Transformation of the paradigm in intestinal failure; future prognostication and quality of life, not just survival.

Andrew Robert Barclay MD[1], Paul Henderson PhD[2,3]

1. Department of Paediatric Gastroenterology, Royal Hospital for Children, Glasgow, UK
2. Department of Paediatric Gastroenterology and Nutrition, Royal Hospital for Sick Children, Edinburgh, UK
3. Child Life and Health, University of Edinburgh, Edinburgh, UK

Address for Correspondence

Dr Andrew R Barclay

Department of Paediatric Gastroenterology.

Royal Hospital for Sick Children

1345 Govan Road

Glasgow UK

Fax 0044 141 451 6576

Phone 0044 141 451 6575

Email: andrew.barclay@ggc.scot.nhs.uk

Dr Barclay and Dr Henderson received no additional support in the writing of this article

Dr Barclay and Dr Henderson have no relevant conflicts of interest in the writing of this article

Word Count 718

Figures 1

Dr Barclay reviewed the article on two occasions and primarily wrote the manuscript

Dr Henderson reviewed the article after acceptance to *the journal* and assisted in the writing of the manuscript

The use of parenteral nutrition (PN) has been the mainstay of treatment for intestinal failure (IF) for over 40 years. Until relatively recently the major complications of PN, namely sepsis and IF-associated liver disease (IFALD), have been the primary limiters of good long-term outcome (1). The multifactorial developments of the last decade have transformed the paradigm for patients with long term (Type III) IF, often evidenced by the serial publications of the Paris group (2-5). The authors of the article in this issue of *JPGN* (6) should be congratulated on the outcomes described; 98% 10 year survival, in a cohort with a median duration of 10 months PN, represents a new aspiration for professionals looking after these children. However their stratification of patients by diagnostic category and weaning prognostic factors sheds new light on the possibilities for patients with 'potentially irreversible IF' (ultra short segment short bowel syndrome [SBS], neuromuscular disease [NMD] and mucosal disorders [MUD]).

As with previous studies the authors conclude, through multivariate analysis, that SBS characteristics (>40cm small bowel, preserved ileocaecal valve and preserved colon) predict enteral weaning, but non-weaning is no longer predictive for death or IFALD. With only one death in the cohort, the Paris group now describe equitable survival for NMD and MUD despite reduced likelihood of weaning (41% and 14% respectively). This represents a triumph for NMD patients, for whom outcomes and quality of life have lagged behind other IF diagnoses. Indeed the absolute number and proportion of NMD patients on long-term PN has risen considerably in the last two decades (2, 7), but again the authors' study describes equitable outcomes for the first time. These gains may also be secondary to organisation of specialist services for complex NMD within supra-regional motility units. With the prospect of novel restorative therapies for NMD on the horizon (8), this lends more favour to long term PN as a therapy versus small bowel transplantation in such cases. Whilst small bowel transplantation continues to have an important role for patients with 'potentially irreversible IF', the reduction in morbidities and resultant improvement in quality of life demonstrates a shrinking proportion of patients requiring intervention despite year-on-year rises in the incidence of diseases requiring long-term PN (9).

What this paper clearly articulates is an expectation for patients with 'potentially irreversible IF' to spend the majority of time in the community, free from major morbidity and particularly IFALD. Their serial publication in this field is also a firm advocate of the role of

the large specialist service dedicated to all aspects of care of ‘potentially irreversible IF’. The evolution of the nutrition support team, led primarily by the paediatric gastroenterology multidisciplinary team (MDT), into larger interdepartmental intestinal rehabilitation programmes (IRP) has been advocated by many large centres and the transformative effect of this is beyond reproach (10). However, despite systematic review, the analyses of the individual elements and organisation of the IRP remain elusive in terms of an evidence-based appraisal of the contributions of specialist PN/lipid prescribing, sepsis prevention, intestinal lengthening surgery, specialist motility expertise and other MDT input (Figure 1). We anticipate potential future publication from the Paris group on individual aspects of their care, to aide professionals to replicate these outcomes.

