World Journal of Gastroenterology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.3748/wjg.v4.iSuppl2.10

World J Gastroenterol 1998 October 15; 4(Suppl2): 10-15
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

Is there a pathologic basis for gastrointestinal dysmotility?

Eamonn MM Quigley

Eamonn MM Quigley, Section of Gastroenterology/Hepatology, Department of Internal Medicine, University of Nebraska Medical Center Omaha, NE 68198-2000, United States

Author contributions: The author solely contributed to the work.

Correspondence to: Eamonn MM Quigley, MD, FACG, FRCP, FACP, Section of Gastroenterology/Hepatology, Department of Internal Medicine, University of Nebraska Medical Center Omaha, NE 68198-2000, United States

Received: August 8, 1998
Revised: September 2, 1998
Accepted: September 28, 1998
Published online: October 15, 1998

Quigley EMM. Is there a pathologic basis for gastrointestinal dysmotility? *World J Gastroenterol* 1998; 4(Suppl2): 10-15 Available from: URL: http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/10.htm DOI: http://dx.doi.org/10.3748/wjg.v4.iSuppl2.10

INTRODUCTION[1-10]

Based on their high prevalence in clinical practice, there has been an understandable tendency, in the area of gastrointestinal motility, to focus on "functional" disorders. Thus, considerable time and energy has been expended on the performance, analysis and interpretation of motility studies in such disorders as non-cardiac chest pain, non-ulcer dyspepsia (NUD), irritable bowel syndrome (IBS) and idiopathic constipation. I believe it is fair to say that the role of motility in these disorders remains debated and controversial. Progress in this area has been limited by the lack of truly objective criteria for the definition of these disorders-none is based on a clearly defined biochemical or pathological abnormality. The utilization of these disorders as templates for the evaluation of motility tests is clearly, therefore, fraught with problems.

If a definition for a disorder is not uniform, then different study population may not be comparable. Given the non-specificity of many of the symptoms experienced by these patients, it is also likely that each category, whether it be IBS or NUD, includes a heterogeneous collection of patients—a factor that may exert a significant influence on the likelihood of finding a motility "abnormality " in a particular study group. Studies in this area are also hampered by the ap parent ubiquity of epi-phenomenology. Thus, it is often difficult to unravel th e confounding effects of stress, anxiety, depression, patient expectations and various therapeutic interventions, and to truly decide what motor abnormalities a re primary or secondary. Therapeutic trials in disorders such as non-ulcer dyspepsia or the irritable bowel syndrome have led to the greatest frustration. It s hould come as no surprise that trials of therapy in a disorder whose definition is difficult and which may encompass entities of varying pathophysiology often lead to inconclusive and disappointing results. When such studies are performed in major referral centers, the influence of selection bias and, in particular, of "learned illness behavior" must be borne in mind—the patient studied in these centers may be very different from those seen in the community. The motility literature is dominated, therefore, by conflicting data on the role of dysmotility, on the value of various types of motility studies and the efficacy of motility-altering drugs in functional disorders; syndromes which share a lack of a clearly defined basic pathology. The goal of this presentation is to remind the audience of those motility disorders which have a pathologic basis, whose pathophysiology is understood either in part or in whole, and which may serve as better templates for the evaluation of motility and its therapy.

ENTERIC NEUROPATHOLOGY[11-27]

Before describing those "organic disorders" associated with dysmotility, it seems only reasonable to discuss, in brief, the techniques of enteric neuropathology. It must be admitted, from the outset, that this is very much a minority sport. Several technical problems have limited our ability to examine pathological tissue from the muscle or nervous system of the gut. First and foremost, any complete evaluation of intestinal muscle or nerve must be performed on a full thickness specimen of the gut wall. Up until recently, this has required open laparotomy and full thickness biopsy or examination of tissue removed during the course of a gastrointestinal surgical procedure. More recently, some centers have developed the technique of laparoscopic intestinal biopsy, and validated its utility in the diagnosis of intestinal myopathy and neuropathy. This procedure has usually been performed in the context of the laparoscopic placement of intestinal feeding or decompression rubes in patients with severe dysmotility syndromes. Some have raised concerns regarding the safety of this procedure, cautioning of the possible development of post operative adhesions and related obstruction. A second major hurdle relates to the processing and interpretation of the biopsy material. While the morphology of the intestinal muscle layers can be evaluated using conventional hematoxylin-and eosin-stained sections, this technique is inadequate for the study of enteric neurons. Large amounts of fatty constituents of neurons are lost during dehydration, clearing, and paraffin infiltration of tissue for hematoxylin-eosin histology, leading to artifactual vacuolization and other defects, and axonal and dendritic processes cannot be seen. Traditional transverse sections provide a poor demonstration of the myenteric and submucosal plexuses—these are best visualized when seen in a flat, en face view. Specimens for the evaluation of enteric neurons need, therefore, to be specially prepared and mounted. Staining of these sections is particularly important and potentially problematic. The standard technique in use is the silver method. The gut is fixed

