.1μM/15min at Week 1. The apparent increased potassium secretion by the autotransplanted ileum was therefore not proven statistically.

For Week 2, the study would have detected a change in secretion of 49.2μM/15min. The difference in means is 52.0μM/15min, but this fails to be significant by ANOVA which takes all the variability among dogs into account.

The experiments at Week 8 would have detected an increase or decrease in secretion of 16.8μM/15min, while for Week 9 it was 33.4μM/15min.

Potassium secretion by autotransplanted ileum was not significantly increased.

Time of study was significant: there was a decrease in potassium secretion between the early experiments at Weeks 1 and 2 when compared to the later experiments at Week 8 and Week 9. This occurred in both groups of dogs, but was most marked in the autotransplanted ileum. The fall in potassium secretion in the control ileum between Week 1 and Week 9, was only 14.7μM/15min. The potassium secretion in

autotransplanted ileum was much higher at Weeks 1 and 2 than in the control dogs but fell to almost similar values by Week 9. This, however, represented a decrease in potassium secretion by autotransplanted ileum of 42.1μM/15min. Despite this, the difference in potassium secretion was not statistically significant between the autotransplants and the control dogs at Week 1 or 2. Greater variability in potassium secretion was seen in the autotransplanted dogs as manifested by a large standard deviation (Table 5.21, page 96) , and confirmed by the ANOVA tables, and the wide confidence intervals.

This experiment suggests that at the early stage after autotransplantation, the ileum secretes an increased amount of potassium, a change which does not persist with time. This increased secretion may be due to the loss of sympathetic innervation, which may be a transient effect, seen only in the first two of weeks after denervation. Equally, the fall to normal levels may be due to the mucosa becoming accustomed to the lack of sympathetic input, or it may be the effect on the mucosa of the loop being isolated, resulting in mucosal atrophy.

TRANSIT TIME

Jejunum

Autotransplantation : is significant ($p<0.025$).

Week of study : no effect ($p=0.734$).

Transit	Control Mean (min)	AutoTx Mean (min)	95% C.I.of the difference
	4.6	5.9	0.1, 2.5

Since the effect of week of study was not significant, a single confidence interval was generated.

The confidence interval dictates that these experiments would have detected an increase or a decrease in transit of 0.7min. The prolonged transit seen in the autotransplants was significant.

The transit time in the autotransplanted jejunal loops was longer than that of the control loops. Transection of the distal duodenum separates the autotransplanted jejunum from

the proximal pacemakers in stomach and duodenum; these control the frequency of the migrating motor complex (the "duodenal brake"). This leaves the jejunal myoelectric activity under the control of the most proximal jejunal pacemaker which cycles at a faster rate than the duodenal pacemaker. This results in each MMC having a shorter period, but fewer MMC's occur. This is due to the occurrence of prolonged episodes of irregular spiking activity, which results in a slower transit time. Since transection instantly cuts off proximal pacemaker control the effect on transit is immediate. Regeneration of enteric neurones across an anastomotic line only allows passage of the migrating myoelectric complex on a regular basis after 12 weeks. Both these facts can explain why the prolongation of transit is seen at Week 1 and persists at Week 9.

Ileum

Autotransplantation : no effect (p=0.345).

Week of study : no effect (p=0.082).

Transit	Control Mean (min)	AutoTx Mean (min)	95% C.I.of the difference
	8.2	9.5	-2.0, 4.4

Since the effect of week of study is not significant, a single confidence interval was generated.

These experiments would have detected an increase or a decrease in transit of over 3.2min.

Ileal transit time was not significantly altered by autotransplantation.

Unlike the situation in the jejunum, the increase in transit time in the ileum was not significant despite there being an identical difference in the mean transit time. This was due to greater variability in the ileal dogs. It is possible that a true difference in transit did exist; this may have been proven statistically if more dogs had been studied.

Summary

Autotransplantation did not affect absorption of volume of perfusate, sodium or chloride, nor did it alter potassium secretion in either jejunum or ileum, with this saline solution.

An effect is noted with week of study. Volume, sodium and chloride absorption were reduced at Week 9 when compared to Week 1, but only in the ileum. Potassium secretion was reduced in both jejunum and ileum at Week 9 when compared to Week 1.

Transit time was significantly slower after autotransplantation in the jejunum. Although it was slowed by the same amount in autotransplanted ileum, as compared to control ileum, this failed to achieve statistical significance. This is most easily explained by the increased variability in transit times observed in ileal dogs.

SODIUM CHLORIDE ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	1B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	17.5	9.9	cannula	9.9	24.3	23.6	11.5	20.8	-0.6
	23.7	11.8	came	14.1	11.8	17.6	19.5	9.9	14.7
		11.8	out	16.4			16.0	19.4	17.8
MEAN	**20.6**	**11.2**		**13.5**	**18.0**	**20.6**	**15.7**	**16.7**	**10.6**
SODIUM (%/15 mins)	18.3	7.7		8.7	23.8	23.9	16.2	21.1	2.4
	25.3	11.9		16.3	13.3	19.9	28.5	14.2	19.1
		12.6		18.2			20.8	20.3	20.2
MEAN	**21.8**	**10.7**		**14.4**	**18.6**	**21.9**	**21.8**	**18.5**	**13.9**
CHLORIDE (%/15 mins)	20.7	3.3		9.7	21.3	28.5	10.9	21.7	0.9
	25.7	12.5		18.2	11.1	19.9	24.8	17.1	19.0
		16.9		23.3			15.5	20.1	20.0
MEAN	**23.2**	**10.9**		**17.1**	**16.2**	**24.2**	**17.1**	**19.6**	**13.3**
POTASSIUM EXCRETION (µmol/15mins)	72.4	76.5		70.7	60.4	64.6	68.7	65.3	86.5
	65.7	71.9		65.1	80.3	80.1	62.1	62.3	70.1
		81.7		67.0			64.7	65.3	81.4
MEAN		**76.7**		**67.6**	**70.3**	**72.3**	**65.2**	**64.3**	**79.3**
PEG RECOVERY (%)	94.1	88.0		92.9	91.6	89.7	96.9	86.7	106.0
	97.9	91.2		95.3	94.5	85.0	95.6	99.4	99.8
		94.7		96.2			89.7	89.9	85.0
MEAN	**96.0**	**91.3**		**94.8**	**93.0**	**87.3**	**94.1**	**92.0**	**96.9**
TRANSIT TIME (mins)	7.1	3.8		3.6	3.4	6.3	2.3	5.0	9.8
	7.2	4.1		3.8	3.3	5.0	2.5	2.8	4.2
		6.0		4.2			2.9	3.5	5.8
MEAN	**7.1**	**4.6**		**3.7**	**3.3**	**5.6**	**2.6**	**3.7**	**6.6**

TABLE 5.1 : EXPERIMENTS AT WEEK 1

SODIUM CHLORIDE ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	1B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	17.7	13.5	cannula	11.9	10.0	12.9	17.7	10.2	18.2
	24.5	19.3	came	6.9	12.9	11.4	19.2	14.7	23.3
	23.5	26.3	out		14.3		17.8	13.8	28.8
		24.6			11.4		17.6	11.8	
MEAN	**21.9**	**20.9**		**9.4**	**12.1**	**12.1**	**18.1**	**12.6**	**23.4**
SODIUM (%/15 mins)	18.5	14.9		14.2	11.6	10.9	20.4	16.7	21.3
	23.1	22.2		12.5	14.5	11.4	21.0	15.5	24.4
	27.4	19.9			15.7		18.9	15.1	29.3
		28.9			12.0		22.0	14.1	
MEAN	**23.0**	**21.5**		**13.3**	**13.4**	**11.2**	**20.6**	**15.3**	**25.0**
CHLORIDE (%/15 mins)	18.9	17.9		13.6	13.8	15.0	26.0	13.4	21.2
	24.3	24.9		5.8	13.0	10.8	21.9	19.0	20.2
	22.2	15.6			13.6		20.3	16.5	25.3
		29.5			9.9		20.6	20.4	
MEAN	**21.8**	**22.0**		**9.7**	**12.6**	**12.9**	**22.2**	**17.3**	**22.2**
POTASSIUM EXCRETION (μmol/15mins)	66.3	77.5		57.7	77.0	76.3	74.9	66.5	71.9
	62.2	72.9		69.7	80.0	84.6	78.6	66.1	70.9
	61.7	68.4			81.5		75.8	72.6	72.7
		62.1			88.2		77.9	56.0	
MEAN	**63.4**	**70.2**		**63.7**	**81.7**	**80.4**	**76.8**	**65.3**	**71.8**
PEG RECOVERY (%)	101.1	97.9		98.9	97.6	88.5	94.0	88.4	96.6
	93.0	92.7		96.6	90.7	96.1	88.9	92.3	86.0
	95.3	89.0			98.7		86.7	88.7	85.0
		99.0			100.2		88.0	93.8	
MEAN	**96.5**	**94.6**		**97.7**	**96.8**	**92.3**	**89.4**	**90.8**	**89.2**
TRANSIT TIME (mins)	6.9	7.1		6.2	2.5	6.6	2.1	4.1	4.1
	5.0	4.0		6.3	3.8	5.0	3.8	5.6	4.8
	3.3	3.4			3.4		4.4	6.0	3.6
		3.1			4.7		2.3	3.6	
MEAN	**5.1**	**4.4**		**6.2**	**3.6**	**5.8**	**3.1**	**4.8**	**4.2**

TABLE 5.2 : EXPERIMENTS AT WEEK 2

SODIUM CHLORIDE ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	1B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	Died	Fistula	4.8	Fistula	10.6	Ripped	13.6	18.0	-4.2
	stomal		9.6		10.1	out	10.6	22.6	9.1
	prolapse		2.4		16.3	loop	17.5	29.8	6.3
MEAN			**5.6**		**12.3**		**13.9**	**23.5**	**3.7**
SODIUM (%/15 mins)			6.6		10.8		19.1	22.7	-2.0
			11.9		12.7		11.8	24.2	9.3
			4.9		17.9		17.4	29.7	7.8
MEAN			**7.8**		**13.8**		**16.1**	**25.5**	**5.0**
CHLORIDE (%/15 mins)			2.7		8.1		13.6	21.0	-7.1
			11.5		17.4		8.8	23.4	5.6
			5.8		15.3		16.9	32.5	4.1
MEAN			**6.7**		**13.6**		**13.1**	**25.6**	**0.9**
POTASSIUM EXCRETION (μmol/15mins)			68.5		68.0		62.5	62.4	60.5
			64.6		73.7		59.6	59.7	54.3
			65.8		77.9		54.7	42.3	67.4
MEAN			**66.3**		**73.2**		**58.9**	**54.8**	**60.7**
PEG RECOVERY (%)			97.1		92.2		87.5	92.9	112.3
			107.4		95.9		103.1	90.1	96.8
			110.0		93.8		90.4	85.0	113.1
MEAN			**104.8**		**94.0**		**93.7**	**89.3**	**107.4**
TRANSIT TIME (mins)			4.9		4.8		2.9	2.4	2.9
			5.0		3.3		2.4	4.2	2.5
			5.8		9.5		1.8	3.3	2.1
MEAN			**5.2**		**5.9**		**2.4**	**3.3**	**2.5**

TABLE 5.3 : EXPERIMENTS AT WEEK 8

SODIUM CHLORIDE ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	1B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	Died	Fistula	5.7	Fistula	8.3	Ripped	11.1	16.5	13.8
	Stomal		1.0		10.9	out	9.8	17.1	22.0
	prolapse		7.3		9.1	loop	10.1		7.2
			6.5		22.1		15.1		20.3
MEAN			**5.1**		**12.6**		**11.5**	**16.8**	**15.8**
SODIUM (%/15 mins)			8.7		9.2		14.8	18.2	15.2
			1.0		10.2		11.3	21.2	22.4
			8.2		10.3		15.4		8.3
			8.2		19.7		16.0		21.8
MEAN			**6.5**		**12.3**		**14.4**	**19.7**	**16.9**
CHLORIDE (%/15 mins)			6.3		12.3		10.5	16.6	13.2
			8.0		8.8		7.2	16.0	20.3
			9.2		13.9		11.5		5.7
			5.7		18.0		14.0		17.7
MEAN			**7.3**		**13.2**		**10.8**	**16.3**	**14.2**
POTASSIUM EXCRETION (μmol/15mins)			60.8		70.5		72.9	63.5	69.2
			56.4		82.2		62.5	54.5	59.8
			53.6		73.7		57.3		66.9
			59.2		63.3		58.6		63.1
MEAN			**57.5**		**72.4**		**62.8**	**59.0**	**64.7**
PEG RECOVERY (%)			95.7		90.5		92.5	93.5	94.7
			99.4		94.1		86.5	87.5	89.5
			96.0		93.2		97.9		107.5
			92.9		99.8		88.5		93.7
MEAN			**96.0**		**94.4**		**91.3**	**90.5**	**96.3**
TRANSIT TIME (mins)			5.6		3.0		2.4	4.4	4.4
			3.1		5.5		2.2	3.3	3.4
			3.2		4.3		1.7		8.7
			2.7		4.3		1.9		6.8
MEAN			**3.6**		**4.3**		**2.0**	**3.8**	**5.8**

TABLE 5.4 : EXPERIMENTS AT WEEK 9

SODIUM CHLORIDE ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2A	2B	2C	2D	2E	2F	2G	2H
VOLUME (%/15 mins)	9.8	12.5	Unwell	16.5	-14.1	Died	16.3	27.8
	16.8	5.2		7.4	-11.6		15.4	
	12.2			14.0			11.2	
MEAN	**12.9**	**8.8**		**12.6**	**-12.8**		**14.3**	**27.8**
SODIUM (%/15 mins)	13.7	-0.4		26.0	-7.9		25.1	32.4
	17.9	14.3		8.6	-7.3		15.3	
	13.0			15.7			17.6	
MEAN	**14.9**	**6.9**		**16.8**	**-7.6**		**19.3**	**32.4**
CHLORIDE (%/15 mins)	14.4	11.3		23.1	-16.9		23.7	29.1
	20.4	19.1		7.3	-9.5		17.5	
	10.5			13.3			15.9	
MEAN	**15.1**	**15.2**		**14.6**	**-13.1**		**19.0**	**29.1**
POTASSIUM EXCRETION (μmol/15mins)	51.6	66.0		49.9	65.9		76.3	68.4
	45.5	59.1		35.9	49.6		83.3	
	79.6			50.9			87.0	
MEAN	**58.9**	**62.5**		**45.6**	**57.7**		**82.2**	**68.4**
PEG RECOVERY (%)	97.7	93.1		88.4	89.4		105.9	85.5
	86.4	98.2		115.0	98.0		90.7	
	89.6			109.7			104.3	
MEAN	**91.2**	**95.6**		**104.4**	**93.7**		**100.3**	**85.5**
TRANSIT TIME (mins)	3.7	7.7		2.7	7.6		9.1	5.3
	5.6	6.5		2.2	12.8		5.9	
	10.1			5.5			6.8	
MEAN	**6.5**	**7.1**		**3.5**	**10.2**		**7.3**	**5.3**

TABLE 5.5 : EXPERIMENTS AT WEEK 1

SODIUM CHLORIDE ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2A	2B	2C	2D	2E	2F	2G	2H
VOLUME (%/15 mins)	19.6	5.9	Unwell	19.9	25.3	Died	13.4	21.2
	15.0	17.8	Not	22.7	18.0	of	20.9	22.8
	27.6	10.4	studied	26.1	16.0	pneu-		18.8
	24.4			27.6	15.9	monia		21.1
MEAN	**21.6**	**11.4**		**24.1**	**18.8**		**17.1**	**21.0**
SODIUM (%/15 mins)	22.7	6.9		23.4	26.7		20.5	23.0
	18.1	19.1		24.5	18.6		22.7	26.6
	28.7	11.1		27.5	10.0			20.3
	24.7			30.1	17.4			22.5
MEAN	**23.6**	**12.4**		**26.4**	**18.2**		**21.6**	**23.1**
CHLORIDE (%/15 mins)	31.7	8.5		22.5	25.7		16.7	19.8
	21.9	24.1		23.0	14.0		20.1	27.1
	28.0	18.2		26.4	4.8			17.5
	21.9			25.3	13.3			23.9
MEAN	**25.9**	**16.9**		**24.3**	**14.4**		**18.4**	**22.1**
POTASSIUM EXCRETION (μmol/15mins)	61.1	68.2		78.2	47.4		67.7	82.6
	68.1	54.8		74.1	62.8		64.8	71.9
	82.1	54.0		70.1	52.4			79.3
	60.7			66.3	39.4			84.9
MEAN	**68.0**	**59.0**		**72.2**	**50.5**		**66.2**	**79.7**
PEG RECOVERY (%)	89.7	91.9		87.7	88.1		92.4	98.6
	100.1	98.8		92.4	93.4		85.3	92.1
	88.3	108.2		99.2	106.9			89.2
	111.4			87.5	106.9			95.9
MEAN	**97.4**	**99.6**		**91.7**	**98.8**		**88.8**	**93.9**
TRANSIT TIME (mins)	9.2	4.8		3.6	6.3		4.1	6.8
	7.8	4.6		5.8	4.4		6.1	5.1
	7.3	5.6		5.7	5.6			7.0
	8.3			3.6	4.8			5.5
MEAN	**8.1**	**5.0**		**4.7**	**5.3**		**5.1**	**6.1**

TABLE 5.6 : EXPERIMENTS AT WEEK 2

SODIUM CHLORIDE ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2A	2B	2C	2D	2E	2F	2G	2H
VOLUME (%/15 mins)	Fistula	5.8	14.2	22.9	5.7	Died	7.7	28.6
		3.4		17.2	4.8	of	12.8	28.4
		14.3			11.7	pneu-	15.4	
						monia		
MEAN		**7.8**	**14.2**	**20.0**	**7.4**		**12.0**	**28.5**
SODIUM (%/15 mins)		7.6	17.8	26.8	9.5		9.1	33.8
		5.7		18.5	8.3		17.2	34.1
		17.0			14.7		16.8	
MEAN		**10.1**	**17.8**	**22.6**	**10.8**		**14.4**	**33.9**
CHLORIDE (%/15 mins)		10.2	17.0	23.4	5.7		5.7	23.1
		6.5		17.3	3.0		16.1	31.4
		20.5			10.6		14.4	
MEAN		**12.4**	**17.0**	**20.3**	**6.4**		**12.1**	**27.2**
POTASSIUM EXCRETION (μmol/15mins)		66.2	57.4	54.3	37.4		40.3	65.3
		65.1		61.9	44.3		41.2	80.8
		54.2			40.1		75.3	
MEAN		**61.8**	**57.4**	**58.1**	**40.6**		**52.3**	**73.0**
PEG RECOVERY (%)		106.1	102.1	88.5	92.8		86.2	91.6
		104.6		86.1	88.1		99.0	90.8
		89.0			92.8		99.3	
MEAN		**99.9**	**102.1**	**87.3**	**91.2**		**94.8**	**91.2**
TRANSIT TIME (mins)		9.0	3.8	5.4	1.9		7.3	2.9
		8.7		3.9	3.8		11.0	5.0
		8.4			4.1		4.7	
MEAN		**8.7**	**3.8**	**4.6**	**3.3**		**7.7**	**3.9**

TABLE 5.7 : EXPERIMENTS AT WEEK 8

SODIUM CHLORIDE ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2a	2B	2C	2D	2E	2F	2G	2H
VOLUME (%/15 mins)	Fistula	9.4	24.4	11.8	5.0	Died	15.3	22.3
		9.2	22.7		6.0	of	13.7	21.1
		7.7			5.9	pneu-		30.5
		18.1			12.3	monia		21.9
MEAN		**11.1**	**23.5**	**11.8**	**7.3**		**14.5**	**23.9**
SODIUM (%/15 mins)		11.6	26.5	14.5	7.0		18.2	25.1
		10.1	24.5		7.5		15.6	23.2
		8.0			6.6			31.7
		16.4			13.5			23.8
MEAN		**11.5**	**25.5**	**14.5**	**8.6**		**16.9**	**25.9**
CHLORIDE (%/15 mins)		22.7	27.1	13.2	2.0		14.5	16.7
		11.8	20.2		5.0		12.4	17.1
		14.8			7.3			30.4
		16.1			10.7			18.3
MEAN		**16.3**	**23.7**	**13.2**	**6.2**		**13.4**	**20.6**
POTASSIUM EXCRETION (μmol/15mins)		61.6	64.8	49.4	55.4		61.8	71.6
		60.4	62.7		53.1		54.2	72.6
		73.2			54.6			35.8
		56.0			41.2			74.5
MEAN		**62.8**	**63.7**	**49.4**	**51.1**		**58.0**	**63.6**
PEG RECOVERY (%)		93.7	90.7	91.9	98.4		94.2	93.1
		93.6	101.3		102.6		87.5	85.2
		112.8			90.0			88.4
		114.0			88.3			92.1
MEAN		**103.5**	**96.0**	**91.9**	**94.8**		**90.8**	**89.7**
TRANSIT TIME (mins)		6.0	4.8	4.6	2.1		4.0	4.3
		6.7	12.8		3.1		4.6	3.8
		8.2			2.3			3.7
		8.6			3.2			5.5
MEAN		**7.4**	**8.8**	**4.6**	**2.7**		**4.3**	**4.3**

TABLE 5.8 : EXPERIMENTS AT WEEK 9

SODIUM CHLORIDE ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	26.5	23.6	28.7	38.5	49.2	6.5
	31.4	39.0	33.2	44.4		35.6
		39.3	27.1	28.7		
MEAN	**28.9**	**34.0**	**30.0**	**37.3**	**49.2**	**21.0**
SODIUM (%/15 mins)	32.1	27.3	30.2	42.6	54.0	10.8
	38.8	44.8	35.7	48.5		39.8
		42.0	30.3	31.9		
MEAN	**35.4**	**38.0**	**32.1**	**41.0**	**54.0**	**25.3**
CHLORIDE (%/15 mins)	36.5	26.8	33.1	44.9	59.2	7.9
	37.4	47.4	38.4	48.7		35.2
		46.0	28.1	35.4		
MEAN	**36.9**	**40.1**	**33.2**	**43.0**	**59.2**	**21.5**
POTASSIUM EXCRETION (μmol/15mins)	104.1	62.3	77.4	67.8	102.0	79.9
	60.7	72.3	69.9	53.4		62.3
		59.4	71.3	69.0		
MEAN	**82.4**	**64.7**	**72.9**	**63.4**	**102.0**	**71.1**
PEG RECOVERY (%)	91.8	86.4	91.1	87.2	93.5	107.6
	85.0	94.5	88.5	95.7		87.1
		94.2	98.2	106.2		
MEAN	**88.4**	**91.7**	**92.6**	**96.4**	**93.5**	**97.3**
TRANSIT TIME (mins)	13.5	3.1	15.7	10.6	8.4	6.8
	11.0	8.2	11.8	8.8		8.8
		5.9	9.6	16.4		
MEAN	**12.2**	**5.7**	**12.4**	**11.9**	**8.4**	**7.8**

TABLE 5.9 : EXPERIMENTS AT WEEK 1

SODIUM CHLORIDE ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	31.3	26.2	33.9	47.8	35.0	25.0
	20.0	23.3	19.6	43.9	22.4	32.7
	26.7	20.2	14.9	40.1	38.1	19.1
		34.7	28.3			
MEAN	**26.0**	**26.1**	**24.2**	**43.9**	**31.8**	**25.6**
SODIUM (%/15 mins)	34.8	28.7	38.4	51.0	38.1	28.3
	25.5	27.8	23.6	47.6	28.0	36.1
	30.4	23.9	19.9	42.3	41.7	23.9
		35.6	33.8			
MEAN	**30.2**	**29.0**	**28.9**	**47.0**	**35.9**	**29.4**
CHLORIDE (%/15 mins)	38.2	36.4	35.7	55.3	40.5	28.0
	28.8	26.5	25.6	49.3	27.1	43.7
	32.6	20.0	18.3	42.5	46.5	18.2
		35.4	33.2			
MEAN	**33.2**	**29.6**	**28.2**	**49.0**	**38.0**	**30.0**
POTASSIUM EXCRETION (μmol/15mins)	64.2	76.0	69.5	66.3	111.2	59.9
	55.9	76.1	74.7	54.6	107.1	60.3
	73.2	144.3	97.1	52.1	85.3	60.3
		66.3	99.1			
MEAN	**64.4**	**90.1**	**85.1**	**57.7**	**101.2**	**60.2**
PEG RECOVERY (%)	92.6	88.2	87.6	88.7	105.3	97.7
	86.1	96.5	106.2	97.5	98.6	93.0
	96.5	108.3	95.1	86.7	108.3	91.1
		89.8	93.1			
MEAN	**91.7**	**95.7**	**95.5**	**91.0**	**104.1**	**93.9**
TRANSIT TIME (mins)	13.3	8.3	14.9	16.1	5.6	9.3
	7.8	6.5	15.0	12.7	5.6	8.8
	8.9	7.2	14.9	9.8	7.8	9.8
		9.0	16.1			
MEAN	**10.0**	**7.7**	**15.2**	**12.9**	**6.3**	**9.3**

TABLE 5.10 : EXPERIMENTS AT WEEK 2

SODIUM CHLORIDE ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	25.8	31.4	41.2	35.4	18.1	18.4
	25.7	27.9	28.5	45.1	14.5	26.5
		29.2	37.0	43.8	19.2	36.3
MEAN	**25.7**	**29.5**	**35.6**	**41.4**	**17.3**	**27.1**
SODIUM (%/15 mins)	18.5	37.3	47.7	37.9	21.6	21.4
	31.4	33.9	35.2	50.0	20.8	29.2
		34.4	45.6	51.0	21.6	38.9
MEAN	**24.9**	**35.2**	**42.0**	**46.3**	**21.3**	**29.8**
CHLORIDE (%/15 mins)	14.1	39.1	48.7	40.5	24.3	24.5
	28.5	38.6	32.4	51.3	24.1	41.0
		39.0	44.8	52.2	27.6	39.8
MEAN	**21.3**	**38.9**	**42.0**	**48.1**	**25.3**	**35.1**
POTASSIUM EXCRETION (μmol/15mins)	69.9	59.9	69.8	54.5	63.5	70.1
	69.8	44.4	77.7	48.2	87.5	67.3
		48.8	66.5	67.1	82.9	65.8
MEAN	**69.8**	**51.0**	**71.2**	**56.6**	**78.0**	**67.7**
PEG RECOVERY (%)	109.7	87.4	85.4	85.0	92.3	90.0
	91.1	85.0	92.8	86.7	90.3	97.8
		86.3	85.3	90.1	97.2	95.9
MEAN	**100.4**	**86.2**	**87.8**	**87.3**	**93.3**	**94.6**
TRANSIT TIME (mins)	13.1	6.1	8.6	2.5	6.6	6.8
	9.0	3.1	7.1	3.9	8.4	6.3
		2.9	8.0	5.9	12.2	6.0
MEAN	**11.0**	**4.0**	**7.9**	**4.1**	**9.1**	**6.4**

