PERSPECTIVE

Royal Australasian College of Surgeons

The Exocrine Appendix. Darwin's vestige

Small organs in less accessible places are at risk of being under appreciated. In the early 1950's the father of transplantation immunology and Nobel laureate Sir Peter Medawar, described the Thymus as 'a vestigial organ in the neck of no biological significance'.[1] This was proved wrong quite quickly, but Darwin's assessment of the appendix continues to resonate.

Charles Darwin (1809–1882) observed correctly that all great apes and man (Hominidae) had an appendix. He concluded that the more primitive species remained arboreal and foliferous (leaf eaters) and needed a large caecum to ferment the bulky cellulose containing diet into usable fatty acids. As the apes evolved, they descended to the ground and became frugivorous (fruit eating) and their sugars digested in the small bowel by enzymatic hydrolysis in the usual way. The caecum, Darwin hypothesized, then became smaller, the appendix appearing prominent, and therefore a remnant, a vestige of a once useful organ, the caecum.[2]

In Darwin's time not many taxa had been studied for the presence of the appendix. Since then, many studies have been performed within the primate taxa and the appendix is seen in many species of Lorises, Lemurs, New and Old-World Monkeys, and in all Apes. The appendix is also established in Rabbits, and more recently in Echidna and Platypus.

In a study of 361 species across the mammalian phylogeny, 50 were found to have an appendix. There were seen to be 38 evolutionary events establishing an appendix, with six losses. This was much more than could be expected by chance, strong evidence that the appendix conferred a selective advantage in mammalian evolution. This study also concluded that Darwin's assertion regarding the relationship between the size of the caecum and that of the appendix was incorrect. Rather in the course of evolution the entire length of the colon and caecum is related to the size of the appendix.[3,4]

In a similar French taxonomic study examining 258 mammalian species the appendix was seen to arise 16 times and lost just once. But they go on to make a remarkable claim; the presence of the appendix is related to increased longevity among species controlled for body size, and this is due to a decrease in extrinsic mortality. The explanation proposed, that gut infections are common causes of primate mortality (including in humans), and having an appendix to repopulate the gut with symbionts after enteric infection had selective advantage by decreasing extrinsic mortality.[5] The same group also studied 1251 captive primates belonging to 45 species over a 20 year period, comparing morbidity from diarrheal disease in groups with and without an appendix. They identified a lower risk of severe diarrheal disease, particularly early in life among primates with an appendix than without.[6]

Researchers from Duke University[7,8] drew attention to the presence of biofilms in the human gut, particularly in the appendix and proximal colon, while the distal colon and rectal mucosa were relatively bare, mucus being adherent to solid stool. They suggested that commensal organisms in the human colon could be maintained and renewed through biofilms detached from the appendix, particularly after episodes of infectious gastro-enteritis, a common occurrence worldwide. They also reviewed the literature on Clostridium difficile (CD) colitis, and conclude that an intact appendix does not protect from an initial attack of CD after broad spectrum antibiotic use, but does have an effect in preventing recurrent CD.[9] Mucus layers in the colon and appendix, the essential barrier separating the gut from the microbiota, consist of MUC2 a gel forming glycoprotein. This is packed into dense vesicles in epithelial goblet cells and expand by a factor between 100 and 1000 by volume when hydrated and exocytosed into the lumen of the gut as three-dimensional mucosal sheets.[10] These form into the biofilm, an inner largely sterile glyco-calyx containing immunoglobulin A and antibacterial peptides secreted by Paneth cells, and an outer layer containing the microbiota. As a major secondary lymphoid organ, the appendix is an intermediary between the microbiota and the immunological toolkit of the gut, likely to have a role in the establishment of tolerance and sensitivity.[11,12]

The mucus secreting activity of the appendix in humans was studied by Wangensteen who showed a secretion pressure approaching systolic blood pressure developed reliably within 24 h in the normal obstructed appendix (Fig. 1).[13] He also observed that secretion in the rabbit appendix was increased by catharsis. The appendix has prominent muscular layers[11] and an autonomic innervation, and this process of active secretion into the caecum, an exocrine function, supports the observations of the Duke University group.