for a week or two in buffered formalin, then impregnated with a strong silver nitrate solution, the excess silver washed out with formalin and the bound silver developed with strong ammoniacal silver nitrate or silver diamine. This is not an easy technique—if successful, the entire plexus is stained brown against a lighter muscle background. It is evident from the above that enteric neuropathology is a highly specialized and technically demanding technique. Not surprisingly, few centers can provide this level of expertise, and, in particular, are sufficiently experienced to interpret these sections. This remains a further limitation to progress in this area. There is a great need for an expansion of availability of these enteric neuropathological services and for standardization of their interpretation. Until this is achieved, enteric neuronal pathology will remain beyond the reach of most physicians and their patients. Though not included as a standard component of diagnostic enteric neuropathology, considerable information has recently been provided by immunohisto-chemical studies of the enteric nervous system. Using specific antibodies, deficiencies of various neurotransmitter substances often described in a number of clinical disorders. This again, however, is a technically exacting technique.

Parallels between the enteric and central nervous systems are increasingly appreciated—the description of a variety of pathological findings in the autonomic and enteric nervous systems in Parkinson' s disease has provided a clinically relevant example of such parallelism.

WHAT CAN WE LEARN FROM "ORGANIC" DYSMOTILITY SYNDROMES?

It should be no surprise, based on the above, that detailed descriptions of enteric myopathies or neuropathies remain limited. More commonly, these organic disorders are defined on the basis of the occurrence of a dysmotility syndrome in a patient with a clearly-defined disease process. Typical examples of the latter would include post-operativeileus, Ogilvie's syndrome and the various manifestations of diabetic gastroenteropathy. Important lessons regarding the pathophysiology of dysmotility can also be gleaned from iatrogenic motility disorders (whether induced by medications, radiation therapy, or surgical intervention) and various models of experimentally-induced dysmotility.

Lessons from the Classics (and the Tropics)[28-52]

Perhaps the most detailed information on the basic pathophysiology of motor disorders has been gleaned from three rather rare disorders, namely, achalasia, infantile hypertrophic pyloric stenosis and Hirschsprung's disease. Each of these disorders has been characterized by neuronal loss within the affected segment, an d when examined in further detail by the specific dropout of VIP- and NO-containing neurons. Loss of nitrergic neurons appears to be highly characteristic of the aganglionic segment in both achalasia and Hirschsprung's disease. It is important to remember that very similar changes have been described in a much more common disorder, on a worldwide basis, namely Chagas' disease. We have much to learn from this disorder which affects many millions, especially in South America.

Further abnormalities, of particular interest to the physiologist and pathophysiologist, have been demonstrated in pyloric stenosis. These findings relate to a group of highly specialized cells known as the interstitial cells of Cajal. These cells, which appear to be of fundamental importance in motility through their ability to generate the basic electrical rhythm of the intestine, have been the subject of considerable interest in recent years. A "knockout" animal model has been developed whereby interstitial cell development can be arrested—this leads to the loss of electrical rhythmicity throughout the intestine, but does not necessarily impair the generation of contractions or the peristaltic reflex. Now, two groups have reported a deficiency of interstitial cells in the hypertrophied segment in pyloric stenosis.

Studies in Hirschsprung's disease have provided additional insights. It is evident for example, that there is some overlap between Hirschsprung's disease and that group of disorders referred to as intestinal neuronal dysplasia. Though the hallmark of the latter disorder is hyperganglionosis rather than aganglionosis, affected individuals have severe dysmotility symptoms usually manifested by intractable constipation. It is also clear that in some patients with "Hirschsprung's disease" the aganglionosis may extend to involve the entire colon or, indeed, the small intestine. Similar overlap has been suggested between achalasia and the pseudo-obstruction syndromes.

