# Research Project Report

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## Project Title
Collagen Abnormalities in patients with Rectal Prolapse

## Start date
April 2010

## Finish date
April 2014

## Lay Summary (max 500 words)
Rectal prolapse occurs when the rectum (the terminal part of the large intestine) descends to lie outside the anus. It is a common problem, affecting up to 10% of the population.

It is characterised by the external protrusion of the rectum and is extremely distressing for patients. It may also be a cause of faecal incontinence and in elderly patients may be the cause of admission to care homes. Understanding of the causes of rectal prolapse is poor. Traditionally it was viewed as a disorder of elderly women who acquired pelvic floor weakness during childbirth. However, this fails to account for the condition occurring in men or in women who have never had children.

We aim to increase understanding of the causes of rectal prolapse by studying the structures that support the rectum to determine why they may be weaker in patients with prolapse, and the reasons this weakness develops. We will do this by sampling the tissues that are attached to the rectum in patients with and without prolapse and studying their chemical composition.

## Background (purpose for project)
This project arises from research carried out by my predecessor Mr Edward Smyth, who was a recipient of a BDRF consumables grant 2 years ago. The funding was used to initiate a study with the aim of characterising the pathophysiology of rectal prolapse. This distressing condition that has been inadequately researched. Indeed there is virtually no basic science literature on this subject. The research to date has yielded some interesting results and raised further important questions. The results will form the basis of a DPhil thesis and publications arising from it, and the research has generated a number of national and international presentations.

## Introduction
Historically, the aetiology of rectal prolapse has been associated with obstetric-related trauma resulting in a weak pelvic floor. However as men, nulliparous women and even children can suffer from this disorder, it seems as though the aetiology must be multifactorial. The work carried out to date compared results on multiparous women, with those from nulliparous women and those from men. It also noted other patient characteristics, particularly benign joint hypermobility syndrome (BJH).
Methods

Participants with rectal prolapse were prospectively recruited to the study (n=105). Control tissue was taken from individuals undergoing colonic cancer surgery (n=12). Individuals were assessed for their connective tissue status and grouped according to parity and gender. Analyses focussed on presenting demographics and surgical outcomes in patients with respect to connective tissue status, changes in the extracellular matrix in relation to prolapse, systemic changes in connective tissue components.

Results and discussion

It was found that a proportion of patients have heritable predisposition to altered connective tissue biology in that they had benign joint hypermobility syndrome. These patients typically presented younger and fared less well with surgical treatments than those with normal connective tissue status. The extracellular matrix had a number of changes in association with the condition, collagen types 1 and 3 were altered in comparison to control and an overall increase in the elastic fibres of the pelvic connective tissues was noted. Alterations in the elastic fibres within the dermis of patients were also identified and suggests that a systemic disorder of connective tissue may account for the development and progression of the condition in some individuals. The pelvic connective tissues themselves were noted to have a number of changes with respect to the disorder, an increase in MMP 1 was noted and this was linked to a reduction in connective tissue supports surrounding the rectum. The growth factor TGF β may play a role in modulating this process and a reduction in the expression of this growth factor was found to be associated with the development of external prolapse. We found that cellularity was increased in response to the process of prolapse in females, but in males this process was attenuated. In addition it was also noted that in some females the cells did not differentiate to the type normally identified in the pelvic connective tissues.

Conclusion

The experimental findings suggest that in some individuals a combination of a systemic connective tissue disorder, altered collagen ratios and an environment favouring tissue degradation may account for the development and progression of rectal prolapse.

Recommendations for future work

Our immediate objectives, based on results to date, are:-
(i) to determine the molecular basis of the underlying connective tissue defect in a subgroup of patients with rectal prolapse
(ii) to determine activity of proteolytic enzymes in rectal prolapse tissues in relation to tissue damage and to investigate possible initiating factors involved in this activity
(iii) to determine cellular responses in dermal cells and in cells from prolapse tissue in the same patients in order to determine if responses to wounding or shearing forces
(iv) to relate all these cellular and molecular responses to patient characteristics, symptoms at presentation, BJH, and treatment outcome.

References

2. Collinson, R., et al., The emerging role of internal rectal prolapse in the aetiology of
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