TABLE 5.11 : EXPERIMENTS AT WEEK 8

SODIUM CHLORIDE ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	34.1	15.6	21.0	51.9	27.2	24.8
	31.9	28.1		24.2	15.0	16.0
		20.4			23.3	
MEAN	**33.8**	**21.4**	**21.0**	**38.0**	**21.8**	**20.2**
SODIUM (%/15 mins)	38.7	23.2	22.9	58.6	27.8	26.8
	38.0	35.4		29.3	17.9	22.6
		26.1			25.4	
MEAN	**38.3**	**28.2**	**22.9**	**43.9**	**23.7**	**24.7**
CHLORIDE (%/15 mins)	41.8	18.4	21.9	58.0	35.3	22.8
	40.3	35.8		27.9	17.4	21.1
		26.8			26.8	
MEAN	**41.0**	**27.0**	**21.9**	**42.9**	**26.5**	**21.9**
POTASSIUM EXCRETION (μmol/15mins)	68.3	60.1	59.5	60.0	63.0	54.3
	57.7	48.1		61.2	79.4	48.4
		83.0			68.6	
MEAN	**63.0**	**63.7**	**59.5**	**60.6**	**70.3**	**51.4**
PEG RECOVERY (%)	85.0	88.5	93.1	89.4	92.5	111.9
	85.1	91.0		98.8	91.6	93.9
		92.2			100.7	
MEAN	**85.1**	**90.6**	**93.1**	**94.1**	**94.9**	**102.9**
TRANSIT TIME (mins)	5.6	3.7	6.3	4.6	6.1	8.2
	5.2	3.3		5.9	9.4	5.3
		5.5			7.5	
MEAN	**5.4**	**4.2**	**6.3**	**5.2**	**7.7**	**6.8**

TABLE 5.12 : EXPERIMENTS AT WEEK 9

SODIUM CHLORIDE ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H.
VOLUME (%/15 mins)	33.1	20.8	31.0	28.5	45.7	37.0	53.9	Not
	30.3	21.6	12.7	50.5	34.6	48.8	43.9	studied
		51.5	17.2		46.7	47.6	67.6	
MEAN	**31.7**	**31.3**	**20.3**	**39.5**	**42.3**	**44.5**	**55.1**	
SODIUM (%/15 mins)	39.6	23.5	33.8	33.7	54.2	48.6	56.6	
	27.0	26.5	17.6	54.8	38.7	55.3	47.4	
		54.6	22.2		50.8	52.7	71.7	
MEAN	**33.3**	**34.9**	**24.5**	**44.2**	**47.9**	**52.2**	**58.7**	
CHLORIDE (%/15 mins)	43.8	25.8	36.0	35.3	51.5	42.9	58.0	
	31.5	30.9	15.9	57.2	41.4	55.8	47.5	
		55.4	17.5		51.6	55.4	74.1	
MEAN	**37.6**	**37.4**	**23.1**	**46.2**	**48.2**	**51.4**	**59.9**	
POTASSIUM EXCRETION (μmol/15mins)	69.3	202.8	94.8	87.2	349.0	462.9	70.7	
	77.7	122.3	58.2	76.5	166.0	198.8	69.3	
		34.9	60.7		180.0	82.9	89.9	
MEAN	**73.5**	**120.0**	**71.2**	**81.8**	**231.9**	**248.2**	**76.6**	
PEG RECOVERY (%)	109.8	95.7	93.8	85.1	90.2	89.3	95.4	
	100.2	97.5	93.0	89.4	99.9	88.5	94.6	
		91.2	98.8		89.9	86.0	111.8	
MEAN	**105.0**	**94.8**	**95.2**	**87.2**	**92.9**	**87.9**	**100.6**	
TRANSIT TIME (mins)	18.4	9.4	6.5	13.6	14.9	11.1	8.3	
	17.2	11.0	5.2	2.8	8.1	12.3	10.7	
		10.1	5.7		15.2	9.5	15.3	
MEAN	**17.8**	**10.2**	**5.8**	**8.2**	**12.7**	**11.0**	**11.4**	

TABLE 5.13 : EXPERIMENTS AT WEEK 1

SODIUM CHLORIDE ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H
VOLUME (%/15 mins)	38.3	35.6	33.4	40.8	58.2	26.5	28.6	Not
	36.1	39.1	16.1	42.8	28.0	39.2	48.3	studied
		30.0	19.9		30.5	23.8	39.7	
MEAN	**37.2**	**34.9**	**23.1**	**41.8**	**38.9**	**29.8**	**38.9**	
SODIUM (%/15 mins)	48.0	38.5	38.1	48.0	60.5	36.2	32.8	
	38.1	45.9	20.1	49.4	32.4	44.1	51.7	
		35.2	23.3		34.7	29.8	44.1	
MEAN	**43.1**	**39.9**	**27.2**	**48.6**	**42.5**	**36.7**	**42.9**	
CHLORIDE (%/15 mins)	42.6	37.1	38.4	45.4	60.3	33.0	30.9	
	36.8	45.6	14.9	49.1	29.2	45.6	52.0	
		29.7	23.2		32.9	28.4	44.5	
MEAN	**39.7**	**37.5**	**25.5**	**47.2**	**40.8**	**35.7**	**42.5**	
POTASSIUM EXCRETION (μmol/15mins)	74.0	145.4	81.2	262.5	88.1	297.1	110.0	
	76.3	165.1	88.5	110.7	218.3	97.9	49.7	
		197.3	59.4		67.4	161.5	87.0	
MEAN	**75.2**	**169.3**	**76.4**	**186.6**	**124.6**	**185.5**	**82.2**	
PEG RECOVERY (%)	105.4	88.1	95.4	107.3	92.1	108.9	105.3	
	104.2	88.0	112.0	94.5	85.5	90.5	89.7	
		93.0	96.5		92.5	96.4	103.3	
MEAN	**104.8**	**89.7**	**101.3**	**100.9**	**90.0**	**98.6**	**99.4**	
TRANSIT TIME (mins)	9.3	5.2	8.0	18.7	9.8	13.5	9.4	
	6.7	5.6	9.3	10.4	11.0	11.9	6.6	
		7.3	9.7		8.7	15.7	14.8	
MEAN	**8.0**	**6.0**	**9.0**	**14.6**	**9.8**	**13.7**	**10.3**	

TABLE 5.14 : EXPERIMENTS AT WEEK 2

SODIUM CHLORIDE ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H
VOLUME (%/15 mins)	30.7	4.8	Cannula	32.3	27.3	Stoma	37.9	26.8
	13.4	15.0	abscess	48.7	50.6	and	45.2	28.8
		32.6		33.3		loop	25.5	37.5
						eaten		
MEAN	**22.0**	**17.5**		**38.1**	**38.9**		**36.2**	**31.0**
SODIUM (%/15 mins)	35.3	5.9		33.9	33.7		40.6	31.0
	18.5	18.7		52.6	54.0		48.1	31.5
		37.5		36.8			27.6	39.0
MEAN	**26.9**	**20.7**		**41.1**	**43.8**		**38.8**	**33.8**
CHLORIDE (%/15 mins)	38.2	8.4		38.0	33.4		41.5	26.0
	17.0	21.7		55.2	54.4		51.5	27.2
		39.8		38.2			30.0	39.0
MEAN	**27.6**	**23.3**		**43.8**	**43.9**		**41.0**	**30.7**
POTASSIUM EXCRETION (μmol/15mins)	72.4	62.4		54.9	65.9		72.4	25.8
	99.7	50.3		56.7	57.8		95.7	53.1
		101.9		57.4			57.3	53.9
MEAN	**86.0**	**71.5**		**56.3**	**61.8**		**75.1**	**44.3**
PEG RECOVERY (%)	100.0	89.7		100.0	89.5		99.9	104.9
	92.2	92.6		107.0	106.8		95.0	107.9
		87.1		106.3			106.9	97.2
MEAN	**96.1**	**89.8**		**104.4**	**98.1**		**100.6**	**103.3**
TRANSIT TIME (mins)	20.2	14.2		12.3	8.4		7.8	2.4
	10.8	9.4		15.5	6.1		7.1	2.9
		6.7		7.3			9.1	4.7
MEAN	**15.5**	**10.1**		**11.7**	**7.2**		**8.0**	**3.3**

TABLE 5.15 : EXPERIMENTS AT WEEK 8

SODIUM CHLORIDE ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H
VOLUME (%/15 mins)	58.2	16.4	Cannula	37.4	Wrong	Stoma	39.6	22.5
	36.2	23.4	abscess	46.4	NaCl	and	39.3	
	22.8	14.8		42.3	conc.	loop		
						eaten		
MEAN	**39.1**	**18.2**		**42.0**			**39.5**	**22.5**
SODIUM (%/15 mins)	62.8	19.5		40.8			43.6	32.8
	41.8	25.5		51.9			43.1	
	27.8	18.9		45.6				
MEAN	**44.1**	**21.3**		**46.1**			**43.3**	**32.8**
CHLORIDE (%/15 mins)	64.8	12.2		42.9			46.9	35.4
	42.0	24.9		52.1			44.6	
	25.8	15.4		47.4				
MEAN	**44.2**	**17.5**		**47.5**			**45.8**	**35.4**
POTASSIUM EXCRETION (μmol/15mins)	68.1	140.1		45.3			55.8	64.8
	82.0	75.7		148.9			92.6	
	64.6	172.6		89.9				
MEAN	**71.6**	**129.5**		**94.7**			**74.2**	**64.8**
PEG RECOVERY (%)	93.9	107.9		101.3			96.6	90.1
	95.1	88.8		92.7			95.1	
	85.6	98.1		91.3				
MEAN	**91.5**	**98.3**		**95.1**			**95.8**	**90.1**
TRANSIT TIME (mins)	12.7	8.8		7.7			8.2	2.9
	18.4	5.2		3.8			9.0	
	8.4	15.2		13.5				
MEAN	**13.2**	**9.7**		**8.3**			**8.6**	**2.9**

TABLE 5.16 : EXPERIMENTS AT WEEK 9

ANALYSIS OF VARIANCE TABLES : SODIUM CHLORIDE

	Experiment : Jejunum	Criterion : Volume			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	63	63.2	0.28	.603
CASE(TR)	14	3122	223.0	2.52	.018
WK	3	461	153.8	1.74	.182
WKxTR	3	289	96.2	1.09	.371
WKxCASE(TR)	28	2479	88.5	4.52	<.001
ERROR	96	1880	19.6		

The interaction Week x Case (Treatment) is significant and, against its mean square, the interaction Week x Treatment and Week are not significant. The effect of Case (Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

	Control			AutoTx			AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	9	14.3	4.3	7	15.6	6.6	-5.2 , 7.8

	Experiment : Jejunum	Criterion : Sodium			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	140	140.1	0.54	.476
CASE(TR)	14	3658	261.3	3.18	.004
WK	3	314	104.6	1.27	.303
WKxTR	3	245	81.5	0.99	.411
WKxCASE(TR)	28	2300	82.2	3.85	<.001
ERROR	96	2048	21.3		

The interaction Week x Case (Treatment) is significant and, against its mean square, the interaction Week x Treatment and Week are not significant. The effect of Case (Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

	Control			AutoTx			AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	9	16.0	4.3	7	17.9	7.2	-5.0 , 8.9

TABLE 5.17 : RESULTS FOR VOLUME AND SODIUM (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : SODIUM CHLORIDE

	Experiment : Jejunum	Criterion : Chloride			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	94	94.2	0.39	.545
CASE(TR)	14	3419	244.2	2.72	.012
WK	3	429	143.0	1.59	.213
WKxTR	3	254	86.5	0.94	.434
WKxCASE(TR)	28	2513	89.7	3.27	<.001
ERROR	96	2636	27.5		

The interaction Week x Case (Treatment) is significant and, against its mean square, the interaction Week x Treatment and Week are not significant. The effect of Case (Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

	Control			AutoTx			AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	9	15.6	4.5	7	16.9	6.7	-5.3 , 7.9

	Experiment : Jejunum	Criterion : Potassium			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	960	960.2	3.24	.093
CASE(TR)	14	4149	296.4	2.15	.042
WK	3	1723	574.4	4.16	.015
WKxTR	3	29	9.8	0.07	.975
WKxCASE(TR)	28	3865	138.0	2.12	.004
ERROR	96	6243	65.0		

The interaction Week x Case (Treatment) is significant and, against its mean square, the interaction Week x Treatment is not significant. The effects of Week and Case (Treatment) are significant . Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

	Control			AutoTx			AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	8	70.6	5.3	6	62.6	12.2	-21.1 , 5.0
2	8	71.7	7.4	6	65.9	10.2	-17.0 , 5.6
8	5	62.8	7.1	6	57.2	10.7	-18.1 , 6.9
9	5	63.3	5.9	6	58.1	6.5	-13.8 , 3.4

There was a significant reduction in the mean potassium level between weeks 2 and 8.

TABLE 5.18 : RESULTS FOR CHLORIDE AND POTASSIUM (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : SODIUM CHLORIDE

	Experiment : Jejunum		Criterion : Transit Time		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	55	55.0	7.38	<.025
CASE(TR)	14	121	8.65	1.16	.354
WK	3	10	3.2	0.43	.734
WKxTR	3	5	1.6	0.21	.889
WKxCASE(TR)	28	209	7.4	3.11	<.001
ERROR	96	230	2.4		

The interaction Week x Case (Treatment) is significant and, against its mean square, the interaction Week x Treatment and the effects of Week and Case (Treatment) are not significant. The effect of Treatment is significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

	Control			AutoTx			AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	9	4.6	1.0	7	5.9	1.1	0.1 , 2.5

TABLE 5.19 : RESULTS FOR TRANSIT TIME (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : SODIUM CHLORIDE

	Experiment : Ileum		Criterion : Volume		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	358	358.1	0.81	.386
CASE(TR)	12	5311	442.6	5.21	<.001
WK	3	769	256.2	3.02	.034
WKxTR	3	176	58.7	0.69	.560
WKxCASE(TR)	29	2938	101.3	1.19	.264
ERROR	81	6875	84.9		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment. The effects of Week and Case (Treatment) are significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	6	33.3	8.6	7	37.8	11.2	-8.3 , 17.3
2	6	29.6	7.5	7	35.0	6.4	-3.2 , 13.8
8	6	29.4	8.4	6	30.6	9.0	-10.1 , 12.5
9	6	25.9	7.6	5	32.2	11.0	-6.4 , 19.0

There was a progressive decrease in the mean volume over the weeks.

	Experiment : Ileum		Criterion : Sodium		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	509	509.0	1.10	.316
CASE(TR)	12	5569	464.1	5.44	<.001
WK	3	808	269.4	3.16	.029
WKxTR	3	277	92.2	1.08	.362
WKxCASE(TR)	29	3438	118.6	1.39	.127
ERROR	81	6915	85.4		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment . The effects of Week and Case (Treatment) are significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	6	37.6	9.7	7	42.2	11.9	-8.8 , 18.0
2	6	33.4	7.1	7	40.1	6.8	-1.8 , 15.2
8	6	33.4	9.9	6	34.2	9.0	-11.3 , 13.0
9	6	30.3	8.8	5	37.5	10.4	-5.9 , 20.3

There was a progressive decrease in the mean sodium over the weeks.

TABLE 5.20 : RESULTS FOR VOLUME AND SODIUM (ILEUM)

ANALYSIS OF VARIANCE TABLES : SODIUM CHLORIDE

	Experiment : Ileum		Criterion : Chloride		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	318	318.4	0.58	.462
CASE(TR)	12	6613	551.1	5.40	<.001
WK	3	944	314.5	3.08	.032
WKxTR	3	289	96.4	0.94	.423
WKxCASE(TR)	29	3918	135.1	1.32	.164
ERROR	81	20478	102.0		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment. The effects of Week and Case (Treatment) are significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	6	39.0	12.4	7	43.4	11.9	-10.4 , 19.2
2	6	34.2	8.3	7	38.4	6.8	-5.0 , 13.5
8	6	35.1	10.1	6	35.1	9.0	-12.4 , 12.3
9	6	30.2	9.4	5	38.1	12.4	-7.0 , 22.7

There was a significant reduction in the mean chloride level between Week 1 and Week 2.

	Experiment : Ileum		Criterion : Potassium		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	33833	33833.4	4.11	.065
CASE(TR)	12	98681	8223.4	3.63	<.001
WK	3	18865	6288.2	2.77	.047
WKxTR	3	8106	2702.0	1.19	.318
WKxCASE(TR)	29	60344	2080.8	0.92	.590
ERROR	81	183602	2266.7		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment . The effects of Week and Case (Treatment) are significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	6	76.1	14.4	7	129.0	77.7	-20.0 , 126.2
2	6	76.5	18.2	7	128.5	51.7	3.0 , 101.4
8	6	65.7	10.0	6	65.8	14.8	-16.8 , 16.9
9	6	61.4	6.2	5	86.9	26.3	-8.0 , 58.9

There was a significant reduction in the mean potassium level between Week 2 and Week 8.

TABLE 5.21 : RESULTS FOR CHLORIDE AND POTASSIUM (ILEUM)

ANALYSIS OF VARIANCE TABLES : SODIUM CHLORIDE

	Experiment : Ileum		Criterion : Transit Time		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	40	40.4	0.97	.345
CASE(TR)	12	500	41.7	2.49	.022
WK	3	124	41.3	2.47	.082
WKxTR	3	58	19.2	1.15	.347
WKxCASE(TR)	29	485	16.7	2.12	.004
ERROR	81	639	7.88		

The interaction Week x Case (Treatment) is significant and, against its mean square, the interaction Week x Treatment and Week are not significant. The effect of Case (Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	8.2	1.8	8	9.5	3.2	-2.0 , 4.4

TABLE 5.22 : RESULTS FOR TRANSIT TIME (ILEUM)

CHAPTER 6

RESULTS : GLUCOSE

The mean values obtained for absorption in each experiment are shown in Tables 6.1-6.8 (pages 108-115) at the end of this chapter. These also show the mean of all experiments for each dog at each week studied. A total of 150 experiments were carried out in all four groups of dogs and 37 (24.7%) of these were excluded from further analysis because of poor PEG recovery. The number of experiments performed in each group over the two study weeks (Week 1 and Week 8) are as follows:

	Number of experiments	
	Total	**Discarded**
Group 1	39	6 (15.4%)
Group 2	36	12 (33.0%)
Group 3	36	8 (22.2%)
Group 4	39	11 (28.2%)

The poor PEG recovery was not equally distributed amongst all dogs. Instead, several dogs had all three experiments affected and all their data for glucose absorption had to be deleted. This applied to 2H at Week 1(Table 6.1, page 108) and 3A and 4H at Week 8 (Table 6.8, page 115). Some dogs had two of their three studies affected : 1A, 1F, 4A and 4C at Week 1(Table 6.1, page 108), and 2C, 3D and 4E at Week 9 (Table 6.8, page 115). The reason for this remains obscure since all experiments were carried out in identical fashion, using the same equipment and analysed by the same methods on the same machines. While poor PEG recovery was more notable in some dogs than others, the affected dogs occurred randomly in all four groups (chisquare test, p=0.3).

VARIABILITY

As with the 150mmol sodium chloride solution, the solution of 135mmol sodium chloride plus 30mmol glucose also produced results which were affected with significant variability. This is apparent in the jejunal groups of dogs for volume, sodium, chloride

and glucose absorption, where significant variability occurred between dogs over the two study weeks. This is depicted statistically as WKxCASE(TR) , $p < 0.05$. There was no significant variability amongst the dogs themselves in the jejunal groups [CASE(TR), $p > 0.05$]. The situation for the ileal dogs was somewhat different, with significant variability amongst dogs alone for volume, sodium, chloride and glucose [CASE(TR), $p < 0.05$] while this variability is not significant when the effect of week is added in (WKxCASE(TR), $p > 0.05$).

ABSORPTION

The analysis of variance tables and the overall means with the confidence intervals from which the sensitivity of the study is calculated, are at the end of this chapter (Tables 6.9-6.14, pages 116-121).

VOLUME

Jejunum

Autotransplantation : no effect ($p > 0.9$).

Week of study : no effect ($p = 0.357$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	33.1	33.4	-8.1, 8.9

The effect of week of study was not significant, so a single confidence interval exists.

These experiments were capable of detecting an increase or a decrease in absorption of 8.5%/15min.

Autotransplantation produced no alteration in the volume absorbed by the jejunum. The volume absorbed was much greater than with the sodium chloride solution due to the presence of glucose which facilitates absorption, a mechanism which was observed to be intact following autotransplantation.

Ileum

Autotransplantation : no effect ($p=0.2$).

Week of study : is significant ($p<0.001$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
Week 1	59.6	48.8	-23.0, 1.4
Week 8	48.1	42.5	-19.7, 8.5

The effect of week of study was significant, so individual confidence intervals were generated.

At Week 1, these experiments were capable of detecting an increase or a decrease in absorption of greater than 12.2%/15min. At Week 8 the difference which was detectable is 14.1%/15min.

Ileal autotransplantation did not affect volume absorption.

Both groups showed a decrease in volume absorbed at Week 8 when compared with Week 1. This same finding has already been seen with the sodium chloride solution, and is explained by the effect on the mucosa of defunctioning this segment of ileum.

SODIUM

Jejunum

Autotransplantation : no effect ($p>0.5$).

Week of study : no effect ($p=0.417$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	31.6	34.0	-6.1, 10.8

The effect of week of study was not significant so there is a single confidence interval.

These experiments were capable of detecting an increase or a decrease in absorption of greater than 8.4%/15min.

Autotransplantation of the jejunum did not impair sodium absorption.

Ileum

Autotransplantation : no effect (p=0.234).

Week of study : is significant (p=0.007).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
Week 1	63.7	52.5	-23.3, 0.8
Week 8	52.5	49.0	-17.6, 10.6

Two confidence intervals were required since the effect of week of study is significant.

At Week 1, the experiments would have detected an increase or a decrease in absorption of 12.0%/15min. At Week 8, the experiments would have detected a difference of 14.1%/15min.

Sodium absorption was not significantly altered by autotransplantation of the ileum.

Sodium absorption is less at Week 8 than at Week 1 in both control and autotransplanted ileum, indicating that the effect of defunctioning on the mucosa is similar regardless of whether the loop is innervated or not.

CHLORIDE

Jejunum

Autotransplantation : no effect ($p>0.5$).

Week of study : no effect ($p=0.382$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	33.2	34.4	-7.4, 9.9

A single confidence interval exists since the effect of week of study is insignificant.

These experiments would have detected an increase or a decrease in absorption of more than 8.6%/15min.

Chloride absorption remained unchanged after autotransplantation, which is an expected finding since sodium absorption is not altered.

Ileum

Autotransplantation : no effect ($p=0.19$).

Week of study : is significant ($p<0.002$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
Week 1	68.9	59.1	-20.8, 1.1
Week 8	58.0	53.4	-19.4, 10.1

A separate confidence interval for each week exists since the effect of week of study was significant.

At Week 1, these experiments were capable of detecting an increase or decrease in absorption of 10.9%/15min. At Week 8, the difference which the experiments were able to detect was an increase or decrease of over 14.7%/15min.

Chloride absorption in the ileum was not significantly altered by autotransplantation.

The time effect seen was a decrease in chloride absorption in both control and autotransplanted ileum between Week 1 and Week 8. As seen with the jejunum, this parallels the findings for absorption of sodium.

POTASSIUM

Jejunum

Autotransplantation : is significant ($p<0.001$).

Week of study : no effect ($p=0.056$).

Secretion	Control Mean (μM/15min)	AutoTx Mean (μM/15min)	95% C.I.of the difference
	79.8	62.6	-26.5,-8.0

A single confidence interval exists since the effect of week of study was not significant.

These experiments were capable of detecting an increase or a decrease in secretion of more than 9.2μM/15min.

Autotransplanted jejunum secreted less potassium. This result is contrary to what might be expected, since, as described in Chapter 1, the loss of the "sympathetic brake" has been shown to result in increased secretion.

Ileum

Autotransplantation : no effect ($p>0.2$).

Week of study : no effect ($p=0.369$).

Secretion	Control Mean (μM/15min)	AutoTx Mean (μM/15min)	95% C.I.of the difference
	101.7	118.1	-20.0,52.6

The effect of week of study was not significant so a single confidence interval was generated.

These experiments were able to detect an increase or a decrease in secretion of greater than 36.3μM/15min.

Autotransplanted ileum did not secrete an increased amount of potassium.

While the mean potassium secretion of the ileal autotransplant dogs appeared higher than that of the control group, the standard deviations reveal that the potassium secretion by the autotransplanted dogs was more variable and so the difference detected by this series of experiments is insignificant. It is possible that autotransplanted ileum does secrete more potassium, like the jejunum, but more dogs would be required to prove this statistically.

TRANSIT TIME

Jejunum

Autotransplantation : is significant (p=0.018).

Week of study : is significant (p=0.028).

Transit	Control Mean (min)	AutoTx Mean (min)	95% C.I.of the difference
Week 1	4.8	6.4	-0.2, 3.6
Week 8	4.6	5.1	-1.9, 2.7

There was an effect of week of study, therefore there are two confidence intervals.

At Week 1 the experiments were capable of detecting an increase or decrease in transit time of 1.9min. At Week 8, an increase or decrease of 2.3min would have been detected.

Transit time in the autotransplanted jejunum was slower.

The autotransplanted dogs showed a reduction in transit time between Week 1 and Week 8. A slowing of transit in the transplanted group compared to controls is an expected finding since autotransplantation alters motility. The reduction in the transit time by Week 8 implies that a degree of reconnection of enteric neurones across the anastomosis has occurred, allowing the migrating motor complex of the bowel proximal to the transection to propagate distally. This is rather unexpected since it normally takes around 12 weeks before the MMC passes an anastomosis.

Ileum

Autotransplantation : is significant ($p=0.001$).

Week of study : is significant ($p<0.001$).

Transit	Control Mean (min)	AutoTx Mean (min)	95% C.I.of the difference
Week 1	10.7	7.9	-5.5, -0.2
Week 8	6.4	4.0	-4.7, -0.3

There are two separate confidence intervals since the effect of week of study was significant.

At Week 1, these experiments would have detected an increase or decrease in transit of 2.6min. At Week 8, an increase or decrease of 2.2min was detectable.

These experiments showed that autotransplantation of the ileum shortens transit time, contrary to what might have been expected. Both groups also show a decrease in transit time between Week 1 and Week 8. This cannot be accounted for by the proximal bowel transection in the autotransplants, which would have the opposite effect on transit time. Equally the decrease in transit time seen in the control group between Week 1 and Week 8 cannot be explained by that either since there has been no transection of the

duodenum and the loop is in myoneural continuity with the proximal bowel by the seromuscular bridge. These unusual results remain unexplained.

GLUCOSE

Jejunum

Autotransplantation : no effect ($p>0.1$).

Week of study : no effect ($p=0.416$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	78.1	67.7	-18.9,-1.8

A single confidence interval was generated since the effect of week of study was insignificant.

These experiments would have detected an increase or a decrease in absorption of greater than 8.6%/15min.

Autotransplantation did not significantly affect glucose absorption from the jejunum.

Autotransplanted jejunum appears to absorb slightly less glucose than the controls, but this failed to achieve statistical significance. This may mean that a true difference in absorption does exist, but it has not been detected statistically because the number of dogs studied was insufficient.