The description of these various subtle morphological and immunohistochemical abnormalities in these three disorders does not, of course, necessarily imply that these are the primary defects. It has been suggested, for example, that the neuronal injury in both achalasia and Chagas' disease is based on an immune mechanism and specific autoantibodies have been described. Others have described autonomic dysfunction in achalasia and others still have suggested a viral trigger. Given the, albeit anecdotal, association between various "dysmotility" disorders and prior infective episodes, these observations are of considerable interest, and may yet provide important clues to the etiology of a wide variety of common disorders. Both achalasia and Hirschsprung's disease may also occur in the con text of genetically-based disorders with multi organ involvement. Of special interest is the recent description of genetic markers for Hirschsprung's disease. Mapping studies in both man and animal models have suggested that specific genes may be involved: mutations in the RET protooncogene and the endothelin-B receptor gene have been described in an autosomal dominant (with incomplete penetrance) and recessive type of Hirschsprung' s disease, respectively. Mutations of th e RET protooncogene have also been described in MEN 2A, MEN 2B and sporadic medullary and papillary thyroid carcinoma. These genetic abnormalities are thought to result in impaired neural crest migration, colonization or differentiation. Hirschsprung's disease is now regarded as an example of a neurocristopathy-disor ders of the neuronal crest: from the above genetic studies, a basis for the over lap of Hirschsprung's disease with other dysmotility syndromes is revealed.

It is clear, therefore, that highly specialized, sophisticated and focused studies on these, albeit rare but well-defined disorders, are of great importance an d hold considerable promise towards an understanding of dysmotility syndromes in general. In these disorders, where the clinical definition is agreed, manometric criteria are well-defined and pathologic diagnosis is possible, it may well prove possible to define, at the most basic level, relationships between molecular abnormality, physiologic dysfunction, and clinical presentation.

Sizing up the Syndromes[53-106]

At the next level, from a pathologic point of view, are those organic disorders of motility which do not posses a uniform pathology but are defined clinically on the basis of a uniform abnormality of function. These include:

-Diffuse esophageal spasm
-Gastroparesis
-Intestinal pseudo-obstruction
-acute (ileus)
-chronic
-colonic (Ogilvie's syndrome)
-Megacolon

Each of these syndromes includes a wide variety of disorders of varied etiology—what they share is a common abnormality of motor function which can be reproducibly demonstrated by studies of gut anatomy or function (including manometry). For some, such as the many motor manifestations of scleroderma or amyloidosis, a pathologic basis is evident; for others, such as those with post-operative ile us, it is assumed, and for others still the functional abnormality such as gastroparesis remains unexplained. It is in this latter category that we begin to move into the territory of functional disease and so to consider the possible contribution of motor dysfunction to otherwise unexplained symptomatology. For the mo ment, however, we will focus on those individuals with one of the above syndrome s whose symptoms appear to have an organic basis.

Diffuse esophageal spasm (DES) is a rare disorder of esophageal

motor function whose etiology remains undefined. Many patients with "spasm" and more non- specific motor disorders have underlying reflux—an important pathologic basis f or many instances of non-obstructive dysphagia. A recent report provided some fascinating insights into the pathophysiology of spasm by demonstrating the induction of DES by recombinant human hemoglobin, a potent inactivator of nitric oxid e!

Because of the relative accessibility of gastric emptying studies, gastroparesis is probably the most frequently defined abnormality of motor "function". Gastroparesis, in of itself, is a nonspecific finding and may not imply a primary disorder of gastric motor function. Several organic dysmotilities, such as diabetic gastroenteropathy, include gastroparesis as a prominent feature. Studies in this and other organic gastropareses have served to emphasize the complexity of gastric motor function and have emphasized the importance of regional differences in gastric motility as well as the role of visceral afferents, central input and "long" reflexes in the regulation of gastric contractility. It is becoming evident that gastroparesis may be inadequate to describe gastric motor dysfunction in many circumstances; in diabetes, for example, emptying may be accelerated or delayed; following vagotomy disturbed gastric compartmentation may be more prevalent than altered emptying. The inadequacy, up until recently, of our methodologies for the evaluation of any gastric motor function other than emptying may go some way towards explaining our inability to explain many symptoms suggestive of foregut distress.