Whilst these data support the further improvements in long term PN, challenges remain for patients with poorer outcomes, often minor sub-groups of such study, or those with non primary gastrointestinal disorders. Patients with early onset inflammatory and immune-mediated diseases (including autoimmune enteropathy, classified as non-primary gastrointestinal for the purposes of this paper) for example, still report poorer outcomes than the IF group as a whole. Further understanding of the pathogenesis and mechanisms of these diseases will hopefully lead to more targeted therapies, and the ESPGHAN funded GENIUS patient registry is now recruiting to help characterise these diseases(http://www.genius-group.org/). Additionally as all measures for long term PN improve, the boundaries for such therapy will continue to move; mild dysmotility or dysmotility in the context of severe neurodisability are conditions that the NST are being asked to manage more frequently. As it stands the authors’ paper is a welcome addition to the literature and offers us the future agenda for IF, namely the ability to prognosticate for the individual patient and the primary focus to move to quality of life rather than just long term survival.

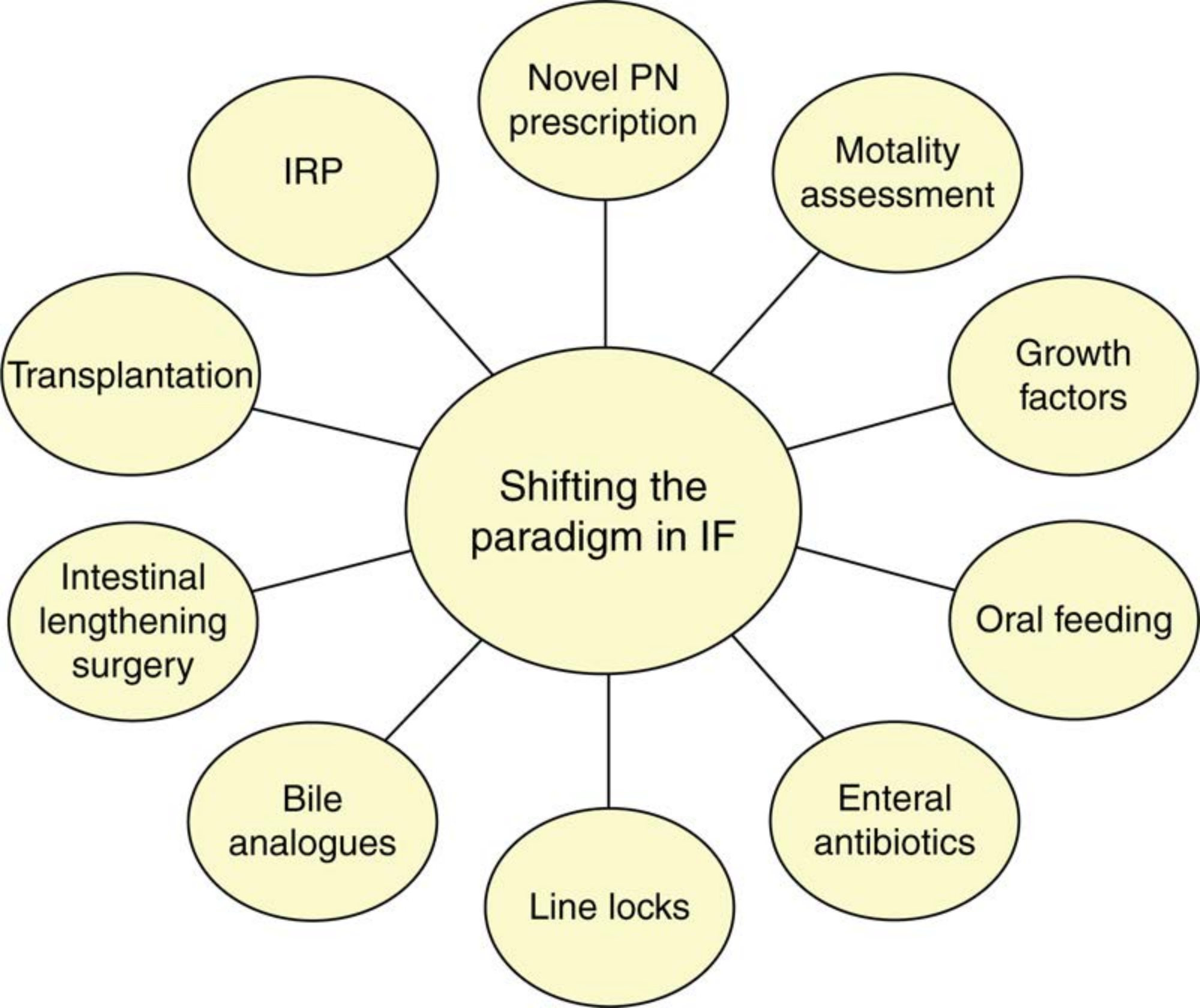
References

1. Di'Antiga L, Goulet O. Intestinal Failure the European view. *J Pediatric Gastroenterol Nutr* 2013;56: 118-27.
2. Colomb V, Dabbas Tyan M, et al. Long-term Outcome of Children Receiving Home Parenteral Nutrition: A 20-year Single-center Experience in 302 Patients. *J Pediatric Gastroenterol Nutr* 2007;44: 347-53
3. Goulet O, Antebe H, Wolf C et al. A new intravenous fat emulsion containing soy bean oil, medium chain tri-glycerides, olive oil and fish oil: A single centre double blind randomised study of efficacy and safety in pediatric patients receiving home parenteral nutrition. JPEN *J Parenteral Enteral Nutr* 2010;34: 485-495