Ileum

Autotransplantation : no effect ($p=0.215$).

Week of study : is significant ($p<0.001$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
Week 1	82.3	75.0	-24.9, 10.4
Week 8	76.0	64.2	-29.0, 5.4

The effect of week of study was significant so two confidence intervals exist.

At Week 1 these experiments were capable of detecting an increase or decrease in absorption of greater than 17.6%/15min. At Week 8, the experiments would have detected an increase or decrease of more than 17.2%/15min.

Glucose absorption by autotransplanted ileum was not significantly altered by autotransplantation.

Ileum exhibits a time-dependent effect, with glucose absorption being significantly reduced at Week 8 compared to Week 1. This was seen to occur similarly in both control and autotransplanted ileum, almost certainly as a result of defunctioning.

Summary

Autotransplantation resulted in no significant alteration in absorption of volume, sodium, chloride or glucose in either jejunum or ileum.

Potassium secretion was decreased in autotransplanted jejunum, but not ileum.

Transit time was affected in both jejunum and ileum: showing an expected increase in autotransplanted jejunum, but paradoxically being shorter in autotransplanted ileum.

Ileum was seen to have a time-dependent effect with absorption of volume, sodium, chloride and glucose as seen at Week 8 when compared to Week 1. This was a decrease which occurred in both control and autotransplanted ileum.

GLUCOSE ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	1B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	51.1	39.2	Cannula	22.6	40.9	24.9	34.2	32.5	36.7
		13.6	came	38.5	45.8		27.9	29.4	43.1
		32.1	out	35.9			44.2	31.3	44.7
MEAN	**51.1**	**28.3**		**32.3**	**43.4**	**24.9**	**35.4**	**31.1**	**41.5**
SODIUM (%/15 mins)	51.0	38.1		18.6	36.8	24.3	25.8	33.1	36.3
		7.0		36.4	43.7		32.2	29.7	44.7
		30.1		34.1			43.9	31.4	43.7
MEAN	**51.0**	**25.1**		**29.7**	**40.4**	**24.3**	**34.0**	**31.4**	**41.6**
CHLORIDE (%/15 mins)	53.3	40.3		23.7	36.5	25.2	19.9	35.7	37.5
		16.9		38.3	45.4		34.7	31.8	44.0
		30.1		35.8			42.5	34.4	44.0
MEAN	**53.3**	**29.1**		**32.6**	**40.9**	**25.2**	**32.4**	**34.0**	**41.8**
POTASSIUM EXCRETION (μmol/15mins)	61.9	82.5		83.2	77.5	72.9	108.9	68.3	83.0
		127.4		67.1	84.7		62.2	65.8	77.9
		95.8		81.0			92.1	82.5	80.1
MEAN	**61.9**	**101.9**		**77.1**	**81.1**	**72.9**	**87.7**	**72.2**	**80.3**
GLUCOSE (%/15MINS)	85.2	86.2		75.8	85.9	63.6	69.0	68.3	88.0
		84.2		73.6	92.1		80.2	65.8	87.4
		83.3		79.9			96.2	70.8	88.8
MEAN	**85.2**	**84.6**		**76.4**	**89.0**	**63.6**	**81.8**	**68.3**	**88.1**
PEG RECOVERY (%)	90.6	103.4		96.3	96.4	100.8	95.5	85.1	93.5
		95.4		101.2	88.3		91.9	91.5	91.6
		110.8		99.3			90.9	85.0	90.4
MEAN	**90.6**	**103.2**		**98.9**	**92.3**	**100.8**	**92.8**	**86.4**	**91.8**
TRANSIT TIME (mins)	7.2	3.8		3.3	9.0	2.8	2.1	6.0	6.3
		4.0		3.6	4.0		3.3	4.0	8.1
				2.6			3.8	5.4	6.5
MEAN	**7.2**	**3.9**		**3.2**	**6.5**	**2.8**	**3.1**	**5.1**	**7.0**

TABLE 6.1 : EXPERIMENTS AT WEEK 1

GLUCOSE ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	2B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	Prolapsed	Fistula	22.9	Fistula	34.0	Ripped	35.3	32.9	20.3
	stoma		17.5		43.8	out	37.2	32.5	25.3
			23.4		17.7	loop	37.0	34.0	35.1
MEAN			**21.3**		**31.8**		**36.5**	**33.1**	**26.9**
SODIUM (%/15 mins)			20.0		31.4		34.1	32.2	17.2
			17.5		41.3		39.1	35.0	21.9
			21.8		12.7		34.2	33.7	35.1
MEAN			**19.8**		**28.5**		**35.8**	**33.6**	**24.7**
CHLORIDE (%/15 mins)			23.7		34.9		34.6	29.0	18.3
			16.2		42.1		38.5	35.4	25.3
			22.9		17.8		32.6	34.9	32.3
MEAN			**20.9**		**31.6**		**35.2**	**33.1**	**25.3**
POTASSIUM EXCRETION (µmol/15mins)			81.6		80.3		76.2	60.9	80.2
			81.8		79.0		73.5	38.2	69.2
			87.6		104.6		68.5	84.2	93.9
MEAN			**83.7**		**88.0**		**72.7**	**61.1**	**81.1**
GLUCOSE (%/15MINS)			76.3		81.4		84.6	70.2	61.4
			72.9		92.1		79.0	55.6	63.8
			84.8		83.9		79.1	79.4	76.4
MEAN			**78.0**		**85.8**		**80.9**	**68.4**	**67.2**
PEG RECOVERY (%)			94.1		90.9		94.5	87.4	107.4
			95.5		88.3		103.1	89.3	100.2
			85.0		106.6		91.5	93.5	102.0
MEAN			**91.3**		**95.3**		**96.4**	**90.1**	**103.2**
TRANSIT TIME (mins)			6.6		3.0		2.3	2.7	2.4
			4.4		11.1		2.2	4.2	1.7
			10.4		4.1		2.3	6.0	6.4
MEAN			**7.1**		**6.1**		**2.3**	**4.3**	**3.5**

TABLE 6.2 : EXPERIMENTS AT WEEK 8

GLUCOSE ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2A	2B	2C	2D	2E	2F	2G	2H	
VOLUME (%/15 mins)	30.9	28.4	Unwell	18.8	27.9	Died	41.4	Poor	
	48.4	25.7	Not	23.2	45.1	of	30.1	PEG	
	20.8	36.5	studied			pneu-		recov-	
						monia		ery	
MEAN	**33.4**	**30.2**		**21.5**	**36.5**		**35.7**		
SODIUM (%/15 mins)	31.3	26.3		21.4	28.6		43.9		
	49.5	24.1		25.5	45.5		30.7		
	18.0	36.4							
MEAN	**32.9**	**28.9**		**23.4**	**37.0**		**37.3**		
CHLORIDE (%/15 mins)	33.8	33.5		24.0	30.0		42.1		
	51.7	25.0		20.8	45.0		30.9		
	17.3	40.8							
MEAN	**34.3**	**33.1**		**22.4**	**37.5**		**36.4**		
POTASSIUM EXCRETION (µmol/15mins)	65.5	90.4		44.5	49.2		90.0		
	65.2	85.1		46.0	51.0		74.8		
	118.8	79.9							
MEAN	**83.2**	**85.1**		**45.2**	**51.1**		**82.4**		
GLUCOSE (%/15mins)	67.0	67.9		33.0	72.2		91.7		
	82.0	66.6		40.2	79.1		74.8		
	77.0	76.9							
MEAN	**75.3**	**70.5**		**36.7**	**75.6**		**83.2**		
PEG RECOVERY (%)	88.6	93.6		89.3	103.4		98.5		
	85.6	93.9		93.9	89.0		87.6		
	92.5	88.1							
MEAN	**88.9**	**91.9**		**91.6**	**96.2**		**93.0**		
TRANSIT TIME (mins)	4.6	1.8		4.6	10.4		9.1		
	4.2	8.0		3.8	4.4		7.4		
	12.3	6.8							
MEAN	**7.0**	**5.5**		**4.2**	**7.4**		**8.2**		

TABLE 6.3 : EXPERIMENTS AT WEEK 1

GLUCOSE ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2A	2B	2C	2D	2E	2F	2G	2H
VOLUME (%/15 mins)		26.3	42.0	52.4	20.0	Died	7.7	50.2
		19.9		36.3	25.8	of	29.6	36.3
					18.9	pneu-		
						monia		
MEAN		**23.1**	**42.0**	**44.3**	**21.6**		**18.6**	**43.2**
SODIUM (%/15 mins)		24.9	41.7	57.4	17.5		9.8	49.7
		21.2		42.3	25.1		30.2	36.1
					20.9			
MEAN		**23.0**	**41.7**	**49.8**	**21.2**		**20.0**	**42.9**
CHLORIDE (%/15 mins)		25.5	44.7	56.5	19.1		8.5	47.9
		20.1		42.2	25.3		29.4	33.4
					21.8			
MEAN		**22.8**	**44.7**	**49.3**	**22.1**		**18.9**	**40.6**
POTASSIUM EXCRETION (µmol/15mins)		62.1	64.7	50.4	66.3		45.9	59.4
		57.4		55.4	57.9		32.0	40.6
					49.8			
MEAN		**59.7**	**64.7**	**52.9**	**58.0**		**38.9**	**50.0**
GLUCOSE (%/15mins)		65.5	79.5	86.2	52.7		35.9	80.0
		53.1		70.2	61.2		40.0	62.7
					49.6			
MEAN		**59.3**	**79.5**	**78.2**	**54.5**		**37.9**	**71.3**
PEG RECOVERY (%)		91.3	94.4	92.1	89.6		87.4	92.1
		105.4		92.1	88.8		91.1	85.9
					100.0			
MEAN		**98.3**	**94.4**	**92.1**	**92.8**		**89.2**	**89.0**
TRANSIT TIME (mins)		5.2	12.8	5.1	3.9		4.4	6.0
		3.4		6.5	2.8		2.0	4.1
					4.5			
MEAN		**4.3**	**12.8**	**5.8**	**3.7**		**3.3**	**5.0**

TABLE 6.4 : EXPERIMENTS AT WEEK 8

GLUCOSE ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	57.4	44.9	66.9	78.0	71.5	47.6
	42.9	42.1	69.4	74.2	49.2	62.1
		61.4		77.1	55.3	
MEAN	**50.1**	**49.5**	**68.1**	**76.4**	**58.7**	**54.8**
SODIUM (%/15 mins)	65.9	54.1	70.3	80.2	75.8	49.6
	52.9	51.4	71.0	76.0	49.7	65.6
		60.0		79.8	56.2	
MEAN	**59.4**	**55.2**	**70.6**	**78.7**	**60.6**	**58.6**
CHLORIDE (%/15 mins)	70.8	59.5	71.5	84.2	79.3	56.6
	60.0	54.0	72.5	81.2	67.3	70.3
		62.1		83.0	67.5	
MEAN	**65.4**	**58.5**	**72.0**	**82.8**	**71.4**	**63.4**
POTASSIUM EXCRETION (µmol/15mins)	118.2	86.1	97.2	60.4	117.3	106.1
	97.0	133.2	108.5	63.4	180.7	84.3
		82.5		64.6	133.7	
MEAN	**107.6**	**100.6**	**102.8**	**62.8**	**143.9**	**95.2**
GLUCOSE (%/15mins)	54.5	72.1	91.8	94.6	88.4	73.8
	49.5	79.2	97.0	98.1	95.1	86.0
		89.6		93.6	91.0	
MEAN	**52.0**	**80.3**	**94.4**	**95.4**	**91.5**	**79.9**
PEG RECOVERY (%)	86.6	85.9	85.0	111.3	99.7	109.4
	104.0	87.8	87.5	92.8	101.1	95.4
		93.1		101.3	89.9	
MEAN	**95.3**	**88.9**	**86.8**	**101.8**	**96.9**	**102.4**
TRANSIT TIME (mins)	10.0	5.1	7.4	15.6	15.0	16.1
	7.8	6.0	15.9	5.0	9.7	12.6
		7.6		17.9	9.4	
MEAN	**8.9**	**6.2**	**11.6**	**12.8**	**11.4**	**14.3**

TABLE 6.5 : EXPERIMENTS AT WEEK 1

GLUCOSE ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	Poor	32.2	55.2	64.9	30.5	47.5
	PEG	41.8	46.7		40.1	40.3
	recov-	40.7	61.1		44.2	46.8
	ery					
MEAN		**38.2**	**54.3**	**64.9**	**38.3**	**44.9**
SODIUM (%/15 mins)		32.0	63.9	68.5	35.7	52.3
		47.7	55.9		43.2	41.8
		48.1	65.3		48.2	47.2
MEAN		**42.6**	**61.7**	**68.5**	**42.4**	**47.1**
CHLORIDE (%/15 mins)		43.4	66.9	76.1	42.9	54.3
		52.5	59.5		51.3	45.5
		51.2	66.6		57.8	50.3
MEAN		**49.0**	**64.3**	**76.1**	**50.7**	**50.0**
POTASSIUM EXCRETION (µmol/15mins)		108.0	77.3	83.8	122.7	112.5
		75.4	90.2		158.7	99.6
		70.5	103.4		125.8	102.5
MEAN		**84.6**	**90.3**	**83.8**	**135.7**	**104.9**
GLUCOSE (%/15mins)		73.2	69.0	96.6	57.8	70.9
		66.5	68.2		66.8	77.1
		65.5	76.5		73.6	84.5
MEAN		**68.4**	**71.2**	**96.6**	**66.0**	**77.5**
PEG RECOVERY (%)		91.7	85.0	90.7	88.5	94.5
		93.0	97.1		100.0	93.9
		90.9	93.4		93.2	109.2
MEAN		**91.9**	**91.8**	**90.7**	**93.9**	**99.2**
TRANSIT TIME (mins)		3.0	8.7	8.0	7.6	6.2
		4.6	4.6		4.5	5.0
		5.5	14.8		5.0	6.0
MEAN		**4.4**	**9.4**	**8.0**	**5.7**	**5.7**

TABLE 6.6 : EXPERIMENTS AT WEEK 8

GLUCOSE ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H
VOLUME (%/15 mins)	46.4	48.8	42.6	61.0	46.0	57.1	32.1	Not
		48.0		62.2	44.6	60.4	29.6	studied
		51.2		66.0			47.0	
MEAN	**46.4**	**49.3**	**42.6**	**63.1**	**45.3**	**58.7**	**36.2**	
SODIUM (%/15 mins)	47.0	61.5	46.3	64.1	48.9	63.5	35.5	
		56.7		66.3	47.4	63.4	31.2	
		53.9		70.7			47.0	
MEAN	**47.0**	**57.4**	**46.3**	**67.0**	**48.2**	**63.4**	**37.9**	
CHLORIDE (%/15 mins)	55.8	58.9	50.4	68.1	50.5	65.8	50.5	
		61.2		69.3	56.2	81.8	47.0	
		56.6		73.6			55.8	
MEAN	**55.8**	**58.9**	**50.4**	**70.3**	**53.3**	**73.8**	**51.1**	
POTASSIUM EXCRETION (μmol/15mins)	100.6	65.5	97.6	61.3	255.2	141.4	218.9	
		74.6		84.8	193.2	94.5	206.2	
		63.1		124.9			160.4	
MEAN	**100.6**	**67.7**	**97.6**	**90.3**	**224.2**	**117.9**	**195.2**	
GLUCOSE (%/15mins)	80.9	59.9	65.2	76.9	66.3	69.5	84.8	
		72.6		79.1	76.8	81.8	88.9	
		71.6		76.7			84.9	
MEAN	**80.9**	**68.0**	**65.2**	**77.6**	**71.5**	**75.6**	**86.2**	
PEG RECOVERY (%)	111.3	93.2	98.8	89.9	86.0	97.6	95.6	
		86.2		91.7	90.7	96.8	107.4	
		88.1		93.2			104.1	
MEAN	**111.3**	**89.2**	**98.9**	**91.6**	**88.3**	**97.2**	**102.4**	
TRANSIT TIME (mins)	8.4	10.3	3.1	5.4	8.5	7.5	8.1	
		10.7		10.6	7.0	7.9	10.5	
		7.1		3.7			9.8	
MEAN	**8.4**	**9.4**	**3.1**	**6.6**	**7.8**	**7.7**	**9.5**	

TABLE 6.7 : EXPERIMENTS AT WEEK 1

GLUCOSE ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H
VOLUME (%/15 mins)	53.1	24.9	Cannula	45.3	45.6	Stoma	40.7	Poor
	17.6	37.4	abscess	46.9		and	43.3	PEG
	48.4	37.4		67.2		loop	38.5	recov-
						eaten		ery
MEAN	**39.7**	**33.2**		**53.1**	**45.6**		**40.8**	
SODIUM (%/15 mins)	55.3	29.4		50.6	50.8		44.3	
	30.2	49.3		53.5			45.7	
	60.2	50.7		73.1			39.7	
MEAN	**48.6**	**43.1**		**59.1**	**50.8**		**43.2**	
CHLORIDE (%/15 mins)	62.0	36.6		53.8	52.8		53.6	
	30.7	56.1		54.1			54.1	
	63.1	52.3		76.0			50.4	
MEAN	**51.9**	**48.3**		**62.8**	**52.8**		**52.7**	
POTASSIUM EXCRETION (µmol/15mins)	65.3	86.8		80.1	102.9		148.5	
	74.5	87.3		72.7			139.6	
	159.4	205.3		63.0			140.5	
MEAN	**99.7**	**126.5**		**71.9**	**102.9**		**142.9**	
GLUCOSE (%/15mins)	71.7	52.0		65.8	65.3		80.2	
	29.3	61.3		52.9			84.5	
	59.7	61.8		64.2			83.8	
MEAN	**53.6**	**58.4**		**61.0**	**65.3**		**82.8**	
PEG RECOVERY (%)	86.7	86.7		100.7	92.3		98.6	
	88.4	92.1		94.0			101.1	
	90.9	106.4		95.1			96.7	
MEAN	**88.7**	**95.1**		**96.6**	**92.3**		**98.8**	
TRANSIT TIME (mins)	3.9	11.3		3.2	3.9		3.5	
	2.4	6.2		2.9			2.6	
	2.1	3.7		2.4			3.2	
MEAN	**2.8**	**7.1**		**2.8**	**3.9**		**3.1**	

TABLE 6.8 : EXPERIMENTS AT WEEK 8

ANALYSIS OF VARIANCE TABLES : GLUCOSE

	Experiment : Jejunum	Criterion : Volume			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	1	1.3	<.01	>.900
CASE(TR)	14	1632	116.6	.50	.863
WK	1	231	231.2	1.00	.357
WKxTR	1	8	8.0	.03	.859
WKxCASE(TR)	6	1391	231.9	3.35	.011
ERROR	34	2355	69.3		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	9	33.1	8.6	7	33.4	6.8	-8.1 , 8.9

	Experiment : Jejunum	Criterion : Sodium			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	64	64.5	0.23	>.500
CASE(TR)	14	1778	127.0	0.45	.896
WK	1	213	213.1	0.76	.417
WKxTR	1	22	21.7	0.08	.790
WKxCASE(TR)	6	1684	280.7	3.35	.011
ERROR	34	2848	83.8		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	9	31.6	8.9	7	34.0	6.6	-6.1 , 10.8

TABLE 6.9 : RESULTS FOR VOLUME AND SODIUM (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : GLUCOSE

	Experiment : Jejunum	Criterion : Chloride			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	26	25.7	0.09	>.500
CASE(TR)	14	1505	107.5	0.38	.934
WK	1	249	248.8	0.89	.382
WKxTR	1	9	8.8	0.03	.865
WKxCASE(TR)	6	1680	279.9	3.69	.006
ERROR	34	2580	75.9		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

	Control			AutoTx			AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	9	33.2	9.0	7	34.4	6.5	-7.4 , 9.9

	Experiment : Jejunum	Criterion : Potassium			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	2831	2830.6	13.99	<.001
CASE(TR)	14	5138	367.0	1.81	.078
WK	1	792	792.0	3.91	.056
WKxTR	1	186	186.5	0.92	.344
WKxCASE(TR)	6	2486	414.4	2.05	.086
ERROR	34	6882	202.4		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment, Week, and Case (Treatment). The effect of Treatment is significant

From the above analysis an appropriate way of summarising the effect of the treatment is to use the individual results, which give the following:

	Control			AutoTx			AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	34	79.8	15.6	24	62.6	19.5	-26.5 , -8.0

There was a significant reduction in the mean potassium level in the autotransplant group.

TABLE 6.10 : RESULTS FOR CHLORIDE AND POTASSIUM (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : GLUCOSE

	Experiment : Jejunum	Criterion : Transit Time			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	35	35.3	6.26	.018
CASE(TR)	14	152	10.8	1.92	.061
WK	1	30	29.7	5.27	.028
WKxTR	1	1	1.2	0.22	.645
WKxCASE(TR)	6	35	5.8	1.03	.424
ERROR	33	185.8	5.63		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Case (Treatment). The effects of Week and Treatment are significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the individual results for each week and treatment, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	18	4.8	2.0	12	6.4	3.1	-0.2 , 3.6
8	15	4.6	2.9	12	5.1	2.8	-1.9 , 2.7

The mean Transit Time was higher for the autotransplant group than the control group and for Week 1 compared to Week 8.

	Experiment : Jejunum	Criterion : Glucose			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	1185	1185.2	1.58	>.100
CASE(TR)	14	2449	174.9	0.23	.988
WK	1	570	570.3	0.76	.416
WKxTR	1	19	19.1	0.03	.878
WKxCASE(TR)	6	4494	749.0	14.03	<.001
ERROR	34	1815	53.4		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	9	78.1	7.9	7	67.7	8.0	-18.9 , -1.8

Thus there is marginal evidence that jejunal autotransplantation results in a lower mean glucose level.

TABLE 6.11 : RESULTS FOR TRANSIT TIME AND GLUCOSE (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : GLUCOSE

	Experiment : Ileum		Criterion : Volume		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	646	646.3	1.90	0.20
CASE(TR)	11	3738	339.8	4.76	<.001
WK	1	980	980.4	13.74	<.001
WKxTR	1	167	167.1	2.34	.136
WKxCASE(TR)	8	468	58.5	0.82	.591
ERROR	33	2355	71.4		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment. The effects of Week and Case (Treatment) are significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	6	59.6	10.7	7	48.8	9.3	-23.0 , 1.4
8	5	48.1	11.5	5	42.5	7.4	-19.7 , 8.5

The difference between weeks was significant with 95% CI of -14.8 , -4.2 .

	Experiment : Ileum		Criterion : Sodium		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	545	545.2	1.59	.234
CASE(TR)	11	3779	343.5	4.94	<.001
WK	1	582	581.9	8.37	.007
WKxTR	1	249	248.6	3.58	.067
WKxCASE(TR)	8	437	54.6	0.79	.619
ERROR	33	2294	69.5		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment. The effects of Week and Case (Treatment) are significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	6	63.7	9.1	7	52.5	10.5	-23.3 , 0.8
8	5	52.5	11.9	5	49.0	6.6	-17.6 , 10.6

The difference between weeks was significant with 95% CI of -12.9 , -1.7 .

TABLE 6.12 : RESULTS FOR VOLUME AND SODIUM (ILEUM)

ANALYSIS OF VARIANCE TABLES : GLUCOSE

	Experiment : Ileum		Criterion : Chloride		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	519	518.8	1.95	.190
CASE(TR)	11	2922	265.7	4.49	<.001
WK	1	701	700.5	11.83	.002
WKxTR	1	140	140.1	2.37	.134
WKxCASE(TR)	8	314	39.3	0.66	.719
ERROR	33	1954	59.2		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment. The effects of Week and Case (Treatment) are significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	6	68.9	8.5	7	59.1	9.4	-20.8 , 1.1
8	5	58.0	11.9	5	53.4	4.8	-19.4 , 10.1

The difference between weeks was significant with 95% CI of -12.6 , -3.4.

	Experiment : Ileum		Criterion : Potassium		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	2569	2569.1	1.08	>.200
CASE(TR)	11	46455	4223.2	1.78	.211
WK	1	2143	2142.8	0.90	.369
WKxTR	1	1791	1790.6	0.76	.410
WKxCASE(TR)	8	18944	2368.0	2.76	.019
ERROR	33	28319	858.1		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	101.7	21.9	7	118.1	34.7	-20.0 , 52.6

TABLE 6.13 : RESULTS FOR CHLORIDE AND POTASSIUM (ILEUM)

ANALYSIS OF VARIANCE TABLES : GLUCOSE

	Experiment : Ileum		Criterion : Transit Time		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	111	110.9	12.40	.001
CASE(TR)	11	176	16.0	1.79	.096
WK	1	222	222.1	24.83	<.001
WKxTR	1	0	0.2	0.02	.877
WKxCASE(TR)	8	53	6.6	0.74	.655
ERROR	33	295	8.9		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Case (Treatment). The effects of Week and Treatment are significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the individual results for each week and treatment, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	15	10.7	4.4	15	7.9	2.4	-5.5 , -0.2
8	13	6.4	3.0	13	4.0	2.4	-4.7 , -0.3

There was a significant reduction in mean Transit Time from Week 1 to Week 8, the 95% CI being (-7.3, -1.3) for the controls and (-5.8 , -2.1) for the autotransplants.

	Experiment : Ileum		Criterion : Glucose		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	782	782.2	1.73	.215
CASE(TR)	11	4968	451.6	7.62	<.001
WK	1	1702	1702.3	28.74	<.001
WKxTR	1	0	0.3	0.00	.948
WKxCASE(TR)	8	987	123.4	2.08	.066
ERROR	33	1955	59.2		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment. The effects of Week and Case (Treatment) are significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	6	82.3	16.3	7	75.0	7.4	-24.9 , 10.4
8	5	76.0	12.3	5	64.2	11.2	-29.0 , 5.4

The difference between weeks was significant with 95% CI of -19.8 , -5.2 .

TABLE 6.14 : RESULTS FOR TRANSIT TIME AND GLUCOSE (ILEUM)

CHAPTER 7

RESULTS : GLYCINE

The mean values obtained for absorption in each experiment are shown in Tables 7.1-7.8 (pages 131-138) at the end of this chapter. These also show the mean value for all the experiments for each dog at each week studied. A total of 153 experiments were carried out in all four groups of dogs and 28 (18.3%) of these were excluded from further analysis because of poor PEG recovery. The number of experiments performed in each group over both study weeks (Week 1 and Week 8) were as follows:

	Number of experiments	
	Total	**Discarded (%)**
Group 1	39	2 (5.1%)
Group 2	39	12 (30.8%)
Group 3	36	7 (19.4%)
Group 4	39	7 (17.9%)

The experiments with poor PEG recovery were evenly spread out among the dogs in the ileal groups (Groups 3 and 4), but were significantly more in the jejunal autotransplant group (Group 2) than in the jejunal control group (Group 1) (chisquare test, $p<0.05$). Two dogs had a major problem with PEG recovery; Dog 2H had no valid experiments at Week 1, and only one out of three was valid at Week 8. There was no obvious cause for this. Dog 3A was similar, with no valid experiments at Week 1 but two of three with valid PEG recovery at Week 8.