The term *chronic intestinal pseudo-obstruction* refers to a diverse and hete rogeneous group of disorders with somewhat similar clinical features regardless of etiology. Patients typically present with repeated episodes of nausea, vomiting and abdominal pain and distention. On clinical grounds, they are often suspected initially of having a mechanical obstruction. Many patients are subjected to more than one diagnostic laparotomy before the correct diagnosis is even considered. Stasis may lead to bacterial colonization, with the subsequent development of diarrhea, steatorrhea, weight loss, and nutritional problems. In some individuals, constipation may be prominent, and in acute episodes, abdominal distension may be striking. This syndrome may be the intestinal manifestation of a systemic disorder (a secondary pseudo-obstruction) or may reflect a primary disorder of the intestinal musculature or its neural apparatus (primary chronic idiopathic intestinal pseud o-obstruction, or CIIP). Whether the disorder is primary or secondary, other parts of the GI tract may be involved, as well as extra-intestinal organs, in particular the urinary tract.

The pseudo-obstruction syndromes provide several insights into our understanding of gastrointestinal dysmotility. Some disorders are based on a primary pathologic abnormality of intestinal muscle and/or nerve. Of the many causes of pseudo-obstruction, scleroderma and the other mixed connective tissue diseases are by far the most common. In its earlier stages, sclerodermatous involvement of the small intestine results in motility changes indicative of a neuropathic process, and recent studies suggest an autoimmune-mediated injury to intestinal nerves. In the later, much more familiar stages, the predominant features are those of a diffuse myopathic disorder; biopsies demonstrate the widespread replacement of the circular muscular layer, in particular, by fibrosis. Manometric studies demonstrate marked hypoactivity, and radiologic studies dilatation of the intestine with megaduodenum and megacolon being particularly prominent. In its advanced s tage, scleroderma serves as an excellent model of an intestinal myopathy.

The range of neuropathic disorders that may result in the pseudo-obstruction syndrome provide considerable insights into the various levels at which intestinal motility is controlled, and may, therefore, be potentially disrupted. These dis orders include those well-described, though very rare, disorders where the path ology lies within the enteric nervous system itself; so-called visceral neuropa thies. Disorders of the autonomic nervous system (*e.g.*, diabetes mellitus, familial dysautonomia, ganglioneuromatosis and paraneoplastic neuropathy), disorders of the spinal cord and central nervous system (*e.g.*, brain stem and spinal cord space- occupying lesions) and a variety of hormonal disorders (hypothyroidism, hypoparathyroidism) may also result in CIIP. Through actions at various levels, a variety of external agents may also cause a pseudo-obstruction syndrome. Important and common examples include radiation enteropathy and the effects of such drugs as opiates, anticholinergics and antineoplastics (*e.g.* vincristine).

Acute *gastroparesis, ileus* and *Ogilvie's syndrome* represent the various manifestations of acute intestinal pseudo-obstruction. Gastroparesis is, perhaps, the least common of these disorders, but is often overlooked, as gastric distention may not be clinically evident, especially in the sedated or anesthetized subject. It is important to remember that acute gastric dilatation has also bee n reported following blunt abdominal trauma, and has been commonly described among transplant patients, being reported in 24% of heart/lung transplant recipient s, for example.

Ileus has come to be regarded as a physiologic response to surgery, and abdominal surgery, in particular—its duration being well related to the extent of the intra-abdominal procedure. The pathogenesis of post-operative ileus, has been extensively investigated. Such investigations have again highlighted the complexity of the control of motor activity. Clinical and experimental studies have, for example, revealed evidence for a role for the central nervous system (through corticotrophin-releasing factor), autonomic neurons (and especially sympathetic hyperactivity), enteric neurons (through the release of inhibitory neurotransmitters in the gut wall), and most recently for afferent neurons. With regard to the latter, a role for both splanchnic, capsaicin-sensitive afferents and CGRP have been proposed.The primacy of any or all of these mechanisms has not been established. It should come as no surprise, therefore, that therapeutic maneuvers based on a single mechanism have proved disappointing.