4. Goulet O, Dabbas-Tyan M, Talbotec C et al. Effect of recombinant human growth hormone on intestinal absorption and body composition in children with short bowel syndrome. JPEN *J Parenteral Enteral Nutr* 2010; 34:513-20
5. Halac U, Lacaille F, Joly F et al. Microvillous Inclusion Disease: How to improve the prognosis of a severe congenital enterocyte disorder. JPEN *J Parenteral Enteral Nutr* 2011; 52: 460-5
6. Petit L-M, Gerard D, Ganousse-Mazeron S et al. Weaning off prognosis factors of home parenteral nutrition for children with primary digestive diseases. *J Pediatric Gastroenterol Nutr* Journal to supply ref
7. Barclay AR, Henderson P, Gowen H et al. The continued rise of paediatric home parenteral nutrition use: Implications for service and the improvement of longitudinal data collection. *Clinical Nutr* 2014 Nov 20. pii: S0261-5614(14)00290-8.
8. Burns AJ, Thapar N. Neural stem cell therapies for enteric nervous system disorders. *Nat Rev Gastroenterol Hepatol.*2014;11: 317–28
9. Ganouuse-Mazeron S, Lacaille F, Colomb-Jung V et al. Assessment and outcome of children with intestinal failure referred for intestinal transplantation. *Clin Nutr* 2015; 34: 428-35.
10. Stanger J D, Oliveira C, Blackmore C et al. The impact of multi-disciplinary intestinal rehabilitation programs on the outcome of pediatric patients with intestinal failure: A systematic review and meta-analysis. *Journ Pediatr Surg* 2013; 48:983-92.

Figure Legend

Figure 1: Shifting the paradigm in intestinal failure over the last decade as evidenced by the Paris Group.

IRP; Intestinal Rehabilitation Programme


Shifting the paradigm in IF
Novel PN prescription
IRP
Motality assessment
Transplantation
Growth factors
Intestinal lengthening surgery
Oral feeding
Bile analogues
Enteral antibiotics
Line locks