VARIABILITY

Once again there is significant variability between dogs. This occurred with WKxCASE(TR) [comparing dogs of all groups over the weeks of study] for volume, sodium, chloride and glycine absorption in the jejunum and also for CASE(TR) [comparison among dogs of all groups] for potassium in the jejunum, and for sodium, chloride and glycine in the ileum.

ABSORPTION

The analysis of variance tables and the overall means with confidence intervals are at the end of this chapter (Tables 7.9-7.14, pages 139-144).

VOLUME

Jejunum

Autotransplantation : no effect ($p>0.4$).

Week of study : no effect ($p=0.375$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	14.2	15.2	-4.6, 6.7

The effect of week of study was not significant, so a single confidence was created.

These experiments were capable of detecting an increase or a decrease in absorption of more than 5.6%/15min.

Jejunal autotransplantation did not alter the volume of perfusate absorbed from this glycine solution.

Ileum

Autotransplantation : is significant ($p=0.03$).

Week of study : no effect ($p=0.356$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	38.4	34.6	-9.4, 1.7

A single confidence interval exists since the effect of week of study is not significant.

Absorption from the autotransplanted ileum was reduced.

The difference in mean absorption was 3.8%/15min, which is significant by ANOVA. This significant reduction in volume absorbed was not seen with sodium or chloride, which usually parallel it, this may mean that true significance does not exist.

SODIUM

Jejunum

Autotransplantation : no effect ($p>0.1$).

Week of study : no effect ($p=0.32$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I. of the difference
	16.0	18.0	-3.5, 7.6

The single confidence interval indicates that the effect of week of study was not significant.

These experiments were able to detect an increase or decrease in absorption of greater than 5.5%/15min.

Sodium absorption was unaltered by autotransplantation of the jejunum.

Ileum

Autotransplantation : no effect ($p=0.159$).

Week of study : no effect ($p=0.205$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	43.4	37.4	-15.0, 3.1

A single confidence interval indicates that the effect of week of study was not significant.

These experiments were capable of detecting an increase or decrease in absorption of greater than 9.0%/15min.

As with jejunum, ileal autotransplantation had no effect on sodium absorption.

CHLORIDE

Jejunum

Autotransplantation : no effect ($p>0.3$).

Week of study : no effect ($p=0.247$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	15.7	17.0	-4.0, 6.7

A single confidence interval exists since the effect of week of study was not significant.

These experiments would have detected an increase or decrease in absorption of more than 5.3%/15min.

Chloride absorption was not altered by jejunal autotransplantation; a finding which parallels that for sodium absorption.

Ileum

Autotransplantation : no effect (p=0.138).

Week of study : no effect (p=0.174).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	45.3	39.3	-14.9, 2.9

The effect of week of study was not significant, so there is a single confidence interval.

These experiments were capable of detecting an increase or decrease in absorption of greater than 8.9%/15min.

Chloride absorption was unaltered in the autotransplanted ileum.

POTASSIUM

Jejunum

Autotransplantation : no effect (p=0.868).

Week of study : is significant (p<0.001).

Secretion	Control Mean (μM/15min)	AutoTx Mean (μM/15min)	95% C.I.of the difference
Week 1	72.8	77.6	-49.0,58.3
Week 8	57.8	52.8	-18.0, 8.0

There is a separate confidence interval for each week, since the effect of week of study was significant.

At Week 1, these experiments were able to detect an increase or decrease in secretion of over 53.6μM/15min. At Week 8, the experiments would have detected an increase or decrease of greater than 13.0μM/15min.

Potassium secretion in autotransplanted jejunum was unaffected by autotransplantation.

There was a time effect which resulted in potassium secretion decreasing between Week 1 and Week 8 in both the control and autotransplant groups.

Ileum

Autotransplantation : no effect (p=0.254).

Week of study : is significant (p=0.02).

Secretion	Control Mean (μM/15min)	AutoTx Mean (μM/15min)	95% C.I.of the difference
Week 1	92.7	109.2	-20.0, 53.4
Week 8	69.0	80.2	-8.9, 31.3

The effect of week of study was significant: two separate confidence intervals were generated.

At Week 1 these experiments were capable of detecting an increase or decrease in secretion of over 36.7μM/15min. At Week 8, an increase or decrease in secretion of over 20.1μM/15min would have been detected.

Autotransplantation had no significant effect on potassium secretion in the ileum.

The time-specific effect was the same as that observed in the jejunum; there was a decrease in potassium secretion from Week 1 to Week 8 in both groups.

TRANSIT TIME

Jejunum

Autotransplantation : is significant (p=0.003).

Week of study : no effect (p=0.151).

Transit	Control Mean (min)	AutoTx Mean (min)	95% C.I.of the difference
	4.4	5.9	0.3, 2.6

A single confidence interval exists since the effect of week of study was not significant.

These experiments were capable of detecting an increase or decrease in transit time of 1.1min.

Autotransplantation significantly increased transit time.

This expected increase in transit time is not altered from Week 1 to Week 8, indicating that the enteric neurones have not yet regenerated across the anastomotic site which would allow the migrating myoelectric complex to pass.

Ileum

Autotransplantation : no effect (p=0.702).

Week of study : is significant (p<0.001).

Transit	Control Mean (min)	AutoTx Mean (min)	95% C.I.of the difference
Week 1	9.3	10.0	-2.0, 3.4
Week 8	6.9	6.1	-2.7, 1.2

The effect of week of study was significant so two separate confidence intervals were produced.

The experiments at Week 1 were capable of detecting an increase or decrease in transit time of over 2.7min. At Week 8, the experiments would have detected an increase or decrease of over 1.9min.

Transit time in the ileum was not significantly altered by autotransplantation.

Transit time was slower in the autotransplanted ileum at Week 1, but by Week 8, transit in autotransplanted ileum was actually faster than in the controls. The reason for this is not clear, nor is the reason for transit time becoming shorter from Week 1 to Week 8 in both groups of dogs.

GLYCINE

Jejunum

Autotransplantation : no effect ($p>0.05$).

Week of study : no effect ($p=0.426$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	75.2	66.2	-15.6, -2.4

The effect of week of study is not significant, so a single confidence interval exists.

These experiments would have detected an increase or decrease in absorption of over 6.6%/15min.

Jejunal autotransplantation did not result in a statistically significant decrease in glycine absorption.

It may be that glycine absorption is impaired in autotransplanted jejunum, but this study has not studied enough dogs to prove it.

Ileum

Autotransplantation : is significant (p=0.039).

Week of study : no effect (p=0.571).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	83.4	72.3	-22.3, 0.1

A single confidence interval exists since the effect of week of study was not significant.

These experiments were capable of detecting an increase or decrease in glycine absorption of over 11.1%/15min.

Glycine absorption was reduced by autotransplantation of the ileum.

Summary

Absorption of sodium and chloride was not affected by autotransplantation of jejunum or ileum.

Volume of perfusate absorbed was only reduced in autotransplanted ileum, not jejunum.

Potassium secretion was unaffected by autotransplantation in both jejunum and ileum.

Transit was significantly slower in autotransplanted jejunum, but was not affected by autotransplantation of the ileum. Ileum, however, was found to have a significantly shorter transit time at Week 8 than at Week 1 in both groups of dogs.

Glycine absorption was significantly impaired in autotransplanted ileum.

A time effect was noted only with potassium secretion; this was significantly reduced at Week 8 as compared to Week 1. This occurred in both jejunum and ileum, and in both control and autotransplant groups.

GLYCINE ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	1B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	26.3	12.8	Cannula	10.1	12.4	18.6	20.8	12.1	17.5
	27.7	5.3	came	11.1	13.2	14.1	18.3	9.2	19.7
	29.3	1.9	out	17.1	8.6	13.3	12.1	9.1	31.0
MEAN	**27.8**	**6.7**		**12.8**	**11.4**	**15.3**	**17.1**	**10.1**	**22.7**
SODIUM (%/15 mins)	26.6	15.3		9.3	14.4	19.6	25.6	18.7	18.8
	29.3	11.2		12.5	14.5	18.4	23.0	12.5	17.3
	30.2	2.3		19.2	11.9	13.4	14.9	10.3	32.4
MEAN	**28.7**	**9.6**		**13.7**	**13.6**	**17.1**	**21.2**	**14.6**	**12.8**
CHLORIDE (%/15 mins)	27.1	17.7		10.5	14.5	18.6	22.7	19.9	16.4
	30.2	7.8		9.0	9.1	17.0	27.8	12.7	21.2
	29.0	5.6		15.8	10.0	15.1	16.4	10.3	33.3
MEAN	**28.8**	**10.4**		**11.8**	**11.2**	**16.9**	**22.2**	**14.3**	**23.6**
POTASSIUM EXCRETION (µmol/15mins)	57.1	110.9		47.7	81.7	65.9	55.7	74.5	75.3
	61.4	125.8		48.2	78.5	58.4	56.4	80.4	77.1
	59.8	96.6		85.8	76.0	59.4	72.2	66.0	77.1
MEAN	**59.4**	**111.1**		**60.6**	**78.7**	**61.2**	**61.4**	**73.6**	**76.5**
GLYCINE (%/15mins)	88.5	69.7		49.3	80.0	88.8	85.3	77.7	83.3
	78.1	71.9		47.1	76.9	72.7	80.4	74.4	86.0
	74.0	60.7		91.0	77.0	73.7	76.6	69.3	91.7
MEAN	**80.2**	**67.4**		**62.5**	**78.0**	**78.4**	**80.8**	**73.8**	**87.0**
PEG RECOVERY (%)	89.1	104.9		91.9	99.1	95.7	85.7	89.3	106.3
	88.8	92.9		103.8	97.0	96.3	86.5	98.9	109.5
	94.8	110.6		96.6	100.8	94.5	93.3	101.2	88.8
MEAN	**90.9**	**102.8**		**97.4**	**99.0**	**95.5**	**88.5**	**96.5**	**101.5**
TRANSIT TIME (mins)	8.7	4.7		5.3	4.8	4.6	2.0	6.6	2.1
	10.0	2.8		2.5	4.9	8.6	4.0	6.8	1.7
	3.8	2.1		4.1	5.2	3.1	4.9	4.2	6.4
MEAN	**7.5**	**3.2**		**4.0**	**5.0**	**5.4**	**3.6**	**5.9**	**3.4**

TABLE 7.1 : EXPERIMENTS AT WEEK 1

GLYCINE ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	1B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	Prolapse	Fistula	6.8	Fistula	15.1	Ripped	9.9	23.2	12.8
	of		14.1		-4.9	out	11.1	11.0	16.9
	stoma		8.2			loop	15.7		19.6
MEAN			**9.7**		**5.1**		**12.2**	**17.1**	**16.4**
SODIUM (%/15 mins)			9.4		17.1		13.6	28.1	12.6
			14.1		-5.8		12.8	12.3	19.6
			8.2				14.0		19.5
MEAN			**10.6**		**5.7**		**13.5**	**20.2**	**17.2**
CHLORIDE (%/15 mins)			11.2		13.0		12.6	24.8	11.9
			20.4		-1.3		11.1	11.7	16.1
			12.3				11.2		16.4
MEAN			**14.6**		**5.9**		**11.6**	**18.2**	**14.8**
POTASSIUM EXCRETION (μmol/15mins)			56.4		69.7		50.4	43.7	55.7
			58.2		80.2		47.1	62.7	56.8
			53.3				50.3		54.7
MEAN			**56.0**		**74.9**		**49.3**	**53.2**	**55.7**
GLYCINE (%/15mins)			69.2		84.3		81.3	70.1	67.0
			79.3		74.0		72.7	71.5	69.2
			74.7				77.3		69.2
MEAN			**74.4**		**79.1**		**77.1**	**70.8**	**68.5**
PEG RECOVERY (%)			96.1		102.0		90.0	85.4	100.4
			102.2		106.4		100.7	102.5	89.0
			95.8				92.3		85.0
MEAN			**98.0**		**104.2**		**94.3**	**93.9**	**91.1**
TRANSIT TIME (mins)			3.6		6.4		1.6	2.1	2.9
			2.7		4.9		2.0	2.3	7.8
			4.0				2.8		5.4
MEAN			**3.4**		**5.6**		**2.1**	**2.2**	**5.4**

TABLE 7.2 : EXPERIMENTS AT WEEK 8

GLYCINE ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2A	2B	2C	2D	2E	2F	2G	2H
VOLUME (%/15 mins)	8.7	2.2	Unwell	19.7	29.4	Died	16.8	Poor
	10.6	4.7	Not	18.4	21.6	of	14.9	PEG
			studied			pneu-	7.5	recov-
						monia		ery
MEAN	**9.6**	**3.4**		**19.0**	**25.5**		**13.1**	
SODIUM (%/15 mins)	12.3	4.7		24.3	31.0		18.3	
	15.8	5.2		20.9	22.4		20.0	
							11.2	
MEAN	**14.1**	**4.9**		**22.6**	**26.7**		**16.5**	
CHLORIDE (%/15 mins)	12.2	8.1		20.7	29.6		14.1	
	12.9	9.2		19.3	21.6		18.5	
							5.0	
MEAN	**12.5**	**8.6**		**19.9**	**25.6**		**12.5**	
POTASSIUM EXCRETION (µmol/15mins)	150.7	90.4		38.0	46.3		66.6	
	133.5	78.7		37.7	49.6		82.8	
							77.5	
MEAN	**142.1**	**84.5**		**37.8**	**47.9**		**75.6**	
GLYCINE (%/15mins)	60.0	56.0		54.3	74.2		74.7	
	67.0	56.4		49.9	77.9		81.2	
							71.9	
MEAN	**63.5**	**56.2**		**53.1**	**76.0**		**75.9**	
PEG RECOVERY (%)	104.1	94.3		88.5	92.5		100.3	
	87.9	108.4		94.9	88.8		96.7	
							90.5	
MEAN	**96.0**	**101.3**		**91.7**	**90.6**		**95.8**	
TRANSIT TIME (mins)	6.2	5.0		2.8	4.7		12.9	
	10.3	7.1		4.9	6.7		7.1	
							5.8	
MEAN	**8.2**	**6.0**		**3.8**	**5.7**		**8.6**	

TABLE 7.3 : EXPERIMENTS AT WEEK 1

GLYCINE ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2A	2B	2C	2D	2E	2F	2G	2H
VOLUME (%/15 mins)	Fistula	7.6	20.1	17.7	9.1	Died	11.3	22.9
		10.1	23.3		14.3	of	7.7	
		16.1	29.3		9.5	pneu-		
						monia		
MEAN		**11.3**	**24.2**	**17.7**	**11.0**		**8.5**	**22.9**
SODIUM (%/15 mins)		11.5	24.1	21.3	11.7		13.4	24.9
		10.5	27.5		18.3		11.8	
		17.5	29.8		12.5			
MEAN		**13.2**	**27.1**	**21.3**	**14.2**		**12.6**	**24.9**
CHLORIDE (%/15 mins)		13.8	26.0	19.4	10.3		10.3	21.5
		14.1	28.4		16.5		8.0	
		23.6	28.3		13.4			
MEAN		**17.2**	**27.6**	**19.4**	**13.4**		**9.1**	**21.5**
POTASSIUM EXCRETION (µmol/15mins)		55.6	50.7	45.8	39.5		68.7	55.5
		59.2	40.8		48.8		67.4	
		55.1	45.8		46.6			
MEAN		**56.6**	**45.8**	**45.8**	**45.0**		**68.0**	**55.5**
GLYCINE (%/15mins)		64.9	60.7	62.3	61.1		75.0	79.2
		64.9	68.4		61.2		65.0	
		69.2	79.6		49.6			
MEAN		**66.3**	**69.6**	**62.3**	**57.3**		**70.0**	**79.2**
PEG RECOVERY (%)		91.5	112.4	94.7	91.2		86.0	105.7
		95.3	87.5		88.1		88.8	
		99.5	91.1		94.7			
MEAN		**95.4**	**97.0**	**94.7**	**91.3**		**87.4**	**105.7**
TRANSIT TIME (mins)		5.1	8.3	4.7	3.1		5.4	6.6
		6.1	5.6		2.9		6.7	
		3.7	5.0		4.6			
MEAN		**5.0**	**6.3**	**4.7**	**3.5**		**6.0**	**6.6**

TABLE 7.4 : EXPERIMENTS AT WEEK 8

GLYCINE ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	Poor	28.6	36.1	47.0	46.3	21.4
	PEG	50.4	46.5	38.2	55.4	47.4
	recov-	33.1	47.8	46.2	38.8	
	ery					
MEAN		**37.4**	**43.5**	**43.8**	**46.8**	**34.4**
SODIUM (%/15 mins)		37.4	44.7	49.8	51.2	25.2
		53.4	55.6	43.8	61.2	51.3
		35.4	54.5	49.5	41.8	
MEAN		**42.1**	**51.6**	**47.7**	**51.4**	**38.2**
CHLORIDE (%/15 mins)		37.8	43.6	51.2	53.1	31.2
		55.9	55.4	42.2	64.1	54.5
		39.4	53.1	51.6	50.5	
MEAN		**44.4**	**50.7**	**48.3**	**55.9**	**42.8**
POTASSIUM EXCRETION (µmol/15mins)		163.1	108.0	92.8	81.6	93.4
		79.6	89.2	77.9	118.0	70.6
		77.8	82.4	53.9	109.0	
MEAN		**106.8**	**93.2**	**74.9**	**102.9**	**82.0**
GLYCINE (%/15mins)		55.3	86.0	85.6	90.8	87.0
		88.2	77.1	82.6	95.3	93.3
		79.9	90.6	83.6	93.1	
MEAN		**74.5**	**84.6**	**83.9**	**93.1**	**91.1**
PEG RECOVERY (%)		93.0	88.0	88.2	85.2	88.1
		89.7	97.5	91.3	88.8	85.0
		87.8	96.6	87.5	94.9	
MEAN		**91.2**	**94.0**	**89.0**	**89.6**	**86.5**
TRANSIT TIME (mins)		7.8	8.2	8.7	9.6	8.8
		6.0	9.5	9.6	15.2	8.4
		4.1	8.4	13.7	12.8	
MEAN		**6.0**	**8.7**	**10.7**	**12.5**	**8.6**

TABLE 7.5 : EXPERIMENTS AT WEEK 1

GLYCINE ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	38.4	27.2	32.0	51.9	24.7	34.7
	43.4	43.2	35.3		34.8	28.2
			39.9		25.2	34.6
MEAN	**40.9**	**35.2**	**35.7**	**51.9**	**28.2**	**32.5**
SODIUM (%/15 mins)	44.5	33.0	35.7	56.5	27.7	38.1
	48.4	37.1	41.7		37.0	31.2
			45.9		31.9	39.2
MEAN	**46.5**	**35.0**	**41.1**	**56.5**	**32.2**	**35.8**
CHLORIDE (%/15 mins)	46.3	36.2	38.5	57.3	29.6	38.9
	52.4	40.8	43.8		41.9	30.3
			46.5		27.4	38.4
MEAN	**49.3**	**38.5**	**42.9**	**57.3**	**33.0**	**35.9**
POTASSIUM EXCRETION (μmol/15mins)	74.4	51.4	72.4	51.5	73.5	61.8
	73.2	73.5	81.7		67.4	73.1
			76.1		72.8	62.6
MEAN	**73.8**	**62.4**	**76.7**	**51.5**	**71.2**	**65.8**
GLYCINE (%/15mins)	82.3	67.8	77.1	84.9	73.6	82.8
	89.6	89.0	89.2		80.6	81.3
			82.8		76.5	82.3
MEAN	**85.6**	**78.4**	**83.0**	**84.9**	**76.9**	**82.1**
PEG RECOVERY (%)	90.4	93.5	103.3	85.2	86.7	94.5
	91.3	106.0	95.4		86.5	86.9
			91.7		94.2	100.5
MEAN	**90.8**	**99.5**	**96.8**	**85.2**	**89.1**	**94.0**
TRANSIT TIME (mins)	4.4	3.6	6.2	7.2	8.5	7.8
	9.4	4.5	10.9		4.9	9.2
			10.3		5.4	4.0
MEAN	**6.9**	**4.0**	**9.1**	**7.2**	**6.3**	**7.0**

TABLE 7.6 : EXPERIMENTS AT WEEK 8

GLYCINE ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H
VOLUME (%/15 mins)	7.2	39.2	21.7	41.5	36.5	57.4	35.9	Not
	45.5	39.5	16.1	33.7	41.0	32.6	17.8	studied
		25.6		48.6		46.2	54.0	
MEAN	**26.3**	**34.8**	**18.9**	**41.3**	**38.7**	**45.4**	**35.9**	
SODIUM (%/15 mins)	13.4	43.2	26.3	48.7	41.8	60.6	42.0	
	49.3	42.2	19.9	37.1	44.6	36.1	21.7	
		27.6		53.4		52.5	57.1	
MEAN	**31.3**	**37.7**	**23.1**	**46.4**	**43.2**	**49.7**	**40.3**	
CHLORIDE (%/15 mins)	13.5	46.2	30.4	49.7	43.3	63.3	43.5	
	47.8	42.2	22.7	44.8	42.7	43.3	25.3	
		34.9		54.2		53.0	60.9	
MEAN	**30.6**	**41.4**	**26.5**	**49.6**	**43.0**	**53.2**	**43.2**	
POTASSIUM EXCRETION (µmol/15mins)	101.9	47.9	68.2	308.4	207.7	90.0	186.8	
	67.5	31.2	56.9	117.8	92.5	87.9	127.1	
		39.1		101.0		157.5	76.6	
MEAN	**84.7**	**39.4**	**62.5**	**175.7**	**150.1**	**111.8**	**130.2**	
GLYCINE (%/15mins)	66.1	76.5	62.4	72.6	77.8	90.8	74.3	
	83.1	82.0	50.5	78.2	82.8	83.8	72.4	
		55.6		87.4		85.6	83.2	
MEAN	**74.6**	**71.4**	**56.5**	**79.4**	**80.3**	**86.7**	**76.6**	
PEG RECOVERY (%)	96.1	92.3	93.1	89.1	94.5	93.3	88.6	
	87.8	96.1	98.7	89.4	85.4	94.7	113.6	
		115.0		107.2		101.5	89.4	
MEAN	**91.9**	**101.3**	**95.9**	**95.2**	**90.0**	**96.5**	**97.2**	
TRANSIT TIME (mins)	13.0	6.4	6.6	10.7	9.9	11.7	8.7	
	9.5	7.2	7.0	6.0	6.9	7.7	22.5	
		7.3		10.7		13.6	15.5	
MEAN	**11.3**	**7.0**	**6.8**	**9.1**	**8.4**	**11.0**	**15.6**	

TABLE 7.7 : EXPERIMENTS AT WEEK 1

GLYCINE ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H
VOLUME (%/15 mins)	18.9	25.2	Cannula	37.9	52.0	Stoma	21.9	16.2
	31.0	32.8	abscess	42.0	35.2	and	39.4	33.8
				44.3		loop	37.2	
						eaten		
MEAN	**24.9**	**29.0**		**41.4**	**43.6**		**32.8**	**25.0**
SODIUM (%/15 mins)	21.8	31.7		39.8	58.4		23.5	21.6
	37.7	38.6		45.9	39.7		36.7	40.7
				47.9			39.5	
MEAN	**29.8**	**35.2**		**44.5**	**49.0**		**33.2**	**31.1**
CHLORIDE (%/15 mins)	20.9	34.0		45.9	59.5		26.5	17.3
	39.4	40.6		48.2	42.3		39.7	40.1
				50.5			44.5	
MEAN	**30.1**	**37.3**		**48.2**	**50.9**		**36.9**	**28.7**
POTASSIUM EXCRETION (µmol/15mins)	57.4	140.3		98.2	76.6		71.1	41.2
	157.6	83.2		54.4	47.2		78.7	96.5
				54.5			65.3	
MEAN	**107.5**	**111.7**		**69.0**	**61.9**		**71.7**	**68.8**
GLYCINE (%/15mins)	51.5	81.9		86.6	94.2		58.7	38.7
	75.0	79.1		80.4	85.8		80.8	62.3
				78.9			78.5	
MEAN	**63.2**	**80.5**		**82.0**	**90.0**		**72.7**	**50.5**
PEG RECOVERY (%)	86.0	92.3		95.6	112.2		87.9	90.1
	86.8	96.8		91.9	95.2		106.6	111.4
				94.8			90.5	
MEAN	**86.4**	**94.5**		**94.1**	**103.7**		**95.0**	**100.7**
TRANSIT TIME (mins)	6.8	3.8		7.8	2.3		4.9	2.8
	4.9	7.6		11.1	7.6		9.0	4.6
				3.8			8.7	
MEAN	**5.8**	**5.7**		**7.6**	**4.9**		**7.5**	**3.7**

TABLE 7.8 : EXPERIMENTS AT WEEK 8

ANALYSIS OF VARIANCE TABLES : GLYCINE

	Experiment : Jejunum	Criterion : Volume			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	42	41.8	0.55	>.400
CASE(TR)	14	1930	137.9	1.81	.238
WK	1	70	69.8	0.92	.375
WKxTR	1	0	0.2	0.00	.961
WKxCASE(TR)	6	456	76.0	3.47	.008
ERROR	37	811	21.9		

The interaction Week x Case (Treatment) is significant and , against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination , which gives the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	13	14.2	6.3	11	15.2	7.1	-4.6 , 6.7

	Experiment : Jejunum	Criterion : Sodium			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	114	114.0	1.57	>.100
CASE(TR)	14	1830	130.7	1.81	.240
WK	1	85	85.1	1.18	.320
WKxTR	1	4	4.1	0.06	.819
WKxCASE(TR)	6	434	72.3	2.64	.031
ERROR	37	1015	27.4		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	13	16.0	6.2	11	18.0	7.0	-3.5 , 7.6

TABLE 7.9 : RESULTS FOR VOLUME AND SODIUM (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : GLYCINE

	Experiment : Jejunum	Criterion : Chloride			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	61	60.8	0.86	>.300
CASE(TR)	14	1657	118.3	1.67	.273
WK	1	117	116.6	1.65	.247
WKxTR	1	25	25.0	0.35	.574
WKxCASE(TR)	6	425	70.8	3.00	.017
ERROR	37	872	23.6		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	13	15.7	6.2	11	17.0	6.4	-4.0 , 6.7

	Experiment : Jejunum	Criterion : Potassium			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	42	42.1	0.03	.868
CASE(TR)	14	20555	1468.2	22.23	<.001
WK	1	1098	1098.3	16.63	<.001
WKxTR	1	101	101.2	1.53	.224
WKxCASE(TR)	6	912	152.1	2.30	.055
ERROR	37	2444	66.1		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment. The effects of Week and Case (Treatment) are significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	8	72.8	17.4	5	77.6	40.8	-49.0 , 58.3
8	5	57.8	10.0	6	52.8	9.1	-18.0 , 8.0

The difference between weeks was significant with 95% CI of -20.8 , -1.2.