Ileus is being increasingly recognized in non-surgical conditions and has been reported in a variety of acute neurological conditions, including spinal trauma and acute neuropathies (such as the Guillain-Barre syndrome and prophyria). Ile us is also a feature of ischemic disorders of the intestine, and is a cardinal manifestation of mesenteric ischemia. Ileus is being increasingly recognized as a manifestation of severe inflammatory disorders of the gastrointestinal tract, e specially in the context of transmural inflammation. A classical example here is severe graft-versus-host disease—in this condition, the development of ileus is most ominous. Ileus may also be seen in relation to apparently remote events such as retroperitoneal hemorrhage, infection or tumor, disorders of the thoracolumbar cord (such as fractures or tumors), and as a non-metastatic manifestation of a variety of tumors.

Though also seen in the post-operative state, *Ogilvie's syndrome* is more commonly seen, nowadays, in the non-surgical patient. It is particularly associated with disease, trauma or surgical procedures in the retroperiteneum, hips, pelvis and lumbosacral spine. Colonic ileus has also been described in association with gynecological surgery, pregnancy, open heart surgery, and cesarean section . As with other forms of ileus, Ogilvie's syndrome has also been described in t he severely ill patient, for example, those with severe burns or overwhelming in fections. Many factors may contribute to the evolution of both ileus and Ogilvie 's syndrome, including electrolyte abnormalities, analgesics and anticholinergic medications.

All of this information indicates that for ileus of any form, where no obvious cause is evident, possible associated lesions, such as pneumonia, spontaneous bacterial peritonitis and intra-abdominal abscess as well as disease of the retroperitoneum, lumbosacral spine, hips and pelvis should be sought.

New Horizons—Infections and Immunity[107-128]

Of considerable clinical importance, several recent studies have suggested an important role for various infections in the pathophysiology of dysmotility syndromes. While both acute and chronic syndromes have been described in association with a variety of infective agents, acute disorders, such as gastroparesis, ileus and megacolon have been best described. Clinicians have recognized for some time that many acute illnesses, including acute viral infections, may be associated with the development of symptoms suggestive of gastric motor dysfunction, and a post-infective irritable bowel syndrome is well recognized, although poorly de fined.

In some instances, viral infections of the gastric mucosa have

been directly linked with disturbed emptying. Important examples here include those instances of cytomegalovirus and herpes simplex virus gastritis, which may occur in immunocom-promised patients. The author has seen a number of liver transplant patients with a profound gastroparesis syndrome in whom cytomegalovirus has been identified in gastric mucosal biopsy specimens, and who have responded dramatically to gancyclovir therapy alone. CMV has been isolated from intestinal ganglion cells and has also been shown to result in a severe ileus and meconium-like syndrome in neonates and a chronic intestinal pseudo-obstruction syndrome in heart/lung tran splant patients. Reports of ileus and Ogilvie's syndrome in relation to disseminated herpes zoster virus infection have also been described. Again, in immunocompromised patients, HZV has been shown to result in infarction of the celiac sympathetic ganglia. Following oral inoculation, herpes simplex virus type 1 has been shown, in immunodeficient mice, to lead to prolonged sustained replication of the virus in the enteric nervous system of the esophagus and stomach as well as in the nodose ganglion. In this particular model, this virus, when administered orally, can result, therefore, in long-term latent infection, with replication confined to the enteric and autonomic nervous systems. This is a particularly intriguing finding, and provides a pathologic basis for a possible role for an initialviral infection in a prolonged motor disorder. The previously mentioned association of viral infections with achalasia is another example of a possible role for a viral initiation. A number of case studies have reported gastrointestinal motor dysfunction in non-immunocompromised patients in relation to other viral infections.Although the evidence for such an association are somewhat inconclusive and a direct cause and effect relationship remains to be established, the suggestion that common viruses, such as members of the herpes simplex virus family, might evoke, in susceptible individuals, dysmotility (through effects on the central nervous system, autonomic supply or the motor apparatus of the gut) is extremely intriguing and deserving of further study. Dysmotility has also been reported in relation to salmonella and strongyloidosis infections, Legionnaire's disease and spontaneous bacterial peritonitis.

Again, at an experimental level, considerable evidence has been advanced to support a role for inflammatory mediators, released from immune cells in the gut wall, in the regulation of smooth muscle and enteric nervous function. It has been suggested, for example, that such interactions might explain motor abnormalities reported in patients with inflammatory bowel disease as well as in infective and parasitic diarrheas.