Intact mucosal barriers shield the mucosa from interacting with gut commensals, though obligate gut pathogens have mechanisms to surmount this.[10,14,15] The patterns of appendix inflammation are increasingly understood, where Complicated Appendicitis represents an Innate Th1, Th17 response causing gangrene,[12,16] and Uncomplicated Appendicitis a Th2 response[17,18] (as in chronic ulcerative colitis,[15] CUC), and a chronic or recurrent clinical presentation. The increasing evidence of the course of CUC being improved by appendicectomy[19] may be related to translocation from the appendix of inflammatory biofilms and activated cytotoxins, onto the relatively bare rectal mucosa, or the systemic effects of appendix inflammation.

Darwin in 1871 understood that in humans, natural selection did not operate in contemporary western civilisations. He attributed this to

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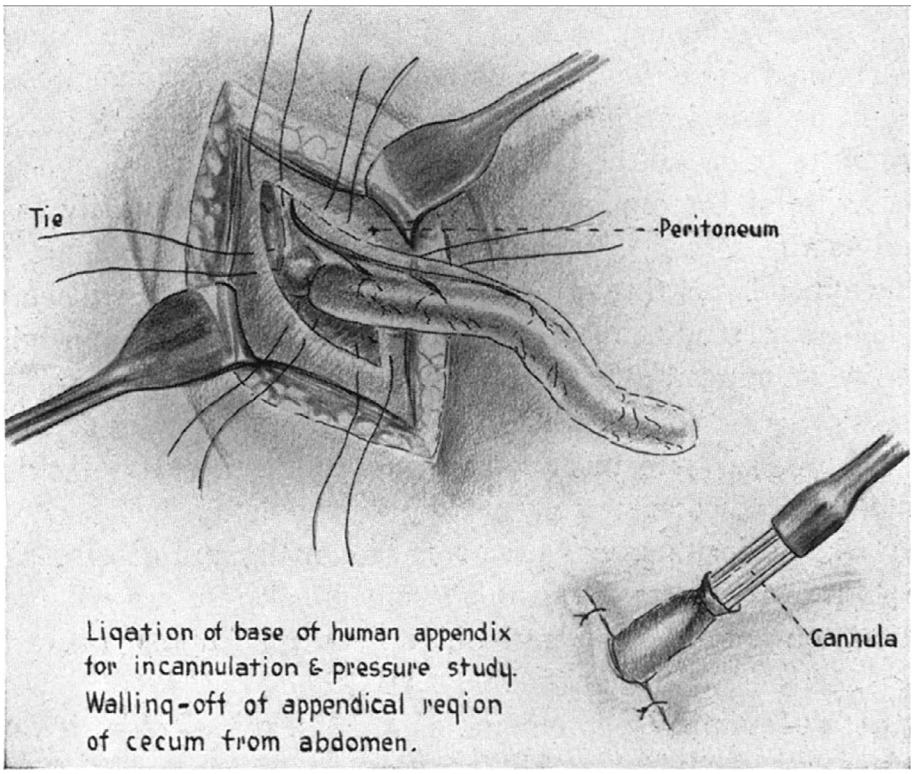

Fig. 1. Wangensteen's experiments on the human appendix. Technique of exteriorizing and obstructing an appendix as employed in this study for purposes of measuring the secretory pressure.

'Altruism' leading to the subsequent development of Socio-Biology (and Eugenics, its turbulent child). The provision of sewage disposal, public sanitation, and clean water among other things as a civic right, reduces the opportunity for and incidence of gastro-intestinal infections, making partly redundant the function of an intact appendix.

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Alan de Costa,*† FRACS
**Department of Surgery, Cairns Hospital, Cairns, Queensland, Australia and †School of Medicine and Dentistry, James Cook University, Cairns, Queensland, Australia*

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