TABLE 7.10 : RESULTS FOR CHLORIDE AND POTASSIUM (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : GLYCINE

	Experiment : Jejunum	Criterion : Transit Time			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	39	38.6	10.41	.003
CASE(TR)	14	87	6.2	1.67	.106
WK	1	8	8.0	2.15	.151
WKxTR	1	1	0.8	0.23	.636
WKxCASE(TR)	6	30	5.0	1.35	.260
ERROR	37	137	3.7		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment, Week, and Case (Treatment). The effect of Treatment is significant.

From the above analysis an appropriate way of summarising the effect of treatment is to use the individual results for each treatment, which gives the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	37	4.4	2.1	24	5.9	2.3	0.35 , 2.65

	Experiment : Jejunum	Criterion : Glycine			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	693	692.8	4.00	>.050
CASE(TR)	14	1915	136.8	0.87	.615
WK	1	115	115.0	0.73	.426
WKxTR	1	55	55.3	0.35	.575
WKxCASE(TR)	6	945	157.5	2.59	.034
ERROR	37	2249	60.8		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	13	75.2	6.6	11	66.2	8.9	-15.6 , -2.4

TABLE 7.11 : RESULTS FOR TRANSIT TIME AND GLYCINE (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : GLYCINE

	Experiment : Ileum		Criterion : Volume		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	526	525.7	5.12	.030
CASE(TR)	12	2306	192.1	1.87	.072
WK	1	90	89.5	0.87	.356
WKxTR	1	34	34.3	0.33	.566
WKxCASE(TR)	8	500	62.5	0.61	.764
ERROR	36	3693	102.6		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment, Week, and Case (Treatment). The effect of Treatment is significant

From the above analysis an appropriate way of summarising the effect of treatment is to use the individual results for each treatment, which gives the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	28	38.4	9.0	32	34.6	12.0	-9.4 , 1.7

	Experiment : Ileum		Criterion : Sodium		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	537	536.9	2.64	.159
CASE(TR)	12	2443	203.5	2.05	.048
WK	1	165	165.4	1.67	.205
WKxTR	1	63	63.1	0.64	.430
WKxCASE(TR)	8	548	68.4	0.69	.697
ERROR	36	3572	99.2		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant .

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	43.4	5.0	8	37.4	9.1	-15.0 , 3.1

TABLE 7.12 : RESULTS FOR VOLUME AND SODIUM (ILEUM)

ANALYSIS OF VARIANCE TABLES : GLYCINE

	Experiment : Ileum	Criterion : Chloride			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	559	558.8	2.52	.138
CASE(TR)	12	2657	221.5	2.42	.020
WK	1	176	176.0	1.93	.174
WKxTR	1	109	109.3	1.20	.281
WKxCASE(TR)	8	683	85.4	0.93	.501
ERROR	36	3289	91.4		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	45.3	4.5	8	39.3	10.0	-14.9 , 2.9

	Experiment : Ileum	Criterion : Potassium			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	2253	2253.1	1.34	.254
CASE(TR)	12	13156	1096.3	0.65	.783
WK	1	9908	9907.8	5.90	.020
WKxTR	1	81	81.0	0.05	.827
WKxCASE(TR)	8	29234	3654.2	2.18	.053
ERROR	36	60413	1678.1		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Case (Treatment). The effect of Week is significant. The effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of week is to use the individual results for each week and treatment, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	14	92.7	26.2	18	109.2	69.2	-20.0 , 53.4
8	14	69.0	9.0	14	80.2	33.9	-8.9 , 31.3

There was a significant reduction in mean potassium secretion from Week 1 to Week 8, the 95% CI being (-39.4 , -8.0) for the Controls and (-67.5 , -9.0) for the autotransplants.

TABLE 7.13 : RESULTS FOR CHLORIDE AND POTASSIUM (ILEUM)

ANALYSIS OF VARIANCE TABLES : GLYCINE

	Experiment : Ileum		Criterion : Transit Time		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	1	1.2	0.15	.702
CASE(TR)	12	194	16.2	2.03	.051
WK	1	125	124.5	15.61	<.001
WKxTR	1	6	5.6	0.70	.408
WKxCASE(TR)	8	81	10.1	1.27	.292
ERROR	36	287	8.0		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Case (Treatment). The effect of Week is significant. The effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the individual results for each week and treatment, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	14	9.3	2.9	18	10.0	4.2	-2.0 , 3.4
8	14	6.9	2.5	14	6.1	2.6	-2.7 , 1.2

There was a significant reduction in mean Transit Time from Week 1 to Week 8, the 95% CI being (-4.6,-0.4) for Controls and (-6.5 , -1.3) for the autotransplants.

	Experiment : Ileum		Criterion : Glycine		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	1500	1500.5	5.37	.039
CASE(TR)	12	3351	279.3	3.58	.002
WK	1	26	25.5	0.33	.571
WKxTR	1	85	85.1	1.09	.303
WKxCASE(TR)	8	687	85.8	1.10	.385
ERROR	36	2806	78.0		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	83.4	3.7	8	72.3	13.1	-22.3 , 0.1

TABLE 7.14 RESULTS FOR TRANSIT TIME AND GLYCINE (ILEUM)

CHAPTER 8

RESULTS : PHENYLALANINE

The mean values obtained for absorption in each experiment are shown in Tables 8.1-8.8 (pages 155-162) at the end of this chapter. These also show the mean value for all the experiments for each dog at each week studied. A total of 150 experiments were carried out in all four groups of dogs and 31 (20.7%) of these were excluded from further analysis because of poor PEG recovery. The number of experiments performed in each group over the two study weeks (Week 1 and Week 8) were as follows:

	Number of experiments	
	Total	**Discarded (%)**
Group 1	39	9 (23.1%)
Group 2	36	8 (22.2%)
Group 3	36	9 (25.0%)
Group 4	39	5 (12.8%)

Once again the experiments with poor PEG recovery were distributed at random among dogs of all groups (chisquare test, $p>0.5$).

VARIABILITY

Inter-dog variability was again significant in the jejunum for volume, sodium and phenylalanine as seen by WKxCASE(TR) [comparing all dogs over weeks of study], and for chloride, potassium and transit time by CASE(TR) [comparing all dogs of both groups]. The ileal dogs exhibited less variability, with significance only reached for volume, sodium and chloride by CASE(TR) [comparing among dogs of both groups].

ABSORPTION

The analysis of variance tables and the mean results of all the phenylalanine experiments are at the end of this chapter (Tables 8.9-8.14, pages 163-168).

VOLUME

Jejunum

Autotransplantation : no effect ($p>0.1$).

Week of study : no effect ($p=0.873$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	12.6	16.3	-3.0, 10.4

The effect of week of study was not significant, so there is one confidence interval.

These experiments were capable of detecting an increase or decrease in absorption of over 5.3%/15min.

Volume of perfusate absorbed from the phenylalanine solution was not altered by autotransplantation of the jejunum.

Ileum

Autotransplantation : no effect ($p=0.494$).

Week of study : no effect ($p=0.883$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	29.6	33.6	-4.2, 12.0

The single confidence interval indicates that effect of week of study was not significant.

These experiments were able to detect an increase or decrease in absorptiom of over 8.1%/15min.

Autotransplantation had no effect on volume of perfusate absorbed from the ileum.

SODIUM

Jejunum

Autotransplantation : no effect ($p>0.3$).

Week of study : no effect ($p=0.928$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	13.5	17.6	-2.5, 10.7

The single confidence interval indicates no significant effect with week of study.

These experiments were able to detect an increase or decrease in absorption of greater than 6.6%/15min.

Sodium absorption was not significantly changed by jejunal autotransplantation.

Ileum

Autotransplantation : no effect ($p=0.443$).

Week of study : no effect ($p=0.801$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	34.0	38.3	-4.2, 12.8

The effect of week of study was not significant, so there is one confidence interval.

These experiments would have detected an increase or decrease in absorption of greater than 8.5%/15min.

Sodium absorption was unaltered by autotransplantation of the ileum.

CHLORIDE

Jejunum

Autotransplantation : no effect (p=0.249).

Week of study : is significant (p=0.018).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
Week 1	15.4	18.3	-5.3, 11.0
Week 8	12.1	16.0	-4.6, 12.4

Since effect of week of study was significant, two separate confidence exist.

At Week 1, the experiments were capable of detecting an increase or decrease in absorption of more than 8.1%/15min. At Week 8, the increase or decrease detectable was 8.5%/15min.

Chloride absorption was not affected by jejunal autotransplantation.

The time-specific effect was reduced chloride absorption in both groups between Week 1 and Week 8. This finding was not seen with sodium, yet absorption of these two ions closely parallels each other. This may mean that significance does not truly exist. This seems likely for two reasons: firstly, chloride absorption was unaffected with time in the jejunum with the other test solutions, and, secondly, sodium absorption from this solution was unaffected with time in the jejunum.

Ileum

Autotransplantation : no effect (p=0.662).

Week of study : no effect (p=0.694).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	35.7	38.3	-6.9, 12.0

There was no effect with week of study, so there is a single confidence interval.

These experiments would have detected an increase or decrease in absorption of greater than 9.4%/15min.

Autotransplantation of the ileum had no effect on chloride absorption.

Week of study made no difference to chloride absorption. This tends to supports the belief that the significant decrease with time seen in the jejunum is spurious, since these experiments with the other solutions have indicated that ileum appears to be more sensitive to defunctioning than jejunum.

POTASSIUM

Jejunum

Autotransplantation : no effect (p=0.572).

Week of study : is significant (p=0.027).

Secretion	Control Mean (μM/15min)	AutoTx Mean (μM/15min)	95% C.I.of the difference
Week 1	75.2	75.8	-21.3, 22.6
Week 8	66.8	54.7	-25.5, 1.3

There is a separate confidence interval for each week since effect of week of study was significant.

At Week 1, these experiments were capable of detecting an increase or decrease in secretion of greater than 21.9μM/15min. The experiments at Week 8 were capable of detecting an increase or decrease of over 13.4μm/15min.

Autotransplantation of the jejunum did not affect potassium secretion.

There was a time-dependent effect on secretion. This was a decrease in potassium secretion in both groups of dogs between Week 1 and Week 8. This was almost certainly the result of defunctioning, with both innervated and denervated loops equally affected.

Ileum

Autotransplantation : no effect (p=0.353).

Week of study : is significant (p=0.01).

Secretion	Control Mean (μM/15min)	AutoTx Mean (μM/15min)	95% C.I.of the difference
Week 1	79.8	130.2	3.0, 97.8
Week 8	70.1	69.0	-13.9, 11.7

The effect of week of study was significant, so two confidence intervals exist.

The experiments at Week 1 were able to detect an increase or decrease in secretion of greater than 47.4μM/15mins. At Week 8, the experiments would have detected an increase or decrease in secretion of more than 12.8μM/15min.

Autotransplantation had no significant effect on ileal potassium secretion.

The time-dependent reduction in potassium secretion was seen in the ileum as well as the jejunum. This decrease was much larger in the autotransplant group. The difference in mean potassium secretion in the two groups at Week 1 failed to achieve significance with the ANOVA due to the very large variability in results obtained from the autotransplanted animals. The confidence interval suggests that a true increase in potassium secretion may have occurred in the autotransplanted ileum at Week 1. This increased secretion returned to normal by Week 8.

TRANSIT TIME

Jejunum

Autotransplantation : no effect (p=0.113).

Week of study : is significant (p=0.009).

Transit	Control Mean (min)	AutoTx Mean (min)	95% C.I.of the difference
Week 1	4.8	6.9	-0.2, 4.4
Week 8	3.9	4.2	-1.5, 2.2

Separate confidence intervals are required since the effect of week of study was significant.

At Week 1, these experiments would have detected an increase or a decrease in transit time of more than 2.3min. At Week 8, the experiments would have detected an increase or decrease of over 1.8min.

No difference in transit time was statistically proven between the autotransplanted jejunum and the controls despite the fact that mean transit time appeared slower in the autotransplants, especially at Week 1. Significance was probably not achieved due to variability.

There was a statistically significant decrease in transit time between Week 1 and Week 8 in both groups of dogs. This remains unexplained.

Ileum

Autotransplantation : no effect ($p=0.2$).

Week of study : is significant ($p<0.001$).

Transit	Control Mean (min)	AutoTx Mean (min)	95% C.I.of the difference
Week 1	8.0	10.0	0.0, 4.1
Week 8	3.9	4.2	-0.6, 3.8

The effect of week of study was again significant, with two confidence intervals necessary.

The experiments at Week 1 were capable of detecting an increase or a decrease in transit of over 2.05min. At Week 8, the experiments would have detected an increase or decrease of over 2.2min.

Autotransplantation of the ileum did not produce a significant change in transit time.

Ileum behaved in similar fashion to jejunum, with no significance found with autotransplantation. Again the mean transit time in the autotransplanted ileum was slower, especially at Week 1, but this just missed statistical significance. A significant decrease in transit was seen in both groups between Week 1 and Week 8. This decrease in the control dogs cannot be explained on the basis of recovery of transmission of the MMC across a proximal anastomosis since there isn't one. Equally, eight weeks was too short a period of time to allow regeneration of enteric neurones to the extent that the proximal MMC would be regularly transmitted across the anastomosis in the autotransplant group. The reason for this marked reduction in transit time between early and late experiments is not known.

PHENYLALANINE

Jejunum

Autotransplantation : no effect ($p>0.1$).

Week of study : no effect ($p=0.32$).

Absorption	Control Mean (5%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	88.	81.6	-12.1, -1.6

The effect of week of study was not significant, so a single confidence interval exists.

The experiments were capable of detecting an increase or a decrease in absorption of greater than 5.2%/15min.

Phenylalanine absorption was not significantly reduced by autotransplantation of the jejunum.

The decrease in phenylalanine absorption seen was not significant by the ANOVA, but the confidence interval not spanning zero indicates that a true difference may exist which has been missed due to the variability within the dogs.

Ileum

Autotransplantation : is significant ($p<0.001$).

Week of study : no effect ($p=0.282$).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	93.4	86.9	-10.3, -2.7

A single confidence interval exists since the effect of week of study was not significant.

The experiments were capable of detecting an increase or a decrease in absorption of over 3.8%/15min.

Autotransplanted ileum had impaired phenylalanine absorption.

Summary

Absorption of volume, sodium, and chloride was not affected by autotransplantation of either jejunum or ileum.

Potassium secretion was unaffected by autotransplantation in both jejunum and ileum.

Phenylalanine absorption was reduced only in autotransplanted ileum.

A time-specific reduction in potassium secretion was observed in both jejunum and ileum in both controls and autotransplants. This same time effect was seen for chloride absorption in jejunum alone.

Transit time was not significantly altered by autotransplantation, but became shorter in both jejunum and ileum at Week 8 when compared to Week 1.

PHENYLALANINE ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	1B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	27.7	4.6	Cannula	6.9	15.8	7.3	15.0	7.1	9.5
	26.4	2.4	came	12.1	16.2			15.3	22.5
		8.2	out	15.0	12.2			17.4	
MEAN	**27.0**	**5.1**		**11.3**	**14.7**	**7.3**	**15.0**	**13.3**	**16.0**
SODIUM (%/15 mins)	28.8	5.9		9.9	16.3	8.1	12.4	9.4	8.1
	26.5	6.0		9.2	18.5			21.5	22.4
		10.4		18.5	6.2			15.2	
MEAN	**27.6**	**7.4**		**12.5**	**13.7**	**8.1**	**12.4**	**15.4**	**15.2**
CHLORIDE (%/15 mins)	31.7	7.3		9.5	13.6	8.5	15.6	13.9	10.5
	27.7	4.4		11.5	18.7			23.7	25.4
		9.1		14.6	6.3			21.5	
MEAN	**29.7**	**6.9**		**11.9**	**12.9**	**8.5**	**15.6**	**19.7**	**18.0**
POTASSIUM EXCRETION (µmol/15mins)	60.9	110.9		81.5	82.9	77.4	74.2	85.9	75.0
	41.5	120.2		59.9	79.1			55.8	67.5
		93.0		73.5	73.7			65.4	
MEAN	**51.2**	**108.0**		**71.6**	**78.6**	**77.4**	**74.2**	**69.0**	**71.2**
PHENYL-ALANINE (%/15mins)	94.5	77.4		86.1	90.6	91.1	94.0	89.8	93.1
	69.7	86.4		91.7	88.1			92.4	87.9
		86.3		85.4	90.7			88.5	
MEAN	**82.1**	**83.4**		**87.7**	**89.8**	**91.1**	**94.0**	**90.2**	**90.5**
PEG RECOVERY (%)	86.6	106.2		96.6	89.7	98.0	92.4	101.0	97.4
	88.3	100.6		96.5	102.4			86.3	87.5
		106.5		107.0	105.5			90.7	
MEAN	**87.4**	**104.4**		**100.0**	**99.2**	**98.0**	**92.4**	**92.7**	**92.5**
TRANSIT TIME (mins)	9.8	5.9		6.1	4.5	3.6	3.6	7.4	4.1
	6.0	2.4		2.0	4.6			3.3	4.3
		4.5		5.2	4.0			6.4	
MEAN	**7.9**	**4.3**		**4.4**	**4.4**	**3.6**	**3.6**	**5.7**	**4.2**

TABLE 8.1 EXPERIMENTS AT WEEK 1

PHENYLALANINE ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	1B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	Prolapse	Fistula	6.8	Fistula	1.0	Ripped	10.8	21.4	14.5
	of		8.9		9.3	out	12.7		14.9
	stoma		7.3			loop	21.8		7.0
MEAN			**7.7**		**5.1**		**15.1**	**21.4**	**12.1**
SODIUM (%/15 mins)			7.4		2.8		11.1	26.9	17.0
			9.4		12.2		13.2		17.2
			10.9				15.9		6.9
MEAN			**9.2**		**7.5**		**18.9**	**26.9**	**13.7**
CHLORIDE (%/15 mins)			13.7		0.8		9.7	18.6	12.5
			7.0		14.2		11.9		15.1
			13.9				12.6		6.9
MEAN			**11.5**		**7.5**		**11.4**	**18.6**	**11.5**
POTASSIUM EXCRETION (µmol/15mins)			60.2		90.1		48.7	63.8	55.7
			67.4		83.0		52.6		61.8
			78.9				52.7		72.4
MEAN			**68.8**		**86.5**		**51.3**	**63.8**	**63.3**
PHENYL-ALANINE (%/15mins)			90.0		90.5		93.7	92.0	82.1
			92.1		91.5		89.9		88.0
			91.7				92.5		85.5
MEAN			**91.3**		**86.7**		**92.0**	**92.0**	**85.2**
PEG RECOVERY (%)			97.7		104.5		92.4	91.4	91.5
			87.6		94.5		85.1		103.7
			93.1				86.9		95.4
MEAN			**92.8**		**99.5**		**88.1**	**91.4**	**96.9**
TRANSIT TIME (mins)			2.5		4.3		2.2	5.7	6.4
			2.5		5.1		2.1		2.4
			3.7				2.3		2.6
MEAN			**2.9**		**4.7**		**2.2**	**5.7**	**3.8**

TABLE 8.2 EXPERIMENTS AT WEEK 8

PHENYLALANINE ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2A	2B	2C	2D	2E	2F	2G	2H
VOLUME (%/15 mins)	9.3	12.9	Unwell	15.2	3.3	Died	19.1	28.9
	22.8	2.4	Not	19.2	19.3	of	21.4	
		4.2	studied			pneu-		
						monia		
MEAN	**16.0**	**6.5**		**17.2**	**11.3**		**20.2**	**28.9**
SODIUM (%/15 mins)	11.5	15.1		18.1	7.1		24.9	27.8
	13.1	3.0		20.2	20.4		27.3	
		5.7						
MEAN	**12.3**	**7.9**		**19.1**	**13.8**		**26.1**	**27.8**
CHLORIDE (%/15 mins)	14.6	22.0		16.9	8.7		20.3	29.5
	10.3	6.9		19.1	19.0		23.3	
		13.0						
MEAN	**12.4**	**14.0**		**18.0**	**13.8**		**21.8**	**29.5**
POTASSIUM EXCRETION (μmol/15mins)	126.7	72.3		30.4	49.1		57.2	75.7
	107.2	74.7		85.2	61.4		91.7	
		77.7						
MEAN	**116.9**	**74.9**		**57.8**	**55.2**		**74.4**	**75.7**
PHENYL-ALANINE (%/15mins)	81.0	87.5		61.0	77.8		91.8	90.8
	78.0	832.7		95.6	95.2		94.2	
		79.1						
MEAN	**79.5**	**83.1**		**77.3**	**86.5**		**93.0**	**90.8**
PEG RECOVERY (%)	95.5	88.8		91.5	93.4		95.8	89.1
	99.9	107.0		91.4	89.1		88.4	
		91.1						
MEAN	**97.7**	**95.6**		**91.4**	**91.2**		**92.1**	**89.1**
TRANSIT TIME (mins)	8.7	11.1		2.4	9.1		8.8	6.0
	9.4	8.3		2.9	4.3		5.4	
		9.6						
MEAN	**9.0**	**9.7**		**2.6**	**6.7**		**7.1**	**6.0**

TABLE 8.3 EXPERIMENTS AT WEEK 1

PHENYLALANINE ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2A	2B	2C	2D	2E	2F	2G	2H
VOLUME (%/15 mins)	Fistula	9.5	22.4	27.3	10.7	Died	9.9	27.0
		15.1	15.1	22.5	10.6	of	6.6	17.8
		14.2	29.3		6.7	pneu-	11.1	
						monia		
MEAN		**12.9**	**22.3**	**24.9**	**9.3**		**9.2**	**22.7**
SODIUM (%/15 mins)		10.2	20.4	27.9	12.8		10.6	29.7
		16.6	15.8	21.7	16.1		8.9	20.0
		15.7	31.7		7.4		11.4	
MEAN		**14.2**	**22.6**	**25.0**	**12.1**		**10.3**	**24.8**
CHLORIDE (%/15 mins)		14.5	23.8	26.8	9.1		4.7	24.0
		11.2	12.7	22.8	10.3		5.4	11.0
		20.2	33.4		6.3		9.0	
MEAN		**15.3**	**23.3**	**24.8**	**8.6**		**6.4**	**17.5**
POTASSIUM EXCRETION (μmol/15mins)		57.9	50.4	59.1	41.4		65.2	72.7
		60.7	45.4	50.8	41.8		35.1	55.0
		61.4	55.3		55.1		57.8	
MEAN		**60.0**	**50.4**	**54.9**	**46.1**		**52.7**	**63.8**
PHENYL-ALANINE (%/15mins)		81.8	87.0	91.1	61.1		72.9	95.1
		89.0	81.2	82.6	66.1		43.7	84.4
		82.6	92.8		67.4		72.2	
MEAN		**84.5**	**87.0**	**86.8**	**64.9**		**62.9**	**89.7**
PEG RECOVERY (%)		99.8	87.6	92.1	86.1		99.3	86.4
		95.0	106.1	86.2	104.5		88.8	94.0
		96.1	92.6		97.8		91.1	
MEAN		**97.0**	**95.4**	**89.2**	**96.1**		**93.1**	**90.2**
TRANSIT TIME (mins)		7.4	7.6	4.2	3.2		3.4	4.6
		3.4	5.6	2.4	3.1		5.2	2.8
		5.7	5.2		2.2		2.8	
MEAN		**5.5**	**6.1**	**3.3**	**2.8**		**3.8**	**3.7**

TABLE 8.4 EXPERIMENTS AT WEEK 8

PHENYLALANINE ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	34.0	28.2	32.9	41.2	44.6	22.0
	25.3	32.0		35.4		24.4
	8.5	31.1		26.9		28.1
MEAN	**22.6**	**30.4**	**32.9**	**34.5**	**44.6**	**24.8**
SODIUM (%/15 mins)	38.7	24.9	36.7	44.0	48.6	26.4
	37.9	34.5		36.2		27.2
	10.8	30.5		28.8		32.2
MEAN	**29.1**	**30.0**	**36.7**	**36.3**	**48.6**	**28.6**
CHLORIDE (%/15 mins)	42.0	29.2	36.7	47.2	54.1	28.3
	30.1	36.7		37.9		28.4
	14.6	37.3		30.3		35.2
MEAN	**28.9**	**34.4**	**36.7**	**38.4**	**54.1**	**30.6**
POTASSIUM EXCRETION (μmol/15mins)	67.1	60.2	114.0	81.5	99.6	100.4
	62.5	80.9		65.0		68.8
	93.1	76.7		65.7		81.9
MEAN	**74.2**	**72.6**	**114.0**	**70.7**	**99.6**	**83.7**
PHENYL-ALANINE (%/15mins)	93.2	94.9	96.2	90.7	98.0	87.4
	93.3	94.6		91.4		89.7
	89.7	94.9		87.2		92.9
MEAN	**92.1**	**94.8**	**96.2**	**89.8**	**98.0**	**90.0**
PEG RECOVERY (%)	87.7	85.0	95.8	86.4	86.2	88.3
	91.3	94.4		100.3		105.9
	89.5	98.6		94.3		94.0
MEAN	**89.5**	**92.7**	**95.8**	**93.7**	**86.2**	**96.1**
TRANSIT TIME (mins)	11.7	5.6	9.4	8.3	10.4	----
	8.3	7.0		6.2		9.3
	7.4	4.2		5.5		10.0
MEAN	**9.1**	**5.6**	**9.4**	**6.7**	**10.4**	**9.6**

TABLE 8.5 EXPERIMENTS AT WEEK 1

PHENYLALANINE ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	32.8	32.9	28.4	31.3	11.2	28.8
		26.6	38.0		25.0	32.9
		27.0			31.7	32.5
MEAN	**32.8**	**28.8**	**33.2**	**31.3**	**22.6**	**31.4**
SODIUM (%/15 mins)	38.1	45.1	37.2	35.1	17.1	30.9
		34.6	43.8		30.9	37.3
		31.1			32.9	36.5
MEAN	**38.1**	**36.9**	**40.5**	**35.1**	**27.0**	**34.9**
CHLORIDE (%/15 mins)	36.1	48.6	38.6	36.6	21.8	30.3
		36.6	43.4		34.0	38.7
		29.8			37.6	36.3
MEAN	**36.1**	**32.8**	**41.0**	**36.6**	**31.1**	**35.1**
POTASSIUM EXCRETION (μmol/15mins)	74.1	49.6	83.9	63.1	99.1	66.9
		49.6	82.6		79.6	66.1
		65.3			68.2	62.8
MEAN	**74.1**	**54.8**	**83.2**	**63.1**	**82.3**	**65.3**
PHENYL-ALANINE (%/15mins)	97.8	92.4	95.0	93.6	86.2	97.4
		93.7	96.6		89.6	96.1
		97.4			95.0	96.7
MEAN	**97.8**	**94.5**	**95.8**	**93.6**	**90.3**	**96.7**
PEG RECOVERY (%)	89.2	95.5	93.6	92.6	98.8	95.2
		87.6	94.5		97.5	88.5
		92.8			91.9	85.0
MEAN	**89.2**	**92.0**	**94.0**	**92.6**	**96.1**	**89.6**
TRANSIT TIME (mins)	5.2	3.0	6.8	5.9	8.6	7.6
		2.0	10.6		6.0	5.3
		3.1			3.8	5.2
MEAN	**5.2**	**2.7**	**8.7**	**5.9**	**6.1**	**6.0**