CONCLUSION

I would suggest that there is ample evidence for a pathologic basis for many dys motility syndromes. In some, albeit rare, instances, characteristic pathological abnormalities have been defined and we are well on our way to an understanding of pathophysiology. In many other disorders, enteric, neural or muscle pathology is either undefined or has not been examined, yet there is considerable evidence to invoke an organic basis for dysmotility. These disorders have shown us that a wide variety of disorders may affect intestinal muscle and nerve, and may also influence motor function through actions in the autonomic nervous system, spinal cord and central nervous system. Circulating hormones and motor-active peptid es also have a role. An important role for infective agents, and viruses in particular, is being increasingly advanced, and mechanisms whereby they may exert their effects are being increasingly understood. In this way, well-defined motility syndromes, such as gastroparesis, ileus, Ogilvie's syndrome, chronic intestinal pseudo-obstruction and megacolon are being increasingly investigated and, in many instances, their etiology understood. Advances in basic investigational tools, as well as increasing access to intestinal tissue, may well provide a "pathologic" basis for at least some of the patients now included under the umbrella of functional disorders, such as non-ulcer dyspepsia and the irritable bowel syndrome.

REFERENCES

1 **McKee DP**, Quigley EM. Intestinal motility in irritable bowel syndrome: is IBS a motility disorder? Part 1. Definition of IBS and colonic motility. *Dig Dis Sci* 1993; **38**: 1761-1772 [PMID: 8404395 DOI: 10.1007/BF01296097]

2 **McKee DP**, Quigley EM. Intestinal motility in irritable bowel syndrome: is IBS a motility disorder? Part 2. Motility of the small bowel, esophagus, stomach, and gall-bladder. *Dig Dis Sci* 1993; **38**: 1773-1782 [PMID: 8404396 DOI: 10.1007/BF01296098]

3 **Quigley EM**. Nonulcer dyspepsia: pathophysiology update. *Hosp Pract (1995)* 1996; **31**: 141-12, 141-12, 156 passim [PMID: 8592011]

4 **Quigley EM**. The irritable bowel syndrome: motility, mind or message? Variations on an enigma. *Dig Dis* 1994; **12**: 69-71 [PMID: 8045029 DOI: 10.1159/000171439]

5 **Quigley EM**. The clinical pharmacology of motility disorders: the perils (and pearls) of prokinesia. *Gastroenterology* 1994; **106**: 1112-1114 [PMID: 8143979]

6 **Quigley EM**. Gastric and small intestinal motility in health and disease. *Gastroenterol Clin North Am* 1996; **25**: 113-145 [PMID: 8682569 DOI: 10.1016/S0889-8553(05)70368-X]

7 **Behrns KE**, Sarr MG. Diagnosis and management of gastric emptying disorders. *Adv Surg* 1994; **27**: 233-255 [PMID: 8140975]

8 **Goyal RK**, Hirano I. The enteric nervous system. *N Engl J Med* 1996; **334**: 1106-1115 [PMID: 8598871 DOI: 10.1056/NEJM199604253341707]

9 **Sarna SK**. Physiology and pathophysiology of colonic motor activity (1). *Dig Dis Sci* 1991; **36**: 827-862 [PMID: 1674470]

10 **Goyal RK**. Changing focus on unexplained esophageal chest pain. *Ann Intern Med* 1996; **124**: 1008-1011 [PMID: 8624051 DOI: 10.7326/0003-4819-124-11-199606010-00010]

11 **Singaram C**, Ashraf W, Gaumnitz EA, Torbey C, Sengupta A, Pfeiffer R, Quigley EM. Dopaminergic defect of enteric nervous system in Parkinson's disease patients with chronic constipation. *Lancet* 1995; **346**: 861-864 [PMID: 7564669 DOI: 10.1016/S0140-6736(95)92707-7]

12 **Edwards LL**, Quigley EM, Pfeiffer RF. Gastrointestinal dysfunction in Parkinson's disease: frequency and pathophysiology. *Neurology* 1992; **42**: 726-732 [PMID: 1565224 DOI: 10.1212/WNL.42.4.726]

13 **Pfeiffer RF**, Quigley EMM, Edwards LL. Gastrointestinal dysfunction in neurological disease. In Korczyn AD, ed.Handbook of Autonomic Nervous System Dysfunction, Marcel Dekker 1995: pp311-339

