reduction in total ERCP numbers was found in the post-MRCP period and the monthly mean number of ERCPs performed was reduced from 22 to 17 per month.

Cannulation failure rates pre-MRCP and post-MRCP were 8.7% (26 ERCPs) and 14.2% (33 ERCPs), respectively. Pre-MRCP introduction, 191 of 272 (70%) successful cannulations were with therapeutic intent. Post-MRCP introduction, 163 of 232 (81%) successful cannulations were with therapeutic intent. Significant increases in the proportion of therapeutic procedures (odds ratio (OR) 1.74 (95% confidence interval (CI) 1.13–2.69; $p=0.012$) and failed cannulations (OR 1.74 (95% CI 1.005–2.99; $p=0.046$) were therefore identified. No significant associations existed between each ERCP indication and failed cannulation. Changes in therapeutic intervention following MRCP introduction for each indication are highlighted in table 1.

We have encountered alterations in ERCP practice following MRCP introduction with fewer, potentially more complex, procedures being performed. Subset analysis found change only in the group with pain, biliary dilatation, with abnormal LFTs $\pm$ CBD stone on USS, potentially reflecting improved identification of duct stones by MRCP. Objective assessment of technical difficulty was not easy, as both trainees and trainers were both involved in performing ERCPs and no validated criteria to assess ERCP difficulty were available during the study period.

MRCP introduction has an impact on ERCP practice. ERCP services and training may require redirection towards fewer but more complex procedures. These changes may necessitate a reduction in the number of cases performed on a list, may result in fewer trainees embarking on ERCP training and, as endoscopy centres require threshold numbers of cases to ensure competency in technique and adequacy of training, may reduce the number of centres able to offer viable training opportunities.

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A novel method to determine small intestinal barrier function in human neonates in vivo

Mucin 2 (MUC2) is the structural component of the protective mucus layer of the gastrointestinal tract, and is secreted by goblet cells.¹ MUC2 is a glycoprotein that contains high amounts of threonine and proline residues.^{2–3} Recently, we showed that almost 90% of dietary threonine is utilised by the intestine of piglets in first pass.⁴ This high visceral threonine requirement presumably reflects the high synthesis rate of MUC2. In this context, threonine might be of critical nutritional importance in maintaining good intestinal barrier function. Neonates with impaired gut function following bowel resection require adequate gut adaptation and recovery of intestinal barrier function to avoid the consequences of malabsorption of dietary nutrients and pathogenic bacterial insults. We therefore used a tracer method to study the role of dietary threonine in intestinal MUC2 synthesis and to calculate the fractional synthetic rate (FSR) of small intestinal MUC2 in human neonates as a parameter for intestinal barrier function.

Five neonates with bowel resection for necrotising enterocolitis were studied

(gestational age 33 ± 1 weeks; four had an ileostomy and one had a jejunostomy). Four weeks postoperatively a continuous [^{13}C] threonine infusion was administered enterally by feeding tube over 12 hours (materials and methods are available as supporting material online on the Gut website at <http://www.gutjnl.com/supplemental>). Using triple CsCl density gradients, mucins were isolated from intestinal outflow fluid collected at three hour intervals over two days.⁵ Mucin containing fractions had a buoyant density between 1.40 and 1.55 g/ml, were stained with periodic acid/Schiff's (PAS) reagent (fig 1A), had an apparent molecular weight of 550 kDa, and corresponded to a peak in the hexose assay (not shown). Western blot analysis using PMH1, a monoclonal antibody specific for MUC2, revealed that pooled PAS positive fractions (that is, fractions 13–15) contained MUC2 (fig 1B, three representative patients).⁶ GC-IRMS analysis demonstrated the presence of the threonine tracer in MUC2 isolated from the intestinal outflow fluid (fig 1C), indicating that dietary threonine was incorporated into MUC2. Threonine enrichment rose linearly during threonine administration and gradually decreased after administration was stopped. Time to absorb threonine and incorporate threonine into MUC2, and subsequently to secrete threonine as part of MUC2 into the intestinal lumen, ranged from approximately six to 10 hours in patients with an ileostomy (table 1). In contrast, MUC2 secretion time for the single patient with a jejunostomy was less than three hours. The linear increase in [^{13}C] enrichment in MUC2 and the luminal [^{13}C] threonine precursor enrichment were used to calculate FSR (see Gut website at <http://www.gutjnl.com/supplemental>). FSR was 12.1–89.7% per day (table 1).

This is the first study which has determined small intestinal MUC2 synthesis in human neonates. FSR of mucosal proteins was 51%/day and 15–29%/day for human

Figure 1 Isolation and characterisation of human mucin 2 (MUC2) in intestinal outflow fluid. Fractions from the third CsCl density gradients were run on sodium dodecyl sulphate-polyacrylamide gels followed by periodic acid/Schiff's (PAS) staining (A). After the final CsCl density gradient, PAS positive fractions were pooled, subjected to western blot analysis, and identified as pure MUC2 (B, pooled fractions of three representative patients). Arrows indicate the positions of the PAS positive bands (A) and of MUC2 (B). (C) Threonine enrichment in purified MUC2 in one representative patient with an ileostomy (PT 4). (D) Ratio (*) of the slope of the linear increase in [^{13}C] threonine enrichment of purified MUC2 versus luminal [^{13}C] threonine precursor enrichment during the experiment for all patients. Fractional synthetic rate can be determined by multiplying the slope (ratio/ Δt) by 24 hours and 100%.