TABLE 8.6 EXPERIMENTS AT WEEK 8

PHENYLALANINE ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H
VOLUME (%/15 mins)	30.0	14.7	29.5	30.4	35.3	37.5	30.0	Not
	37.8	24.9	33.5	31.3	46.7	43.5	37.5	studied
	21.5	28.9		63.3	46.5		45.7	
MEAN	**29.8**	**22.8**	**31.5**	**41.7**	**42.8**	**40.5**	**37.7**	
SODIUM (%/15 mins)	33.5	22.7	33.8	33.8	39.8	41.4	36.9	
	40.6	28.1	37.5	34.7	54.5	47.0	41.7	
	25.6	31.4		70.0	50.3		48.3	
MEAN	**32.2**	**27.4**	**35.6**	**46.2**	**48.2**	**44.2**	**42.3**	
CHLORIDE (%/15 mins)	38.0	24.1	39.2	34.1	41.1	43.7	37.3	
	44.5	29.7	39.5	38.7	52.2	48.1	41.3	
	18.9	34.3		68.8	53.8		51.1	
MEAN	**33.8**	**29.4**	**39.3**	**47.2**	**49.0**	**45.9**	**43.2**	
POTASSIUM EXCRETION (μmol/15mins)	71.7	156.3	122.9	391.1	121.3	68.5	268.6	
	76.8	27.7	72.0	61.1	285.0	93.3	87.3	
	49.9	61.9		235.6	137.0		86.7	
MEAN	**66.1**	**82.0**	**97.4**	**229.3**	**181.1**	**80.9**	**147.5**	
PHENYL-ALANINE (%/15mins)	85.2	84.4	90.7	77.7	93.0	84.5	83.6	
	91.2	56.8	90.9	92.4	93.6	90.0	85.0	
	67.8	91.6		98.1	95.9		88.7	
MEAN	**81.4**	**77.6**	**90.8**	**89.4**	**94.2**	**87.2**	**85.8**	
PEG RECOVERY (%)	86.8	91.7	90.7	90.7	87.6	86.2	95.6	
	90.0	103.3	91.3	102.6	95.3	85.5	96.9	
	91.5	94.4		89.2	95.9		89.7	
MEAN	**89.4**	**96.5**	**91.0**	**94.2**	**92.9**	**85.8**	**94.1**	
TRANSIT TIME (mins)	12.8	12.8	8.1	6.6	11.2	13.1	10.2	
	14.8	5.2	5.9	5.5	14.2	7.8	10.8	
	8.5	7.8		11.6	14.0		8.4	
MEAN	**12.0**	**8.6**	**7.0**	**7.9**	**13.1**	**10.4**	**9.8**	

TABLE 8.7 : EXPERIMENTS AT WEEK 1

PHENYLALANINE ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H
VOLUME (%/15 mins)	7.9	20.2	Cannula	52.9	38.9	Stoma	33.1	19.2
	18.6	27.2	abscess	54.2	40.5	and	38.9	
	44.3	29.8		33.7		loop	57.2	
						eaten		
MEAN	**23.6**	**25.7**		**46.9**	**40.2**		**43.1**	**19.2**
SODIUM (%/15 mins)	15.2	22.5		55.5	43.1		35.0	24.1
	24.6	29.9		59.2	59.8		43.3	
	47.7	34.7		36.8			56.8	
MEAN	**29.2**	**29.0**		**50.5**	**51.4**		**45.0**	**24.1**
CHLORIDE (%/15 mins)	15.8	23.0		59.4	44.2		35.1	17.9
	24.4	31.3		58.6	61.0		43.9	
	49.6	36.6		39.8			60.9	
MEAN	**29.9**	**30.3**		**52.6**	**52.6**		**46.6**	**17.9**
POTASSIUM EXCRETION (µmol/15mins)	61.8	47.4		83.2	63.6		78.5	54.7
	116.8	70.8		48.6	45.8		67.1	
	66.5	74.8		88.7			66.1	
MEAN	**81.7**	**64.3**		**73.5**	**54.7**		**70.6**	**54.7**
PHENYL-ALANINE (%/15mins)	57.9	84.6		95.6	91.0		89.4	68.6
	80.5	91.9		93.3	91.5		88.5	
	89.2	95.7		96.8			98.2	
MEAN	**75.9**	**90.7**		**95.2**	**91.2**		**92.0**	**68.6**
PEG RECOVERY (%)	90.7	86.1		85.3	109.1		85.8	88.0
	89.8	92.0		102.3	104.7		91.3	
	89.8	92.8		111.2			111.4	
MEAN	**90.1**	**90.3**		**95.2**	**106.9**		**96.2**	**88.0**
TRANSIT TIME (mins)	6.3	7.4		12.3	5.4		10.1	4.4
	6.7	12.8		3.7	5.1		3.6	
	7.3	4.2		7.4			11.3	
MEAN	**6.8**	**8.1**		**7.8**	**5.3**		**8.3**	**4.4**

TABLE 8.8 : EXPERIMENTS AT WEEK 8

ANALYSIS OF VARIANCE TABLES : PHENYLALANINE

	Experiment : Jejunum	Criterion : Volume			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	164	164.1	1.93	>.100
CASE(TR)	14	1542	110.2	1.29	.380
WK	1	2	2.3	0.03	.873
WKxTR	1	5	5.2	0.06	.812
WKxCASE(TR)	7	596	85.1	2.88	.018
ERROR	33	977	29.6		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

	Control			AutoTx			AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	9	12.6	6.5	7	16.3	5.7	-3.0 , 10.4

	Experiment : Jejunum	Criterion : Sodium			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	190	190.1	2.48	>.300
CASE(TR)	14	1566	111.9	1.46	.317
WK	1	1	0.7	0.01	.928
WKxTR	1	18	18.2	0.24	.641
WKxCASE(TR)	7	537	76.7	2.80	.021
ERROR	33	904	27.4		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

	Control			AutoTx			AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	9	13.5	6.3	7	17.6	5.9	-2.5 , 10.7

TABLE 8.9 : RESULTS FOR VOLUME AND SODIUM (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : PHENYLALANINE

	Experiment : Jejunum	Criterion : Chloride			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	160	160.0	1.44	.249
CASE(TR)	14	1551	110.8	3.71	.001
WK	1	184	183.9	6.15	.018
WKxTR	1	1	0.9	0.03	.865
WKxCASE(TR)	7	374	53.5	1.79	.123
ERROR	33	987	29.9		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment. The effects of Week and Case (Treatment) are significant. The effect of Treatment is not significant

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	8	15.4	7.2	6	18.3	6.5	-5.3 , 11.0
8	5	12.1	4.0	6	16.0	7.5	-4.6 , 12.4

The difference between weeks was significant with 95% CI of -9.8 , 0.5 .

	Experiment : Jejunum	Criterion : Potassium			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	252	252.5	0.34	.572
CASE(TR)	14	10544	753.2	5.02	<.001
WK	1	801	801.0	5.34	.027
WKxTR	1	56	55.7	0.37	.546
WKxCASE(TR)	7	670	95.7	0.64	.721
ERROR	33	4947	149.9		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment. The effects of Week and Case (Treatment) are significant. The effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	8	75.2	15.8	6	75.8	22.1	-21.3 , 22.6
8	5	66.8	12.8	6	54.7	6.5	-25.5 , 1.3

The difference between weeks was significant with 95% CI of -17.2 , -2.5 .

TABLE 8.10 : RESULTS FOR CHLORIDE AND POTASSIUM (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : PHENYLALANINE

	Experiment : Jejunum Criterion : Transit Time				
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	23	22.5	2.86	.113
CASE(TR)	14	110	7.88	3.12	.004
WK	1	20	19.6	7.76	.009
WKxTR	1	11	10.7	4.24	.048
WKxCASE(TR)	7	18	2.6	1.02	.438
ERROR	33	83	2.5		

The interaction Week x Case (Treatment) is not significant. The effects of Week x Treatment, Week and Case (Treatment) are significant. The effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	8	4.8	1.4	6	6.9	2.5	-0.2 , 4.4
8	5	3.9	1.4	6	4.2	1.3	-1.5 , 2.2

The significant interaction week x treatment is that the mean Transit Time was higher at Week1 after the jejunal autotransplant than at Week 8 or at either week for the controls.

	Experiment : Jejunum Criterion : Phenylalanine				
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	516	515.7	2.84	>.100
CASE(TR)	14	1010	72.2	0.40	.932
WK	1	208	208.0	1.15	.320
WKxTR	1	121	120.9	0.67	.441
WKxCASE(TR)	7	1269	181.3	2.99	.015
ERROR	33	2001	60.6		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	9	88.5	3.7	7	81.6	6.1	-12.1 , -1.6

TABLE 8.11 : RESULTS FOR TRANSIT TIME AND PHENYLALANINE

ANALYSIS OF VARIANCE TABLES : PHENYLALANINE

	Experiment : Ileum		Criterion : Volume		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	101	101.0	0.50	.494
CASE(TR)	12	2438	203.1	2.23	.031
WK	1	2	2.0	0.02	.883
WKxTR	1	18	18.3	0.20	.656
WKxCASE(TR)	9	672	74.7	0.82	.600
ERROR	36	3274	90.9		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	29.6	3.3	8	33.6	9.4	-4.2 , 12.0

	Experiment : Ileum		Criterion : Sodium		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	147	146.6	0.63	.443
CASE(TR)	12	2800	233.3	2.43	.020
WK	1	6	6.2	0.06	.801
WKxTR	1	0	0.4	0.00	.946
WKxCASE(TR)	9	595	66.2	0.69	.714
ERROR	36	3274	90.9		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	34.0	3.0	8	38.3	9.8	-4.2 , 12.8

TABLE 8.12 : RESULTS FOR VOLUME AND SODIUM (ILEUM)

ANALYSIS OF VARIANCE TABLES : PHENYLALANINE

	Experiment : Ileum		Criterion : Chloride		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	48	48.1	0.20	.662
CASE(TR)	12	2881	240.1	2.27	.028
WK	1	17	16.6	0.16	.694
WKxTR	1	50	49.7	0.47	.497
WKxCASE(TR)	9	650	72.3	0.68	.718
ERROR	36	3800	105.6		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	35.7	3.3	8	38.3	10.9	-6.9 , 12.0

	Experiment : Ileum		Criterion : Potassium		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	2693	2692.5	0.89	.353
CASE(TR)	12	37874	3156.2	1.04	.436
WK	1	22729	22729.3	7.49	.010
WKxTR	1	9818	9817.8	3.23	.081
WKxCASE(TR)	9	30421	3380.1	1.11	.379
ERROR	36	109317	3036.6		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Case (Treatment). The effect of Week is significant. The effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the individual results for each week and treatment, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	14	79.8	16.6	19	130.2	96.6	3.0 , 97.8
8	13	70.1	13.8	15	69.0	18.4	-13.9 , 11.7

There was a significant reduction in mean potassium from Week 1 to Week 8, the 95% CI being (-21.9 , 2.4) for the Controls and (-108.8 , -14.0) for the autotransplants.

TABLE 8.13 : RESULTS FOR CHLORIDE AND POTASSIUM

ANALYSIS OF VARIANCE TABLES : PHENYLALANINE

	Experiment : Ileum		Criterion : Transit Time		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	12	12.1	1.70	.200
CASE(TR)	12	105	8.8	1.24	.299
WK	1	98	97.7	13.75	<.001
WKxTR	1	0	0.3	0.05	.827
WKxCASE(TR)	9	71	7.9	1.12	.378
ERROR	35	249	7.1		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Case (Treatment). The effect of Week is significant. The effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the individual results for each week and treatment, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
1	13	8.0	2.2	19	10.0	3.3	-0.0 , 4.1
8	13	5.6	2.4	15	7.2	3.1	-0.6 , 3.8

There was a significant reduction in mean Transit Time from week 1 to week 8, the 95% CI being (-4.2 , -0.5) for the Controls and (-5.0 , -0.6) for the autotransplants.

	Experiment : Ileum		Criterion : Phenylalanine		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	804	803.8	14.73	<.001
CASE(TR)	12	1270	105.8	1.94	.062
WK	1	65	85.0	1.19	.282
WKxTR	1	13	12.7	0.23	.633
WKxCASE(TR)	9	460	51.1	0.94	.506
ERROR	36	1964	54.6		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment, Week, and Case (Treatment). The effect of Treatment is significant

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the individual results for each week and treatment, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	27	93.4	3.4	34	86.9	10.3	-10.3 , -2.7

TABLE 8.14 RESULTS FOR TRANSIT TIME AND PHENYLALANINE

CHAPTER 9

RESULTS : OLEIC ACID

The mean values obtained for absorption in each experiment are shown in Tables 9.1-9.8 (pages 178-185) at the end of this chapter. These also show the mean value for all the experiments for each dog at each week studied. A total of 158 experiments were carried out in all four groups of dogs and 13 (8.2%) of these were excluded from further analysis because of poor PEG recovery. The number of experiments performed in each group over the two study weeks (Week 1 and Week 8) were as follows:

	Number of experiments	
	Total	**Discarded (%)**
Group 1	39	0 (0%)
Group 2	41	4 (9.8%)
Group 3	39	2 (5.1%)
Group 4	39	7 (17.9%)

Once again these experiments with poor PEG recovery were distributed at random among dogs of all groups, with too few lost experiments to perform a chisquare test. The higher discard rate for Group 4 was due to dog 4H who had no valid studies due to poor PEG recovery at Week 9, and dog 4E who lost two of three studies for the same reason.

VARIABILITY

The dogs exhibited variability in their results with the oleic acid solution as with the other test solutions. In the jejunum this was reflected in CASE(TR) [variation when all dogs, control and autotransplant, are compared together] being statistically significant for all the parameters looked at. In the ileum, this inter-dog variability was detected more often by WKxCASE(TR) [variability among both control and autotransplanted dogs looked at together and compared over the different weeks of study] (Tables 9.9-9.14, pages 186-191).

ABSORPTION

The analysis of variance tables and the overall means for all the experiments are at the end of this chapter (Tables 9.1-9.14, pages 178-191).

VOLUME

Jejunum

Autotransplantation : no effect (p=0.237).

Week of study : no effect (p=0.464).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	-1.0	4.7	-3.7, 15.1

The effect of week of study was not significant, so there is a single confidence interval.

These experiments were capable of detecting an increase or a decrease in absorption of greater than 9.4%/15min.

Jejunal autotransplantation did not affect the volume of perfusate absorbed from this solution.

The control group of dogs had a net secretion in response to the oleic acid solution, while the autotransplanted dogs showed slight absorption. This failed to achieve statistical significance.

Ileum

Autotransplantation : no effect (p=0.87).

Week of study : no effect (p=0.763).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	-8.5	-8.2	-5.7, 6.3

There is a single confidence interval since the effect of week of study was not significant.

These experiments would have detected an increase or decrease in absorption of over 6.0%/15min.

No alteration in sodium absorption occurred after autotransplantation of the jejunum.

Net secretion occurred in both groups.

SODIUM

Jejunum

Autotransplantation : no effect (p=0.245).

Week of study : no effect (p=0.899).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	-1.8	4.4	-4.2, 16.7

There is a single confidence interval since the effect of week of study was not significant.

These experiments were capable of detecting an increase or a decrease in absorption of greater than 10.4%/15min.

Sodium absorption was unaffected by autotransplantation of the jejunum.

Ileum

Autotransplantation : no effect (p>0.4).

Week of study : no effect (p=0.43).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	-6.5	-5.4	-7.7, 9.8

The effect of week of study was not significant, so there is a single confidence interval.

These experiments would have detected an increase or decrease in absorption of greater than 8.7%/15min.

No alteration in sodium absorption occurred with ileal autotransplantation.

CHLORIDE

Jejunum

Autotransplantation : no effect (p=0.644).

Week of study : no effect (p=0.609).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	-0.2	2.3	-9.0, 14.1

The effect of week of study was not significant, so there is a single confidence interval.

These experiments would have detected an increase or a decrease in absorption of greater than 11.6%/15min.

No defect in chloride absorption resulted from jejunal autotransplantation.

Ileum

Autotransplantation : no effect (p>0.9).

Week of study : no effect (p=0.462).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	3.0	1.8	-10.3, 7.9

The effect of week of study was not significant, so there is a single confidence interval.

These experiments were capable of detecting an increase or a decrease in absorption of greater than 9.1%/15min.

Chloride absorption was not significantly altered by ileal autotransplantation.

POTASSIUM

Jejunum

Autotransplantation : no effect (p=0.752).

Week of study : is significant (p=0.039).

Secretion	Control Mean (μM/15min)	AutoTx Mean (μM/15min)	95% C.I.of the difference
Week 2	133.7	134.2	-33.0, 34.3
Week 9	126.5	116.2	-49.0, 28.1

The effect of week of study was significant, so there are two separate confidence intervals.

At Week 1, these experiments were capable of detecting an increase or a decrease in secretion of greater than 33.6μM/15min. At Week 8, the experiments would have detected an increase or decrease of over 38.6μM/15min.

Autotransplantation did not affect potassium secretion by the jejunum.

There was a significant time effect. This was seen as reduced potassium secretion in both control and autotransplanted jejunum at Week 9 when compared to Week 2. This reflects the mucosal response to defunctioning.

Ileum

Autotransplantation : is significant (p=0.018).

Week of study : is significant (p=0.042).

Secretion	Control Mean (μM/15min)	AutoTx Mean (μM/15min)	95% C.I.of the difference
Week 2	162.7	211.0	-2.0, 99.4
Week 9	144.3	173.2	6.0, 52.1

The effect of week of study was significant, so there are two confidence intervals.

At Week 2, these experiments would have detected an increase or decrease in secretion of greater than 48.7μM/15min. At Week 9, the experiments would have detected an increase or decrease of greater than 23.0μM/15min.

Autotransplantation of the ileum resulted in a significant increase in potassium secretion.

The time-dependent effect seen was a significant decrease in potassium secretion in both control and autotransplanted ileum between Week 2 and Week 9.

TRANSIT TIME

Jejunum

Autotransplantation : no effect (p=0.157).

Week of study : no effect (p=0.052).

Transit	Control Mean (min)	AutoTx Mean (min)	95% C.I.of the difference
	3.7	4.7	-0.7, 2.7

The effect of week of study was not significant so there is a single confidence interval.

These experiments would have detected an increase or decrease in transit time of greater than 1.7min.

Transit time was not significantly altered in the autotransplanted jejunum.

Although transit after autotransplantation is slower, this failed to achieve statistical significance.

Ileum

Autotransplantation : no effect (p=0.673).

Week of study : no effect (p=0.565).

Transit	Control Mean (min)	AutoTx Mean (min)	95% C.I.of the difference
Week 2	6.1	4.9	-2.6, 0.2
Week 9	5.0	5.9	-0.9, 2.6

Although week of study was not significant (WK in the ANOVA tables, Table 9.14, page 191), two separate confidence intervals have been generated since the comparison of week and the effect of autotransplantation (WK x TR in the ANOVA tables) is significant; p = 0.039 (Table 9.14, page 191).

At Week 2, these experiments would have detected an increase or decrease in transit time of greater than 1.9mins. At Week 9, an increase or decrease of greater than 1.8mins would have been detected.

Transit time was not significantly altered by autotransplantation of the ileum.

Transit time in the ileum gives a confusing set of results. At Week 2 it appeared to be shorter in the autotransplants than in the controls, when it would be expected to be longer, as occurs at Week 9. In addition, in the autotransplants transit increased by Week 9 while in the controls it decreased. These paradoxical results may be the result of a type II error.

OLEIC ACID

Jejunum

Autotransplantation : no effect (p=0.419).

Week of study : no effect (p=0.104).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	44.5	50.3	-8.9, 20.5

There is a single confidence interval since the effect of week of study was not significant.

These experiments would have detected an increase or decrease in absorption of greater than 14.7%/15min.

Oleic acid absorption was not altered by autotransplantation of the jejunum.

Ileum

Autotransplantation : no effect (p=0.511).

Week of study : no effect (p=0.491).

Absorption	Control Mean (%/15min)	AutoTx Mean (%/15min)	95% C.I.of the difference
	40.4	36.8	-16.3, 9.2

There was no effect with time of study, so a single confidence interval exists.

These experiments would have detected an increase or decrease in absorption of greater than 12.7%/15min.

Oleic acid absorption from autotransplanted ileum was not impaired.

Summary

Absorption of volume, sodium, chloride and oleic acid were not significantly altered by autotransplantation of jejunum or ileum.

Potassium secretion was not altered by autotransplantation in the jejunum, but was increased in autotransplanted ileum.

Transit time was unaltered by autotransplantation in both jejunum and ileum.

A time-dependent effect was seen only with potassium secretion. This was reduced at Week 9 when compared with Week 2 in both jejunum and ileum, and affected both autotransplanted and control small bowel.

OLEIC ACID ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	1B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	Wrong	-1.7	Cannula	11.1	-5.0	-5.2	5.2	-1.6	-8.3
	conc.	-2.0	came	-3.5	-7.1	0.6	-4.4	-0.4	10.6
	oleic	11.8	out		-9.3		6.9	13.4	1.7
	acid				-10.8		-2.8	2.5	8.6
MEAN		**2.7**		**3.8**	**-8.0**	**-2.3**	**1.2**	**3.5**	**3.1**
SODIUM (%/15 mins)		5.5		8.0	-6.8	-10.5	5.0	-6.8	-15.9
		-1.5		-4.5	-8.7	-1.9	-2.3	3.5	9.2
		16.8			-12.4		7.7	12.7	-3.6
					-14.4		0.4	1.8	7.9
MEAN		**6.9**		**1.8**	**-10.6**	**-6.2**	**2.7**	**2.8**	**-0.6**
CHLORIDE (%/15 mins)		2.3		15.0	-11.3	-9.8	2.8	-3.3	-16.1
		-4.4		6.4	-9.5	-1.5	-3.6	6.5	7.6
		12.4			-16.7		9.1	13.5	-5.4
					-16.3		-5.4	4.9	4.3
MEAN		**3.4**		**10.7**	**-13.4**	**-5.7**	**0.7**	**5.4**	**-2.4**
POTASSIUM EXCRETION (μmol/15mins)		120.8		64.2	144.4	170.2	165.4	107.8	156.2
		131.5		146.7	150.4	115.0	189.2	105.5	121.8
		115.0			156.9		134.8	89.2	155.6
					181.6		180.3	100.8	123.1
MEAN		**118.0**		**105.4**	**158.3**	**142.6**	**164.4**	**100.8**	**139.2**
OLEIC ACID (%/15mins)		55.2		25.2	40.3	55.9	69.6	31.7	39.1
		57.6		58.1	44.6	31.1	69.2	29.0	47.9
		67.5			33.9		67.2	32.0	44.5
					42.4		64.4	31.1	53.4
MEAN		**60.1**		**41.6**	**40.3**	**43.5**	**67.3**	**30.9**	**46.2**
PEG RECOVERY (%)		103.7		92.6	106.7	96.4	93.0	99.4	100.0
		100.7		98.5	97.3	108.4	92.5	94.1	93.4
		90.0			101.2		91.6	86.7	93.4
					102.2		89.1	94.5	95.1
MEAN		**98.1**		**95.6**	**101.8**	**102.4**	**91.6**	**93.7**	**95.5**
TRANSIT TIME (mins)		4.6		3.1	2.8	2.3	3.3	5.2	5.1
		4.9		5.7	2.8	8.6	2.0	3.8	2.5
		4.5			2.5		3.8	2.6	2.1
					2.4		2.1	4.0	4.3
MEAN		**4.7**		**4.4**	**2.6**	**5.4**	**2.8**	**3.9**	**3.5**

TABLE 9.1 EXPERIMENTS AT WEEK 2

OLEIC ACID ABSORPTION

JEJUNAL CONTROLS

ABSORPTION	1A	1B	1C	1D	1E	1F	1G	1H	1I
VOLUME (%/15 mins)	Died	Fistula	-8.1	Fistula	-9.5	Ripped	3.8	1.1	-13.6
			-8.8		-6.5	out	1.0	13.4	-0.2
			-14.5		-10.5	loop	-2.3	13.5	-9.1
			-9.4		2.1		-0.1		-0.9
MEAN			**-10.2**		**-6.1**		**0.6**	**9.3**	**-5.9**
SODIUM (%/15 mins)			-8.1		-9.5		5.1	-0.1	-16.5
			-9.8		-6.1		1.2	12.5	-2.2
			-17.4		-10.3		-1.6	16.4	-10.3
			-12.0		0.7		-4.2		-1.0
MEAN			**-11.8**		**-6.3**		**0.1**	**9.6**	**-7.5**
CHLORIDE (%/15 mins)			-8.7		-11.0		1.6	-0.3	-17.0
			-10.5		-12.2		-1.7	11.1	-2.0
			-1.3		-13.3		-5.7	14.3	-12.2
			-5.4		0.7		-0.4		-5.8
MEAN			**-6.5**		**-8.9**		**-1.5**	**8.4**	**-9.2**
POTASSIUM EXCRETION (µmol/15mins)			127.9		183.9		108.4	121.5	156.5
			127.5		145.0		126.4	79.7	123.3
			110.2		158.8		145.0	74.4	132.0
			137.5		119.4		145.4		115.0
MEAN			**125.8**		**151.8**		**131.3**	**91.9**	**131.9**
OLEIC ACID (%/15mins)			37.2		36.0		41.5	44.1	26.9
			44.1		29.4		43.4	44.7	25.2
			34.8		34.0		58.8	46.0	30.7
			44.4		32.2		54.1		34.5
MEAN			**40.1**		**32.9**		**49.4**	**44.9**	**29.3**
PEG RECOVERY (%)			93.3		90.7		88.3	98.1	102.9
			97.1		90.5		93.6	88.9	92.8
			96.5		94.8		104.8	94.2	100.9
			94.8		87.3		99.9		100.6
MEAN			**95.2**		**90.8**		**96.6**	**93.7**	**99.3**
TRANSIT TIME (mins)			4.0		1.7		1.8	3.1	2.1
			4.1		2.6		2.1	2.2	3.2
			4.3		1.7		1.7	2.8	4.4
			2.0		2.4		2.0		3.8
MEAN			**3.6**		**2.1**		**1.9**	**2.7**	**3.4**

TABLE 9.2 EXPERIMENTS AT WEEK 9

OLEIC ACID ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2A	2B	2C	2D	2E	2F	2G	2H
VOLUME (%/15 mins)	Wrong	3.4	Unwell	-0.4	-5.4	Died	4.9	-1.1
	conc.	4.4	Not	-6.0	-7.4	of	9.1	1.3
	oleic	10.4	studied	13.9	-5.6	pneu-		8.9
	acid	3.9		-4.4	-1.6	monia		-6.3
MEAN		**5.5**		**0.8**	**-5.0**		**5.0**	**0.7**
SODIUM (%/15 mins)		5.8		-2.7	-12.8		7.8	-2.8
		5.0		-8.7	-8.8		2.9	2.4
		15.3		12.9	-2.7			16.6
		6.2		-2.5	-6.9			-11.1
MEAN		**8.1**		**-0.2**	**-7.8**		**5.3**	**1.3**
CHLORIDE (%/15 mins)		4.9		-4.3	-8.1		5.4	-8.6
		8.4		-7.4	-12.4		-1.0	-0.5
		12.8		8.6	-6.0			13.1
		5.8		-6.9	-6.3			-15.1
MEAN		**8.0**		**-2.5**	**-8.2**		**2.2**	**-2.8**
POTASSIUM EXCRETION (μmol/15mins)		123.0		154.0	139.7		106.1	183.3
		123.5		187.8	135.1		116.7	181.8
		90.2		88.2	124.8			109.9
		115.4		200.3	83.1			198.5
MEAN		**113.0**		**157.6**	**120.7**		**111.4**	**168.4**
OLEIC ACID (%/15mins)		37.8		51.7	42.6		50.5	65.9
		35.1		72.2	41.5		52.4	73.0
		40.1		36.4	38.9			60.1
		34.3		71.2	36.8			73.4
MEAN		**36.8**		**57.9**	**40.0**		**51.5**	**68.1**
PEG RECOVERY (%)		100.0		101.5	98.7		87.7	90.2
		108.9		98.7	97.6		87.9	92.4
		89.1		99.8	93.3			86.0
		94.8		89.3	100.9			104.4
MEAN		**98.2**		**97.3**	**95.4**		**87.8**	**93.2**
TRANSIT TIME (mins)		4.7		2.6	2.9		5.4	3.3
		5.6		---	2.7		4.5	4.3
		3.9		5.5	5.3			3.1
		3.8		6.6	2.5			4.0
MEAN		**4.5**		**4.9**	**3.3**		**5.0**	**3.7**

TABLE 9.3 EXPERIMENTS AT WEEK 2

OLEIC ACID ABSORPTION

JEJUNAL AUTOTRANSPLANTS

ABSORPTION	2A	2B	2C	2D	2E	2F	2G	2H
VOLUME (%/15 mins)	Fistula	3.0	18.8	3.9	-11.7	Died	8.0	-4.2
		-1.7	28.2	4.4	-14.3	of		-10.7
		4.5		1.6	-7.5	pneu-		6.5
		3.0		6.2	-9.9	monia		
MEAN		**2.2**	**23.5**	**4.0**	**-10.8**		**8.0**	**-2.8**
SODIUM (%/15 mins)		2.2	17.1	-8.6	-10.6		14.6	-2.9
		-1.5	29.0	4.7	-17.3			-10.7
		5.8		3.5	-15.1			4.1
		3.9		6.8	-9.7			
MEAN		**2.6**	**23.0**	**1.6**	**-13.2**		**14.6**	**-3.2**
CHLORIDE (%/15 mins)		11.0	16.4	-8.2	-12.0		6.7	-8.4
		1.0	26.1	2.1	-20.8			-12.9
		7.2		2.1	-20.4			1.4
		5.4		1.5	-10.9			
MEAN		**6.1**	**21.2**	**-0.6**	**-16.0**		**6.7**	**-6.6**
POTASSIUM EXCRETION (µmol/15mins)		75.7	87.1	112.3	108.3		94.0	170.5
		109.9	89.0	144.6	124.7			195.8
		99.2		138.5	98.7			153.7
		117.8		141.1	96.6			
MEAN		**100.6**	**88.0**	**134.1**	**107.1**		**94.0**	**173.3**
OLEIC ACID (%/15mins)		22.0	63.2	50.1	19.0		42.0	68.3
		28.7	69.3	59.9	25.6			63.8
		27.7		58.5	24.7			64.0
		37.7		63.6	20.9			
MEAN		**29.0**	**66.2**	**58.0**	**22.6**		**42.0**	**65.4**
PEG RECOVERY (%)		98.2	86.5	94.2	94.7		89.1	91.2
		100.9	88.2	97.4	99.4			94.0
		98.5		98.5	94.4			90.7
		89.6		89.0	90.3			
MEAN		**96.8**	**87.3**	**94.8**	**94.6**		**89.1**	**92.0**
TRANSIT TIME (mins)		5.9	8.6	2.5	1.7		2.0	3.9
		3.9	7.2	5.9	1.9			3.1
		8.7		3.8	1.7			3.2
		6.0		5.2	4.2			
MEAN		**6.1**	**7.9**	**4.3**	**2.4**		**2.0**	**3.4**

TABLE 9.4 EXPERIMENTS AT WEEK 9

OLEIC ACID ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	-16.2	-12.7	-3.4	-19.9	-7.8	-2.6
	-10.0	-9.5	-11.0	-10.0	-14.2	-9.4
	5.6	-20.1	1.5	-12.8	-15.1	-5.8
	6.5		-9.2			
MEAN	**-3.5**	**-14.1**	**-5.5**	**-14.2**	**-12.4**	**-5.9**
SODIUM (%/15 mins)	-15.0	-13.9	-4.1	-24.6	-4.7	0.5
	-6.2	-14.6	-10.2	-10.7	-12.1	-6.3
	5.2	-10.3	3.7	-14.2	-14.5	-1.1
	11.7		-9.5			
MEAN	**-2.3**	**-12.9**	**-5.0**	**-16.5**	**-10.4**	**-2.3**
CHLORIDE (%/15 mins)	1.8	0.9	5.5	-5.4	4.3	8.4
	3.8	5.9	0.1	-0.5	-0.2	-0.8
	17.0	-14.9	7.8	-2.2	-5.8	8.6
	19.4		-0.2			
MEAN	**10.5**	**-2.7**	**3.3**	**-2.7**	**-0.6**	**5.4**
POTASSIUM EXCRETION (µmol/15mins)	134.6	206.7	133.0	163.3	186.9	118.4
	133.1	283.9	212.5	147.9	219.9	118.4
	124.2	139.0	156.4	163.7	164.5	137.4
	119.9		189.4			
MEAN	**127.9**	**209.9**	**172.8**	**158.3**	**191.3**	**124.7**
OLEIC ACID (%/15mins)	33.1	56.0	36.1	44.0	41.1	36.8
	44.0	65.9	38.5	46.9	41.3	37.9
	38.3	26.3	5.2	56.6	38.4	58.2
	32.9		25.9			
MEAN	**37.1**	**49.4**	**25.3**	**49.2**	**40.3**	**44.3**
PEG RECOVERY (%)	93.6	95.7	93.0	97.8	88.8	91.1
	91.8	92.6	96.2	95.5	90.0	96.8
	97.4	97.9	87.8	97.5	94.6	92.0
	94.9		96.0			
MEAN	**94.4**	**95.4**	**93.2**	**96.9**	**91.1**	**93.3**
TRANSIT TIME (mins)	4.1	5.0	6.1	7.6	6.1	6.1
	5.2	6.1	6.1	8.2	2.1	7.0
	6.0	2.9	7.4	9.8	6.4	7.0
	6.6		6.7			
MEAN	**5.5**	**4.7**	**6.6**	**8.5**	**4.9**	**6.7**

TABLE 9.5 EXPERIMENTS AT WEEK 2

OLEIC ACID ABSORPTION

ILEAL CONTROLS

ABSORPTION	3A	3B	3C	3D	3E	3F
VOLUME (%/15 mins)	-2.4	-15.0	-4.9	-10.6	-19.1	-6.5
	0.9	-5.8	-4.5	-8.8	-6.3	-11.1
	-5.4		-4.2	-4.9	-12.3	-5.0
MEAN	**-2.3**	**-10.4**	**-4.5**	**-8.1**	**-12.6**	**-7.5**
SODIUM (%/15 mins)	6.4	-15.5	0.7	-7.0	-23.9	-9.3
	6.4	0.9	-0.3	-10.1	-6.6	-11.3
	-4.9		9.3	1.0	-13.0	-4.4
MEAN	**2.6**	**-7.3**	**3.3**	**-5.3**	**-14.4**	**-8.3**
CHLORIDE (%/15 mins)	17.1	-4.3	9.8	6.9	-4.8	-1.2
	15.6	8.4	1.0	4.0	2.0	-10.4
	8.4		5.1	10.2	-3.2	0.9
MEAN	**13.7**	**2.1**	**5.3**	**7.0**	**-2.0**	**-3.6**
POTASSIUM EXCRETION (µmol/15mins)	175.4	137.5	156.4	178.5	141.3	107.3
	150.1	147.2	127.4	171.0	129.7	109.7
	143.1		152.3	170.9	156.5	98.3
MEAN	**156.2**	**142.3**	**145.2**	**173.5**	**142.5**	**105.1**
OLEIC ACID (%/15mins)	30.1	44.7	42.5	66.3	25.5	29.6
	26.8	50.4	24.5	59.0	36.4	29.3
	32.4		37.9	65.1	39.7	32.1
MEAN	**29.8**	**47.6**	**35.0**	**63.5**	**33.9**	**30.3**
PEG RECOVERY (%)	85.5	102.0	90.7	86.0	99.3	97.5
	92.1	92.6	104.7	96.3	89.3	96.9
	94.7		102.8	85.9	90.1	89.9
MEAN	**90.8**	**97.3**	**99.4**	**89.4**	**92.9**	**94.8**
TRANSIT TIME (mins)	6.1	2.4	5.2	7.1	5.7	4.6
	4.6	2.0	6.6	6.4	5.1	7.0
	5.3		5.2	6.5	---	3.5
MEAN	**5.3**	**2.2**	**5.7**	**6.7**	**5.4**	**5.0**

TABLE 9.6 EXPERIMENTS AT WEEK 9

OLEIC ACID ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H
VOLUME (%/15 mins)	-4.5	-0.9	-20.1	-2.0	-13.8	-8.4	-5.3	Not
	0.7	-6.4	-21.7	-5.2	5.5	-2.5	-6.4	studied
	-8.6		-13.4	-8.2	-4.9	-5.6	-14.3	
MEAN	**-4.1**	**-3.6**	**-18.4**	**-5.1**	**-4.4**	**-5.5**	**-8.7**	
SODIUM (%/15 mins)	-2.5	-0.4	-19.7	-2.1	-15.6	1.5	-6.8	
	2.2	-0.5	-27.1	2.5	2.4	1.5	-3.1	
	-15.8		-13.6	-8.2	-7.9	-0.3	-14.5	
MEAN	**-5.4**	**-0.4**	**-20.1**	**-2.6**	**-7.0**	**0.9**	**-8.1**	
CHLORIDE (%/15 mins)	6.2	12.9	-12.3	5.8	-6.9	4.0	8.5	
	-0.9	-6.4	-24.3	2.3	12.5	6.0	7.5	
	-3.4		-8.8	-1.4	2.9	10.4	-0.6	
MEAN	**-0.6**	**3.3**	**-15.1**	**2.2**	**2.8**	**6.8**	**5.1**	
POTASSIUM EXCRETION (µmol/15mins)	148.5	208.7	144.4	235.8	206.2	447.7	175.1	
	112.1	288.0	137.5	521.9	211.8	184.4	161.8	
	146.7		195.3	177.8	166.6	187.3	165.7	
MEAN	**135.8**	**248.3**	**159.0**	**311.8**	**194.9**	**273.1**	**167.5**	
OLEIC ACID (%/15mins)	30.9	27.9	30.5	90.8	39.3	54.9	33.7	
	38.2	22.4	24.1	31.8	36.6	41.9	21.0	
	53.9		43.1	39.2	46.4	54.1	18.2	
MEAN	**41.0**	**25.1**	**32.6**	**53.9**	**40.7**	**50.3**	**24.3**	
PEG RECOVERY (%)	86.5	108.4	91.2	86.3	105.1	103.2	87.9	
	87.5	85.6	103.1	98.4	114.0	97.8	95.1	
	104.7		92.0	91.0	89.6	93.9	109.7	
MEAN	**92.9**	**97.0**	**95.4**	**91.9**	**102.9**	**98.3**	**97.6**	
TRANSIT TIME (mins)	5.3	4.8	3.1	3.8	6.4	5.7	2.6	
	5.5	5.8	4.4	4.4	4.8	4.3	6.8	
	3.4		1.9	7.6	5.0	5.9	7.0	
MEAN	**4.7**	**5.3**	**3.1**	**5.3**	**5.4**	**5.3**	**5.5**	

TABLE 9.7 EXPERIMENTS AT WEEK 2

OLEIC ACID ABSORPTION

ILEAL AUTOTRANSPLANTS

ABSORPTION	4A	4B	4C	4D	4E	4F	4G	4H
VOLUME (%/15 mins)	-3.5	-21.1	Cannula	-13.9	-7.5	Stoma	-15.2	Poor
	0.7	-17.5	abscess	9.4		and	-11.7	PEG
		-13.1		-4.0		loop	-5.0	recov-
						eaten		ery
MEAN	**-1.4**	**-17.2**		**-2.8**	**-7.5**		**-10.6**	
SODIUM (%/15 mins)	-3.3	-18.9		-14.8	18.7		-13.8	
	-0.3	-12.9		10.3			-14.2	
		-14.5		-2.4			-12.0	
MEAN	**-1.8**	**-15.4**		**-1.5**	**18.7**		**-13.3**	
CHLORIDE (%/15 mins)	6.9	-14.9		-5.6	24.1		-4.7	
	7.9	-7.5		16.4			-2.0	
		-8.2		9.5			5.7	
MEAN	**7.4**	**-10.2**		**6.8**	**24.1**		**-0.3**	
POTASSIUM EXCRETION (µmol/15mins)	151.0	208.1		125.8	118.0		214.4	
	226.0	161.8		214.0			153.8	
		197.8		156.6			151.6	
MEAN	**188.5**	**189.2**		**165.5**	**118.0**		**173.3**	
OLEIC ACID (%/15mins)	38.7	15.4		29.8	45.1		37.8	
	51.9	12.0		39.0			1.9	
		27.5		31.0			40.2	
MEAN	**45.3**	**18.3**		**33.3**	**45.1**		**26.6**	
PEG RECOVERY (%)	113.3	96.5		115.0	98.0		97.4	
	91.1	103.3		89.4			96.1	
		93.9		92.6			96.2	
MEAN	**102.2**	**97.9**		**99.0**	**98.0**		**96.6**	
TRANSIT TIME (mins)	6.4	7.2		7.0	6.2		2.3	
	5.4	3.2		9.8			7.8	
		5.4		4.8			4.3	
MEAN	**5.9**	**5.3**		**7.2**	**6.2**		**4.8**	

TABLE 9.8 EXPERIMENTS AT WEEK 9

ANALYSIS OF VARIANCE TABLES : OLEIC ACID

	Experiment : Jejunum	Criterion : Volume			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	378	378.3	1.55	.237
CASE(TR)	12	2925	243.7	7.57	<.001
WK	1	17	17.5	0.54	.464
WKxTR	1	5	5.3	0.17	.686
WKxCASE(TR)	7	327	46.7	1.45	.204
ERROR	55	1771	32.2		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	8	-1.0	5.5	6	4.7	10.5	-3.7 , 15.1

	Experiment : Jejunum	Criterion : Sodium			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	491	490.6	1.50	.245
CASE(TR)	12	3937	328.1	6.80	<.001
WK	1	1	0.8	0.02	.899
WKxTR	1	6	5.6	0.12	.734
WKxCASE(TR)	7	394	56.3	1.17	.336
ERROR	55	2654	48.3		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	8	-1.8	6.8	6	4.4	11.2	-4.2 , 16.7

TABLE 9.9 RESULTS FOR VOLUME AND SODIUM (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : OLEIC ACID

	Experiment : Jejunum	Criterion : Chloride			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	89	88.8	0.22	.644
CASE(TR)	12	4751	395.9	8.29	<.001
WK	1	13	12.6	0.26	.609
WKxTR	1	4	3.7	0.08	.780
WKxCASE(TR)	7	289	41.3	0.86	.540
ERROR	55	2626	47.8		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	8	-0.2	8.4	6	2.3	11.4	-9.0 , 14.1

	Experiment : Jejunum	Criterion :Potassium			
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	370	369.7	0.10	.752
CASE(TR)	12	42344	3528.6	5.91	<.001
WK	1	2668	2667.8	4.47	.039
WKxTR	1	20	20.1	0.03	.855
WKxCASE(TR)	7	1998	285.4	0.48	.846
ERROR	55	32832	596.9		

The interaction Week x Case (Treatment) is not significant, nor is the effect Week x Treatment. The effects of Week and Case (Treatment) are significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
2	7	133.7	25.4	5	134.2	26.8	-33.0 , 34.3
9	5	126.5	21.7	6	116.2	32.2	-49.0 , 28.1

The difference between weeks was significant with 95% CI of -22.3 , -4.5.

TABLE 9.10 RESULTS FOR CHLORIDE AND POTASSIUM

ANALYSIS OF VARIANCE TABLES : OLEIC ACID

Experiment : Jejunum Criterion : Transit Time

SOURCE	DF	SS	MS	F	P
TR	1	16	16.1	2.28	.157
CASE(TR)	12	84	7.0	4.50	<.001
WK	1	6	6.2	3.96	.052
WKxTR	1	0	0.1	0.01	.925
WKxCASE(TR)	7	14	2.0	1.31	.264
ERROR	54	84	1.6		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	N	Mean	Stdev	N	Mean	Stdev	95% CI
-	8	3.7	1.1	6	4.7	1.8	-0.7 , 2.7

Experiment : Jejunum Criterion : Oleic Acid

SOURCE	DF	SS	MS	F	P
TR	1	669	668.8	0.70	.419
CASE(TR)	12	11464	955.3	4.32	.031
WK	1	775	774.8	3.50	.104
WKxTR	1	0	0.4	0.00	.967
WKxCASE(TR)	7	1549	221.3	4.31	<.001
ERROR	55	2822	51.3		

The interaction Week x Case (Treatment) is significant and, against its mean square, the interaction Week x Treatment and Week are not significant. The effect of Case (Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Control
Week	N	Mean	Stdev	N	Mean	Stdev	95% CI
-	8	44.5	9.4	6	50.3	15.9	-8.9 , 20.5

TABLE 9.11 RESULTS FOR TRANSIT TIME AND OLEIC ACID (JEJUNUM)

ANALYSIS OF VARIANCE TABLES : OLEIC ACID

	Experiment : Ileum		Criterion : Volume		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	3	3.1	0.03	.870
CASE(TR)	11	1212	110.1	3.16	.003
WK	1	3	3.2	0.09	.763
WKxTR	1	69	69.0	`.98	.166
WKxCASE(TR)	9	273	30.3	0.87	.559
ERROR	45	1568	34.9		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	-8.5	4.1	7	-8.2	5.5	-5.7 , 6.3

	Experiment : Ileum		Criterion : Sodium		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	42	42.0	0.32	>.400
CASE(TR)	11	2386	216.9	1.66	.227
WK	1	89	88.9	0.68	.430
WKxTR	1	5	5.3	0.04	.845
WKxCASE(TR)	9	1173	130.3	2.72	.013
ERROR	45	2155	47.9		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	-6.5	5.6	7	-5.4	8.5	-7.7 , 9.8

TABLE 9.12 RESULTS FOR VOLUME AND SODIUM (ILEUM)

ANALYSIS OF VARIANCE TABLES : OLEIC ACID

	Experiment :Ileum		Criterion : Chloride		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	1	1.5	0.01	>.900
CASE(TR)	11	2274	206.7	1.90	.171
WK	1	64	64.2	0.59	.462
WKxTR	1	5	4.9	0.05	.836
WKxCASE(TR)	9	977	108.5	2.54	.019
ERROR	45	1925	42.8		

The interaction Week x Case (Treatment) is significant and, against its mean square, no other effect is significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	3.0	4.9	7	1.8	9.0	-10.3 , 7.9

	Experiment : Ileum		Criterion : Potassium		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	20086	20086.4	6.05	.018
CASE(TR)	11	61458	5587.1	1.68	.108
WK	1	14613	14613.3	4.40	.042
WKxTR	1	2184	2183.7	0.66	.422
WKxCASE(TR)	9	41493	4610.3	1.39	.221
ERROR	45	149330	3318.4		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Case (Treatment). The effects of Week and Treatment are significant.

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the individual results for each week and treatment, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
2	20	162.7	42.9	20	211.0	102.0	-2.0 , 99.4
9	17	144.3	24.0	12	173.2	36.9	6.0 , 52.1

There was a significant reduction in mean potassium from Week 2 to Week 9, the 95% CI being -42.2 , 5.4 for the controls and -90.0 , 14.0 for the autotransplants.

TABLE 9.13 RESULTS FOR CHLORIDE AND POTASSIUM (ILEUM)

ANALYSIS OF VARIANCE TABLES : OLEIC ACID

	Experiment : Ileum		Criterion : Transit Time		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	1	1.1	0.19	.673
CASE(TR)	11	66	6.0	2.62	.011
WK	1	1	0.8	0.34	.565
WKxTR	1	10	10.3	4.51	.039
WKxCASE(TR)	9	14	1.6	0.70	.706
ERROR	44	101	2.3		

The interaction Week x Case (Treatment) is not significant, nor is the effect of Week. The effects of Week x Treatment and Case (Treatment) are significant. The effect of Treatment is not significant

From the above analysis an appropriate way of summarising the effects of week and treatment is to use the means of each week x treatment combination, which gives the following:

		Control			AutoTx		AutoTx - Cont
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
2	6	6.1	1.4	7	4.9	0.8	-2.6 , 0.2
9	6	5.0	1.5	5	5.9	0.9	-0.9 , 2.6

The significant interaction Week x Treatment is that the mean Transit Time decreased between Weeks 2 and Week 9 for the controls but increased for the autotransplants.

	Experiment : Ileum		Criterion : Oleic Acid		
SOURCE	**DF**	**SS**	**MS**	**F**	**P**
TR	1	247	246.9	0.46	.511
CASE(TR)	11	5876	534.2	3.82	<.001
WK	1	67	67.2	0.48	.491
WKxTR	1	17	17.5	0.12	.725
WKxCASE(TR)	9	1548	172.0	1.23	.301
ERROR	45	14470	139.7		

The interaction Week x Case (Treatment) is not significant, nor are the effects Week x Treatment and Week. The effect Case(Treatment) is significant. Against the Case (Treatment) mean square, the effect of Treatment is not significant.

From the above analysis an appropriate way of summarising the effect of the treatment is to use case means, which give the following:

		Control			AutoTx		AutoTx - Control
Week	**N**	**Mean**	**Stdev**	**N**	**Mean**	**Stdev**	**95% CI**
-	6	40.4	10.1	7	36.8	10.7	-16.3 , 9.2

TABLE 9.14 : RESULTS FOR TRANSIT TIME AND OLEIC ACID (ILEUM)

CHAPTER 10

MORPHOMETRICS

Removal of a length of intestine from the main intestinal stream deprives the mucosa of contact with both intraluminal nutrients, and biliopancreatic secretions. This can lead to mucosal atrophy[218-221], which may result in decreased absorption[223,225]. These findings, however, remain in dispute, since other authors report normal histological appearance and function in isolated small bowel[105,222,230,231]. This controversy has relevance to this study since it utilises modified Thiry-Vella loops, which are isolated from intestinal contents.

Study of the appearance of the villi (morphology) and villus height and crypt depth (morphometrics) of autotransplanted small bowel is of particular interest due to Ballinger's finding of blunting of the intestinal villi following autotransplantation in dogs[72]. Abnormal small bowel morphology can be associated with defects in absorption[233].

Since the question of mucosal atrophy in the Thiry-Vella loop remains to be clarified, all the dogs in this study had histological examination of the small bowel carried out, as described in Chapter 2. The purpose of this was twofold: firstly, to determine whether any changes in morphology or morphometrics do occur in the small bowel mucosa of the modified Thiry-Vella loop, and, secondly, to test the assumption that if atrophy of the mucosa does occur, whether it does so to the same extent in both control and autotransplanted bowel.

PROCEDURE

Each dog which survived to the end of the late studies had histological samples of small bowel taken for the purpose of morphometrics. This involved five animals in Group 1 (jejunal controls), six in Group 2 (jejunal autotransplants), six in Group 3 (ileal controls) and six in Group 4 (ileal autotransplants). Each animal had a sample taken at the initial laparotomy to create the Thiry-Vella loop, and a further two samples taken immediately after sacrificing the dog; giving a total of three separate areas of small bowel for assessment per animal.

HISTOLOGICAL SPECIMENS

All specimens of jejunum and ileum taken for histology were obtained from the antimesenteric aspect of the bowel. This site was selected because it made use of the tissue excised when the seromuscular bridge was created by removal of a 5-7cm length of small bowel. This comprised 50% of the circumference of the bowel wall, taken from the site opposite to the insertion of the mesenteric blood vessels. All samples were of full thickness bowel wall, and were pinned out, mucosa upwards, on a cork sheet and subsequently immersed in formalin. A post-mortem was carried out on all dogs immediately after sacrifice and the specimens for histological examination were taken promptly, before post-mortem autolysis could occur. After fixation, they were stained with haematoxylin and eosin and at least 18 transverse sections taken and mounted on slides.

Histology at Initial Laparotomy

These samples were taken to establish the normal morphology and morphometrics, and act as a baseline against which the later samples could be assessed.

The sample was from jejunum in Groups 1 and 2, and was taken from a site 20cm distal to the ligament of Treitz. The ileal dogs, Groups 3 and 4, had their initial sample taken from the site of their seromuscular bridge, 90cm proximal to the ileocaecal valve. In both autotransplanted groups, sampling was immediately after the autotransplantation procedure had been completed.

Post-mortem Histology of Thiry-Vella Loop

This was taken to compare against the initial morphology, and for comparison with the morphology and morphometrics of the small bowel which remained in continuity.

Samples were taken 10 weeks after the initial specimen. A 5cm length of full thickness bowel wall was taken from the antimesenteric aspect of the bowel at the mid-point of the Thiry-Vella loop.

Post-mortem Histology of Bowel in Continuity

This sample was taken firstly to assess the effect of autotransplantation on small bowel morphology, and secondly, to assess any effect of removal of an 80cm length of bowel on the morphology of the remaining bowel.

In the two jejunal groups of dogs, the sample was taken from a site 20cm distal to the origin of the jejunal loop, while in the two ileal groups of dogs it was taken from a site 20cm proximal to the origin of the ileal loop. These sites were arbitrarily chosen in order to standardise the samples for comparison. Both specimens were obtained, as before, from the antimesenteric aspect of the bowel, and were 5cm in length.

MICROSCOPY

The measurement of villus height and of crypt depth of the small bowel mucosa was carried out by using an optical micrometer attached to the microscope.

Each 5cm section of bowel had three slides made from it. Each slide contained six sections. Only sections where the villi and crypts were seen to be cut at right angles, and therefore seen in their entire length, were used. From each slide three separate villi and crypts were measured using the optical micrometer. A mean value for crypt depth and villus height was derived for each animal. An overall mean value was then obtained for each of the four experimental groups. The results are seen in Table 10.1 (page ???).

STATISTICS

The data has been analysed using analysis of variance. The analysis of variance tables associated with this are shown in Table 10.2. (page 201).

RESULTS

Although no formal measurement was made, it was apparent that the modified Thiry-Vella loop had a smaller diameter than the bowel which had remained in continuity. This

finding was noted in all dogs, regardless of group. Thick mucus was found to be adherent to the mucosa of the loops when they were opened, this was not a feature of the bowel left in continuity. The in continuity bowel appeared to be of normal diameter.