Table 1 Patient characteristics and kinetic parameters of small intestinal mucin 2 (MUC2)

Pt	Sex	GA (weeks)	BW (g)	AS (days)	Cause	Enterostomy	Residual small intestine	MUC2 secretion time (h)	FSR (%/day)
1	F	34	1845	7	NEC (colon)	End-ileostomy	Small intestine without 1.5 cm of the ileum and the ileocaecal valve	<6	19.6
2	M	34	2310	5	NEC (colon)	End-ileostomy	Total small intestine	<7	77.8
3	M	34	1905	6	NEC (colon)	End-ileostomy	Small intestine without 10 cm of the ileum and the ileocaecal valve	<7	89.7
4	M	32	2190	7	NEC (colon)	End-ileostomy	Small intestine without 10 cm of the ileum and the ileocaecal valve	<10	31.1
5†	F	33	1450	6	NEC (jejunum)	Jejunostomy	24 cm jejunum and 25 cm ileum without the ileocaecal valve	<3	12.1
Median		34	1905	6					31.1
Range		32–34	1450–2310	5–7					12.1–89.7

GA, gestational age; BW, birth weight; AS, age at surgery; NEC, necrotising enterocolitis; FSR, fractional synthetic rate.

†Patient with a jejunostomy.

jejunum and ileum, respectively.^{7,8} As the FSR of MUC2 in the present study ranged from 12.1 to 89.7%/day, we conclude that the small intestinal epithelium has a high rate of MUC2 synthesis. Despite its wide range, the FSR of MUC2 might be valuable as a tool to study intestinal barrier function. Serial measurements of FSR of MUC2 may be used to monitor intestinal adaptation, and to assess treatment and feeding options in patients following bowel resection. We consider our data as a starting point to investigate the impact of different pathological situations and interventions, such as medication and nutrition, on the FSR of MUC2, and it could be implemented as a tool to improve medical management of patients with impaired gut function.

In conclusion, the development of a tracer method to determine MUC2 synthesis and the FSR of MUC2 in the small intestine in vivo provides the opportunity to study the determinants of intestinal barrier function in a detailed manner.

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Supporting material is available online on the Gut website at <http://www.gutjnl.com/supplemental>

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Genetic association of Fc receptor-like 3 polymorphisms with autoimmune pancreatitis in Japanese patients

Autoimmune pancreatitis is characterised by irregular narrowing of the main pancreatic duct, swelling of the pancreas, histological evidence of lymphoplasmacytic inflammation, and high serum immunoglobulin G4 (IgG4) concentration.^{1–4} Although the human leucocyte antigen DRB1*0405-DQB1*0401 haplotype has been associated with autoimmune pancreatitis,⁵ the role of genetic factors has not yet been fully defined. A new family of genes called Fc receptor-like genes (FCRLs), which have high structural homology with classical Fcγ receptor genes, has recently been identified.^{6,7} FCRL3 polymorphisms have

been shown to be associated with various autoimmune diseases, such as rheumatoid arthritis, autoimmune thyroid disease, and systemic lupus erythematosus, in Japanese populations.^{8,9} These polymorphisms alter the binding affinity of nuclear factor κB and regulate FCRL3 expression. FCRL3 expression on B cells has been observed in significant amounts and is known to augment autoantibody production in individuals with disease susceptible genotypes.⁸ We therefore investigated the association of disease susceptibility to autoimmune pancreatitis with FCRL3 polymorphisms in a Japanese population. Furthermore, we sought to determine whether serum IgG4 concentration was associated with FCRL3 polymorphisms in patients with autoimmune pancreatitis.

Patients and controls were recruited from Shinshu University Hospital and affiliated hospitals in Japan. The test group consisted of 59 patients with autoimmune pancreatitis, 62 patients with chronic calcifying pancreatitis, and 97 unrelated Japanese controls. The diagnosis of autoimmune pancreatitis was based on clinical, imaging tests, and/or histopathological findings in accordance with the criteria of the Japan Pancreas Society,¹⁰ and all patients fulfilled these criteria. Serum IgG4 concentration was measured as reported previously.³ We found high serum IgG4 concentrations (median 730.0 mg/dl (interquartile range 265.0–1037.5)) in 55 of 59 patients with autoimmune pancreatitis but not in patients with chronic calcifying pancreatitis or controls. We treated 52 of 59 patients with prednisolone, and all patients responded favourably to corticosteroid therapy. DNA was extracted by standard techniques from EDTA blood. All subjects were genotyped for FCRL3 –169, –110, +358, and +1381 by TaqMan assay. The significance of allele distribution between patients with autoimmune pancreatitis and those with chronic calcifying pancreatitis or healthy subjects was tested using the χ^2 method with continuity correction. Serum IgG4 concentrations were regressed on the number of susceptible alleles.

The observed genotype frequencies of patients and controls were in Hardy-Weinberg equilibrium. Analysis of genotype distribution frequencies for FCRL3-110 polymorphisms revealed a significant difference between autoimmune pancreatitis patients