Three comparisons have been made for each of villus height and crypt depth:

1. Week 0 (initial laparotomy) versus Week 10 (post-mortem).

2. Autotransplants versus controls.

3. Jejunum versus ileum.

Time

This examines the effect which 10 weeks of isolation from the intestinal stream has on the mucosa of the T-V loop. It also assesses any compensatory changes in the bowel remaining in continuity, 10 weeks after removal of 80cm of it's initial length.

The mean values for all four groups are summed to obtain a single value for "initial histology". This is repeated for "loop histology" and "in continuity histology", and these 3 values are compared.

Villus Height

Villus height is found to be significantly reduced ($p = 0.013$). Examination of the raw data (Table 10.1, page 200) indicates that mucosal atrophy has occurred in all the defunctioned Thiry-Vella loops, of all four experimental groups.

Crypt Depth

Crypt depth was not significantly altered ($p = 0.417$). This suggests that in this model, if atrophic changes do occur, they must take longer than 10 weeks of defunctioning before becoming evident.

Autotransplantation

Autotransplanted small bowel was compared to control small bowel for each of the three morphological samples.

Villus Height

This was significantly greater in the autotransplanted dogs ($p < 0.001$).

The autotransplant groups have slightly higher villi in the sample for "initial histology". This is the result of chance, since dog allocation to control or autotransplanted groups was random. This is an experimental error

Of greater interest is the finding that villus height within the defunctioned loop is better preserved at Week 10 in the autotransplanted bowel. The explanation for this is not obvious, and contrary to expectation. Since the autotransplanted animals start off with an increased villus height over the controls, the true significance of this finding is unknown.

Morphometrics of the in continuity bowel at Week 10 shows villus height in the dogs who were autotransplanted has remained greater than the villus height of the control dogs.

Crypt Depth

This was not significantly different after autotransplantation ($p = 0.782$).

Unlike the villi, the crypt depth of all four experimental groups was the same when the initial histological sample was taken, and this did not alter in the 10 weeks of the study.

Small Bowel Site

A comparison of jejunum versus ileum was made by combining the results of Groups 1 and 2 at "initial histology", "loop histology" and "in continuity histology", and comparing them against the combined results for Groups 3 and 4.

Villus Height

Villus height is significantly higher in the jejunum ($p < 0.001$).

Crypt Depth

Crypt depth is significantly greater in the jejunum ($p < 0.001$).

The normal pattern of villus height and crypt depth being greater in jejunum than ileum is seen at the start of the study, and this finding is unchanged in both "loop" and "in continuity" bowel, even after autotransplantation. Contrary to Ballinger's findings, small bowel autotransplantation did not affect the morphology of jejunal or ileal mucosa.

DISCUSSION

Analysis of the morphology and morphometrics of jejunum and ileum in this study has resulted in several conclusions:

1. Mucosal atrophy within these defunctioned loops has occurred.

Atrophy occurs in Thiry-Vella loops of both jejunum and ileum, confirming that canine small bowel mucosa, like that of the rat, does undergo some atrophy when it is deprived of intraluminal contents.

This finding may explain the significant reduction in absorption in both controls and autotransplants at the late time points in some of the experiments. This was not seen in all late experiments, and when it did occur, it often only affected one of the parameters being assessed e.g. sodium. All five test solutions produced experiments which exhibited decreased absorption at the late time point. Therefore mucosal atrophy can result in decreased absorption in control and autotransplanted small bowel, but the presence of mucosal atrophy does not guarantee decreased absorption.

2. Mucosal atrophy is less in autotransplanted Thiry-Vella loops.

The finding that the mucosa within autotransplanted T-V loops undergoes significantly less atrophy than the mucosa within control T-V loops, was unexpected. The reason is unclear, but it would seem that denervation may possibly exert a protective effect with regard to maintenance of villus height after defunctioning. Neural pathways may either play a part in recognising lack of luminal nutrients, or possibly exert a tonic inhibition on mucosal growth.

Since autotransplanted mucosa within the defunctioned loop retains villus height better than control mucosa, it could be argued that this may have an influence on absorption from the loop. Theoretically, better preservation of villus height in the autotransplants will allow them to absorb more than the controls, since the increased villus height results in an increased surface area for absorption. Since increased absorption by autotransplanted bowel has not been detected by this study, it can be speculated that a defect in absorption after autotransplantation does exist, but has been compensated for by the increased villus height. Since this study only looked at morphology after ten weeks of defunctioning, it is not clear how early any decrease in villus height takes place. Since villus atrophy as early as Week 1 has never been reported in the dog, this implies that autotransplanted bowel will not have the advantage of an increased villus height, when studied at the early time points. Any defect in absorption produced as a result of denervation or lymphatic transection would be seen at Weeks 1 and 2, rather than at Weeks 8 and 9. This has not been shown. The retained villus height does not appear to give autotransplanted small bowel an absorptive advantage over control bowel.

3. Autotransplantation does not result in morphological abnormalities.

Morphological abnormalities are not found in the bowel which remains in continuity, or in the mucosa of the defunctioned loops. The normal pattern of higher villi and deeper crypts in the jejunum than the ileum is also preserved following autotransplantation. Ballinger's finding of blunting of the villi was not observed in this study[72]. Autotransplanted small bowel, both of the T-V loop and that which remains in continuity with the intestinal stream, does not show any abnormality of villus structure.

4. Removal of 80cm of jejunoileum does not result in compensatory hypertrophy.

The jejunum or ileum left in continuity in both control and autotransplanted animals, does not show a significant increase in villus height or crypt depth following the removal of 80cm of total intestinal length. This emphasises that the diarrhoea which the autotransplanted dogs get is not due to having a short gut, which would have provoked compensatory hypertrophy. Further evidence that loss of an 80cm length does not cause the short gut syndrome is the observation that the control dogs, who have had an equal amount of bowel resected, do not develope diarrhoea.

In summary, denervation and lymphatic transection has no apparent detrimental effect on small bowel morphology or morphometrics when the autotransplanted bowel remains in contact with the luminal contents of the intestine.

SMALL BOWEL MORPHOMETRICS

GROUP	INITIAL HISTOLOGY		LOOP HISTOLOGY		IN CONTINUITY HISTOLOGY	
	Villus Height	Crypt Depth	Villus Height	Crypt Depth	Villus Height	Crypt Depth
1 (n=5)	1010±110	630±80	840±80	630±50	920±50	710±50
2 (n=6)	1070±100	620±50	1020±170	620±30	1110±60	570±60
3 (n=6)	830±50	450±15	530±60	330±30	840±50	480±30
4 (n=6)	890±100	480±50	780±90	470±50	980±60	530±30

Villus height and crypt depth are mean ± standard error of the mean and are in μm.

n = number of dogs in group

Initial histology = taken at initial laparotomy

Loop histology = taken from the Thiry-Vella loop at post-mortem

In continuity histology = taken from the bowel in continuity at post-mortem

TABLE 10.1 : MORPHOMETRIC DATA

ANALYSIS OF VARIANCE TABLE : MORPHOMETRICS

Villus height

SOURCE	DF	SS	MS	F	p
WEEK	2	71817	35908	8.70	0.013
SITE	1	104533	104533	25.33	0.0001
TREAT	1	64533	64533	15.64	0.005
ERROR	7	28883	4126		
TOTAL	11	269767			

Crypt Depth

SOURCE	DF	SS	MS	F	p
WEEK	2	7217	3608	0.99	0.417
SITE	1	90133	90133	24.82	0.0001
TREAT	1	300	300	0.08	0.782
ERROR	7	25417	3631		
TOTAL	11	123067			

WEEK = the separate histological sampling times.

SITE = jejunum versus ileum

TREAT = control versus autotransplant

TABLE 10.2 : RESULTS FOR SMALL BOWEL MORPHOMETRICS

CHAPTER 11

DISCUSSION

This study has shown that extrinsic denervation, disruption of continuity of the intrinsic nervous system, and lymphatic transection does not result in significantly increased secretion or decreased absorption, when assessed by simple nutrients in both jejunum and ileum.

The main theme of the large amount of literature published on small bowel transplantation concerns the immunological sequelae; with little information regarding absorption. The few studies pertaining to absorption are difficult to evaluate for several reasons: different animal models and species have been used (autografts, isografts, and allografts, in rats, dogs and pigs), experiments have been conducted at a variety of different times after transplantation, and a wide variety of test solutions have been utilised to assess absorption. The outstanding feature of most of these studies has been the failure to include a control group, making true comparison to normal absorption impossible. This mixture of studies has resulted in conflicting data with regard to the effect transplantation has on small bowel absorption.

The series of experiments described in this thesis has provided important and previously unknown data about absorption of water, electrolytes, and simple nutrients in both jejunum and ileum after autotransplantation in the dog. This study is of particular relevance since it includes control groups, allowing scientific comparison between absorption in autotransplanted bowel and "normal" bowel.

MODEL SELECTION

The ideal model to study the effect of denervation and lymphatic transection on small bowel absorption needs to exclude the confounding effects of ischaemia, reperfusion and rejection, while retaining portal venous drainage. The bowel structure and motility should closely resemble that of humans.

Rat Model

The rat has been the most extensively studied animal model. The disadvantage with this model is that rats have leaf-shaped intestinal villi and, unlike dogs and man, have migrating myoelectric complexes even in the fed state. The differing villus structure and motility to human intestine, and the rapidity with which defunctioned loops develop mucosal atrophy, make it a model far removed from what may occur in humans.

A further problem with rat studies is that they have produced conflicting results. Heterotopically placed grafts have been shown to have decreased water and sodium absorption at 9 and 21 days[158,159]. This was also noted in denervated Thiry-Vella loops[160,161]. These findings were in small bowel isolated from luminal nutrition, and therefore subject to mucosal atrophy, which may have influenced the results. However, other studies in isolated loops show the contradictory finding of normal water and electrolyte absorption[163,246].

Dog Model

Dogs provide a large animal model with similar intestinal villi and motility patterns to human small bowel, and may be more relevant to study than rats. Despite this, dogs have been far less extensively studied, presumably due to their increased cost over rats, a thrombogenic tendency which results in a high rate of graft loss due to infarction, and difficulty in achieving effective immunosuppression. Of the few studies concerning absorption, most have the major flaw of failing to include control groups[166,193,205-207,209]. Comparisons have usually been made between autografts and allografts, both of which have had extrinsic denervation, disruption of continuity of the intrinsic nervous system, and lymphatic transection. This does not allow the autograft to function as a true control, and attempted comparison between these studies gives conflicting results[109,113,182,200,247,248].

The dog model in this study assesses the true physiological effect of denervation and lymphatic transection on a wide range of simple nutrients. The absorptive pathways of all these nutrients have been previously documented, and all were added to the test solutions in physiological concentrations. The exclusion of multiple confounding factors inherent to true transplantation allows this model to make a valid assessment of the effect of denervation and lymphatic transection on small intestinal absorption. It also allows a true comparison with normal absorption, since control groups of animals are included.

SECRETION

Denervation has been implicated in increased secretion due to the loss of the "sympathetic brake" on intestinal secretion[70]. This increased secretion has been suggested as the cause of the diarrhoea which results after division of the sympathetic nerve supply to the small bowel.

There is no published data on potassium secretion after canine jejunoileal autotransplantation. In this study, potassium secretion provides an important method of assessing secretion from the bowel since no potassium was added to any of the test solutions, allowing it to act as a marker of secretion.

Only experiments with the oleic acid solution produced a significant increase in potassium secretion after autotransplantation, and this only occurred in the ileum. This is almost certainly due to the direct stimulant effect of oleic acid. This prosecretory effect of oleic acid is well documented in both jejunum[249,250], and ileum[251]. Autotransplanted ileum appears to be more sensitive to the irritant effect of oleic acid, the reason for this is unknown.

The original concentration of oleic acid chosen for these experiments was 10mM. This was used only in the early experiments in Dogs 1A and 2A and not included in the final analysis of data since it provoked a net secretion of both fluid and mucus from the loops. The concentration of oleic acid used in subsequent experiments was reduced to 5mM, although even this concentration caused secretion in some dogs, and increased mucus production in all dogs. The oleic acid solution is not physiological, since fats are normally absorbed as mixed micelles, along with triglycerides. It's use in this study was purely as a marker of lymphatic function, since it is a long chain fatty acid known to be absorbed solely by lymphatics.

The confidence intervals indicate that changes in potassium secretion of between 10-80% of that seen in the controls would be detected by these experiments. This range covers experiments with all five test solutions. The experiments with sodium chloride, glucose and oleic acid were the most sensitive, and were capable of detecting a difference in potassium secretion of 10-40%. The amino acid solutions were less sensitive, and would have detected a difference in secretion of 30-80%. This wide range is the result of large variability in potassium secretion by the loops, especially in the autotransplanted dogs. Detection of a change in secretion only when it is more than 50% of the normal secretion, indicates a set of experiments which are not sensitive to moderate changes in secretion.

SENSITIVITY OF STUDY

The inclusion of a minimum of six dogs in each of the experimental groups allows the experiments in this study to have the power to detect a change in absorption of volume, sodium, or chloride varying between 25-50% of normal absorption. No such changes occurred.

Impaired absorption in autotransplanted small bowel can be expected to occur to an extent ranging from no impairment (0% reduction in absorption) to total failure of absorption (100% reduction in absorption). The most likely scenario was envisaged to be between these two extremes. Detection of minor impairments in absorption may have no clinical relevance, since the full length of small bowel has excess absorptive capacity, and should be able to compensate by utilising more of it's length. This study intended to detect a degree of impaired absorption which would be of clinical relevance, estimated to be a reduction in absorption of 50% or more. The information derived from the confidence interval data indicate that the majority of the experiments in this study would have detected a change in normal absorption of between 8-50%. This achieves the aim of being sensitive enough to detect changes which are of clinical relevance.

ABSORPTION

Absorption of electrolytes and simple nutrients following autotransplantation was unchanged, apart from a minor reduction in amino acid absorption in autotransplanted ileum. This agrees with preliminary work in the same animal model, using a mixed glucose and electrolyte solution perfused through modified Thiry-Vella loops[252].

Simple nutrients were chosen for the experimental solutions in view of their well documented absorptive pathways. They were perfused separately in order to assess each single pathway at a time, since amino acids, sodium, and glucose are all known to influence the absorption of each other. This ability of mixed nutrient solutions to influence the absorption of each of the constituents is well documented[253-256].

Glucose

Glucose is perhaps the most studied substance in previous absorption studies. It is an aldohexose which has a minor passive uptake pathway, but is mainly actively absorbed[257]. Rat allografts[158,159] and isografts[164] have impaired glucose absorption, but this has not been seen in dogs[173-177]. Normal glucose absorption after autotransplantation has been confirmed by this study. This has important implications in the clinical setting, since glucose is the main carbohydrate in normal diet.

Active uptake of glucose increases both sodium and water absorption[258]. This can be seen in the comparison of volume, sodium and chloride absorbed by jejunum and ileum from the sodium chloride solution with the absorption from the glucose solution. The percentage of volume, sodium, and chloride absorbed per 15mins is around twice as much when there is 30mM glucose present. This study shows that this normal finding is preserved in the autotransplants.

The sensitivity to detect changes in glucose absorption in this study is within the range of between 13-27% of normal absorption. These experiments are particularly sensitive to small changes in glucose absorption.

Glucose absorption was found to be not altered by autotransplantation of jejunum or ileum.

Amino Acids

Amino acid absorption has seldom been studied. Amino acids form the basic building blocks of proteins, and are required for the constant repair and renewal of tissue around the body. Western diet usually supplies an excess of protein, and these extra amino acids are deaminated by the liver. The only previous study which included a control group was in rats, and showed reduced glycine absorption in isografts, allografts, and denervated Thiry-Vella loops[160,161].

Glycine is a neutral amino acid while phenylalanine is an aromatic amino acid, both are absorbed by different pathways. Amino acid absorption often involves a sodium dependent pathway, although an independent pathway also exists, varying from species to species[259-261]. The normal physiological concentration of free amino acids within

the lumen of the gut appears very variable[262], with free glycine ranging from 0.15-0.70mM and free phenylalanine from 0.3-1.1mM. The concentrations of other amino acids ranged from 0.06-3.6mM[263].This study used a concentration of 2.5mM, which was a physiological concentration, rather than pharmacological.

Using amino acids alone, as monopeptides, is somewhat artificial, since protein is usually absorbed still partly linked as peptide chains of varying length[264]. In this latter form they are actually absorbed more efficiently than monopeptides[265]. While accepting that monopeptides are a less major uptake pathway for protein absorption, they still play a role in normal absorption.

The sensitivity of this study to detect changes in absorption of glycine was between 10-15%, while for phenylalanine it was even more sensitive, with only 4-6% change in absorption being detectable. This degree of sensitivity is the highest achieved in this study.

Absorption of glycine and phenylalanine are both reduced after autotransplantation, but only in the ileum. This abnormality was evident as early as Week 1 and persisted at Week 8.The reduction in amino acid absorption represents an overall reduction in absorptive capacity of around 15% in autotransplanted ileum. Since most amino acid absorption occurs in the jejunum, this would only present a potential problem clinically if a segmental ileal graft was used. If absorption of these monopeptides could be extrapolated to include total protein absorption in autotransplanted small bowel, then there would be little reduction, and this would probably be insignificant clinically. An additional factor to take in to consideration is that the slight reduction in amino acid absorption found by this experiment may not exist in the presence of a mixed nutrient diet.

Oleic Acid

Oleic acid is a long chain (C_{18}) fatty acid which is normally absorbed via the lymphatics[266]. It was used specifically as a marker of lymphatic function, which is of major interest since lymphatics are the main route for fat absorption. The importance of fat absorption lies with the ability of fat to provide a rich source of calories, and the essential fatty acids. Jejunum was originally believed to be the site of fat absorption, but the importance of the ileum has recently been recognised. Studies in patients with small bowel resections showed that ileum can absorb fat effectively[267]. Further studies showed that the ileum has the capacity to absorb fat even when there has not been a

proximal small bowel resection[268,269]. An elegant electron microscopy study showed ileal cells filled with lipid in the same fashion as jejunal cells following an infusion of fat in to the lumen of the bowel[270].

Transected lymphatics are known to reconnect at between 14-21 days[103,106,107], but those within the small bowel mesentery, proximal to the line of transection are dilated, presumably as a result of reduced lymph flow, for at least 4 weeks. It is possible that while the intestinal lymphatics are distended, the total lymph flow remains normal, but the flow rate is slower. This would result in the same net fat uptake. The dogs in this study commenced their oleic acid studies exactly 14 days after the autotransplantation procedure, at a time when lymphatic reconnection may have already taken place. This would explain the normal absorption found in this study. Normal oleic acid absorption at 10-14 days has been shown in grafts placed in the neck[184]. It is possible that both these animals, and the dogs in this study would exhibit impaired oleic acid absorption if they had been studied at Week 1.

Normally 40-50% of oleic acid is normally absorbed, and this uptake occurs solely via lymphatics[271]. Absorption of between 37-50% oleic acid/15mins was achieved in this study, in both early and late experiments.

The oleic acid experiments were relatively insensitive to changes in volume, sodium, and chloride; due to the irritant effect of oleic acid allowing little absorption. The experiments, however, were sensitive to changes in potassium secretion of between 13-33%, and to changes in oleic acid absorption of between 29-35%.

Earlier studies in this same dog model of jejunoileal autotransplantation showed no increase in faecal fat excretion, despite being on a high fat diet[272]. This situation has also been found in pigs after a small bowel transplant[273]. Other studies in dogs have showed impaired oleic acid absorption in autografted jejunum for 4 weeks[105,185], and others have found increased faecal fat content up to 9 months after autotransplantation[186]. The reason for these conflicting results is not clear.

The decrease in absorption seen in both control and autotransplanted bowel at the late study week is almost certainly linked to the changes in mucosal enzyme function caused by the mucosa being out of the nutritive stream of intestinal contents. Autotransplanted and control bowel appear equally affected by this process.

Aetiology of Post-autotransplantation Diarrhoea

Diarrhoea as a characteristic feature in dogs following division of the sympathetic supply to the small bowel has been long documented[71, 72]. It occurred in all autotransplanted dogs in this study, not in the controls, and followed the same pattern as previous authors have described: it is at its most profuse in the early post-operative weeks, appears not to distress the animals, and occurs in all autotransplanted dogs without exception[73,102,112,171,179,203].

Four weeks after autotransplantation, some dogs only have diarrhoea after eating. This tendency to post-prandial diarrhoea continues up until the end of the ten week study period. The cause for this change is not known; reinnervation will not have occurred as early as this, so it implies that a form of adaptation has arisen, possibly in the colon which may be able to absorb more fluid after four weeks.

The potential causes of this diarrhoea include:

(a) increased secretion

(b) malabsorption

(c) altered motility

(d) bacterial overgrowth

This study was designed to look for evidence of increased secretion or malabsorption with a set of solutions covering a wide range of simple nutrients. Since the diarrhoea is at its worst early on, the dogs were studied starting just one week post-operatively, for a two week consecutive period. The experiments were then repeated at Weeks 8 and 9, when the diarrhoea had become less marked. Increased secretion was not found to occur, and absorption of volume of perfusate from all five test solutions was not significantly altered by autotransplantation. The single exception to this occurred with the glycine solution (only in the ileum), this may be a chance statistical finding.

This still leaves the post-autotransplantation diarrhoea to be explained. It is known that feeding enhances jejunoileal absorption[274-276]. Possibly, an absorptive defect may only be detected following a meal, when the absorptive system is challenged. Nerve blockade in dogs (simulating the transplanted state) reduces the post-prandial absorptive response to 50% of normal[277]. However, no reduction in post-prandial absorption following autotransplantation in this model was detected in a study in which experiments were

carried out in both the fasting and the fed state[266]. Since neither malabsorption nor increased secretion occurs following autotransplantation, these do not provide adequate explanation for the occurrence of post-autotransplantation diarrhoea.

Motility is affected by autotransplantation of the jejunoileum. The distal small bowel is removed from the control of the duodenal "brake" and the period of the migrating motor complex (MMC) is shorter in the autotransplanted small bowel. This should result in a shorter transit time, but autotransplanted jejunoileum has fewer MMC's in any 24 hour period than innervated bowel. This is the result of autotransplanted small bowel having long periods of a non-cyclic irregular spike potentials making the occurrence of MMC's variable[199, 200, 202]. The alteration in motility which follows autotransplantation is a potential source of diarrhoea. Autotransplanted jejunum showed evidence of a slower transit time with all five solutions; this was significant in the sodium chloride, glucose and glycine solutions. Transit time in autotransplanted ileum was not significantly different from control ileum. There appeared to be a tendency for the autotransplanted bowel of both groups to have slower transit time; that this was not statistically significant may be due to the great variability seen among the dogs. This variability may be due to studying the dogs during different phases of the MMC. The period of the MMC is variable from dog to dog, but tends to be fairly constant within the same dog. The dogs were therefore studied during all phases of the MMC, and each phase may have a different transit time. Slower transit allows more absorption to occur, since the nutrients remain in contact with the absorptive surface for longer[201]. Absorption from autotransplanted jejunum showing a significantly prolonged transit time, was not found to be altered. This may indicate that the slower transit is not sufficient to affect absorption in these experiments, or that the slower transit is sufficient to mask an impairment of absorption in autotransplanted jejunum. This latter supposition is unlikely in view of the fact that no defect in absorption is detected in autotransplanted bowel in those experiments which did not show a prolonged transit time.

The other possible contender for causing the diarrhoea, since increased secretion and decreased absorption have been excluded, is bacterial overgrowth. This phenomenon is usually linked with blind loops or disordered motility and is associated with malabsorption, and both exist in this model, yet no malabsorption is seen.

CONCLUSION

This study has provided essential physiological background data on absorption from both normal and denervated small bowel. It forms the solid foundation of basic knowledge required to allow further meaningful investigation of the effect of transplantation on small bowel absorption. Only now, with the basic effects of lymphatic transection and denervation clearly documented, can further studies be conducted to assess the effect which the several different components of transplantation injury may have on absorption.

There is clearly no physiological reason for transplanted small bowel to have a major absorptive defect, which is encouraging for the future of clinical small bowel transplantation. As no specific nutrient out of the wide range assessed showed major impairment of absorption, it should permit small bowel transplant patients to be able to enjoy a normal unrestricted diet. If transplantation injury causes no permanent damage to a small bowel graft, and rejection can be controlled, then absorption from the transplanted bowel should be sufficient to sustain life.

FUTURE EXPERIMENTS

With the knowledge that water, electrolytes, and simple nutrients are well absorbed from bowel which has been denervated and suffered lymphatic transection, a solid foundation on which other studies can be based, has been laid.

Simple nutrient solutions are not truly physiological since they are composed of isolated nutrients, instead of a mixture of protein, carbohydrates and fat, which make up the normal diet. The potential that a mixed nutrient solution will exhibit malabsorption exists, perhaps because the capacity of carrier mechanisms is reduced by autotransplantation, and this has not been detected by the single nutrient solutions because the carrier systems have not been saturated. Using a mixed nutrient solution may stress the system sufficiently to allow any defects which may have developed following autotransplantation, to be shown. Alternatively, since some nutrients act synergystically to be absorbed, increased absorption may be detected.

Isolated intestinal loops provide an easily controlled experimental environment, but they are not physiological, since they are deprived of normal intestinal content which is necessary for normal mucosal function. It is possible that both control and autotransplanted loops were sufficiently affected by this that subtle absorptive changes

induced by autotransplantation were missed. This could be determined by repeating the experiments in the intact dog, using a triple lumen tube technique. This would also allow the dogs to act as their own controls, since they could be studied both before and after autotransplantation without progressive atrophy occurring, since no defunctioned loop is involved. This may help to reduce the problem of variability.

Using electrodes attached to the small bowel serosa would allow recording of the phase of the MMC, and enable all experiments to be conducted in all dogs during the same phase. This may decrease the variability seen from experiment to experiment, and from dog to dog, and therefore increase the sensitivity of the study to detect small differences in absorption.

The electrolytes detected in the loop effluent may be composed of a mixture of those which were in the test solution, and those secreted by the bowel. Since only the entire electrolyte content of the effluent was analysed, there is no way of knowing whether the loops exhibited both increased secretion and increased absorption. This measurement of net flux, as done in this study, may be too insensitive to detect small changes in secretion and absorption following autotransplantation. By radio-labelling sodium added to the perfusate, and by measuring the total sodium content of the effluent, it would be possible to detect both secretion of unlabelled sodium by the loop, and absorption of the radiolabelled sodium. This would give a very sensitive assessment of unidirectional flux.

This study has proved that secretion and absorption are unchanged by denervation and lymphatic transection. This now provides the essential basic knowledge of the physiology of small bowel absorption following denervation and lymphatic transection which forms the groundwork on which further studies may be based. Each of the confounding factors involved in transplantation can now be added individually to this model, starting with absorption studies in small intestine subjected to ischaemia and reperfusion, and progressing through preservation, immunosuppression, and finally to allografting. These further experimental steps with this canine model are the logical progression of this work.

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