14 **Schuffler MD**, Jonak Z. Chronic idiopathic intestinal pseudo-obstruction caused by a degenerative disorder of the myenteric plexus: the use of Smith' s method to define the neuropathology. *Gastroenterology* 1982; **82**: 476-486 [PMID: 6172315]

15 **Krishnamurthy S**, Heng Y, Schuffler MD. Chronic intestinal pseudo-obstruction in infants and children caused by diverse abnormalities of the myenteric plexus. *Gastroenterology* 1993; **104**: 1398-1408 [PMID: 7683295]

16 **Abell TL**, Waters B, Duncan U et al. Intraoperative electrophysiology and full-thickness biopsy provide useful diagnostic information in patients with refractory nausea and vomiting. *Gastroenterology* 1994; **106**: A

17 **Familoni BO**, Abell TL, Voeller G. Measurement of gastric and small bowel electrical activity at laparoscopy. *J Laparoendosc Surg* 1994; **4**: 325-332 [PMID: 7833517 DOI: 10.1089/lps.1994.4.325]

18 **Lindberg G**, Iwarzon M, Veress B. Small bowel motility patterns in patients with chronic intestinal pseudo-obstruction. *Gastroenterology* 1994; **106**; A532

19 **Singaram C**, SenGupta A. Histopathology of the enteric neuropathies. From silver staining to immunohistochemistry. *Gastroenterol Clin North Am* 1996; **25**: 183-201 [PMID: 8682572 DOI: 10.1016/S0889-8553(05)70371-X]

20 **Cortesini C**, Cianchi F, Infantino A, Lise M. Nitric oxide synthase and VIP distribution in enteric nervous system in idiopathic chronic constipation. *Dig Dis Sci* 1995; **40**: 2450-2455 [PMID: 7587830 DOI: 10.1007/BF02063253]

21 **Meier-Ruge WA**, Brönnimann PB, Gambazzi F, Schmid PC, Schmidt CP, Stoss F. Histopathological criteria for intestinal neuronal dysplasia of the submucosal plexus (type B) *Virchows Arch* 1995; **426**: 549-556 [PMID: 7655734 DOI: 10.1007/bf00192108]

22 **Ryan DP**. Neuronal intestinal dysplasia. *Semin Pediatr Surg* 1995; **4**: 22-25 [PMID: 7728504]

23 **Takeda S**, Yamazaki K, Miyakawa T, Arai H. Parkinson's disease with involvement of the parasympathetic ganglia. *Acta Neuropathol* 1993; **86**: 397-398 [PMID: 8256591 DOI: 10.1007/BF00369454]

24 **Shankle WR**, Landing BH, Ang SM, Chui H, Villarreal-Engelhardt G, Zarow C. Studies of the enteric nervous system in Alzheimer disease and other dementias of the elderly: enteric neurons in Alzheimer disease. *Mod Pathol* 1993; **6**: 10-14 [PMID: 8426853]

25 **Wakabayashi K**, Takahashi H, Ohama E, Ikuta F. Parkinson's disease: an immunohistochemical study of Lewy body-containing neurons in the enteric nervous system. *Acta Neuropathol* 1990; **79**: 581-583 [PMID: 1972853 DOI: 10.1007/BF00294234]

26 **Krishnamurthy S**, Schuffler MD. Pathology of neuromuscular disorders of the small intestine and colon. *Gastroenterology* 1987; **93**: 610-639 [PMID: 3301518]

27 **Smith B**.The neuropathology of the alimentary tract. London, Edward Arnold,1972

28 **Castex F**, Guillemot F, Talbodec N, Colombel JF, Paris JC, Cortot A. Association of an attack of varicella and an achalasia. *Am J Gastroenterol* 1995; **90**: 1188-1189 [PMID: 7611235]

29 **Robertson CS**, Martin BA, Atkinson M. Varicella-zoster virus DNA in the oesophageal myenteric plexus in achalasia. *Gut* 1993; **34**: 299-302 [PMID: 8386130 DOI: 10.1136/gut.34.3.299]

30 **Eckardt VF**, Stenner F, Liewen H, Röder R, Koop H, Bernhard G. Autonomic dysfunction in patients with achalasia. *Neurogastroenterol Motil* 1995; **7**:

55-61 [PMID: 7627867 DOI: 10.1111/j.1365-2982.1995.tb00209.x]
31 **Mearin F**, Papo M, Malagelada JR. Impaired gastric relaxation in patients with achalasia. *Gut* 1995; **36**: 363-368 [PMID: 7698693 DOI: 10.1136/gut.36.3.363]
32 **Gazarian M**, Cowell CT, Bonney M, Grigor WG. The "4A" syndrome: adrenocortical insufficiency associated with achalasia, alacrima, autonomic and other neurological abnormalities. *Eur J Pediatr* 1995; **154**: 18-23 [PMID: 7895750 DOI: 10.1007/BF01972967]
33 **Guelrud M**, Rossiter A, Souney PF, Rossiter G, Fanikos J, Mujica V. The effect of vasoactive intestinal polypeptide on the lower esophageal sphincter in achalasia. *Gastroenterology* 1992; **103**: 377-382 [PMID: 1634056]
34 **Aggestrup S**, Uddman R, Sundler F, Fahrenkrug J, Håkanson R, Sørensen HR, Hambraeus G. Lack of vasoactive intestinal polypeptide nerves in esophageal achalasia. *Gastroenterology* 1983; **84**: 924-927 [PMID: 6832568]
35 **Mearin F**, Mourelle M, Guarner F, Salas A, Riveros-Moreno V, Moncada S, Malagelada JR. Patients with achalasia lack nitric oxide synthase in the gastro-oesophageal junction. *Eur J Clin Invest* 1993; **23**: 724-728 [PMID: 7508398 DOI: 10.1111/j.1365-2362.1993.tb01292.x]
36 **Niwamoto H**, Okamoto E, Fujimoto J, Takeuchi M, Furuyama J, Yamamoto Y. Are human herpes viruses or measles virus associated with esophageal achalasia? *Dig Dis Sci* 1995; **40**: 859-864 [PMID: 7720482 DOI: 10.1007/BF02064992]
37 **Vanderwinden JM**, Liu H, De Laet MH, Vanderhaeghen JJ. Study of the interstitial cells of Cajal in infantile hypertrophic pyloric stenosis. *Gastroenterology* 1996; **111**: 279-288 [PMID: 8690192 DOI: 10.1053/gast.1996.v111.pm8690192]
38 **Sanders KM**. A case for interstitial cells of Cajal as pacemakers and mediators of neurotransmission in the gastrointestinal tract. *Gastroenterology* 1996; **111**: 492-515 [PMID: 8690216 DOI: 10.1053/gast.1996.v111.pm8690216]
39 **Vanderwinden JM**, Mailleux P, Schiffmann SN, Vanderhaeghen JJ, De Laet MH. Nitric oxide synthase activity in infantile hypertrophic pyloric stenosis. *N Engl J Med* 1992; **327**: 511-515 [PMID: 1378938 DOI: 10.1056/NEJM199208203270802]
40 **Langer JC**, Berezin I, Daniel EE. Hypertrophic pyloric stenosis: ultrastructural abnormalities of enteric nerves and the interstitial cells of Cajal. *J Pediatr Surg* 1995; **30**: 1535-1543 [PMID: 8583319 DOI: 10.1016/0022-3468(95)90151-5]
41 **Ward SM**, Burns AJ, Torihashi S, Harney SC, Sanders KM. Impaired development of interstitial cells and intestinal electrical rhythmicity in steel mutants. *Am J Physiol* 1995; **269**: C1577-C1585 [PMID: 8572188]
42 **Isozaki K**, Hirota S, Nakama A, Miyagawa J, Shinomura Y, Xu Z, Nomura S, Kitamura Y. Disturbed intestinal movement, bile reflux to the stomach, and deficiency of c-kit-expressing cells in Ws/Ws mutant rats. *Gastroenterology* 1995; **109**: 456-464 [PMID: 7542218 DOI: 10.1016/0016-5085(95)90333-X]
43 **Vanderwinden JM**, De Laet MH, Schiffmann SN, Mailleux P, Lowenstein CJ, Snyder SH, Vanderhaeghen JJ. Nitric oxide synthase distribution in the enteric nervous system of Hirschsprung's disease. *Gastroenterology* 1993; **105**: 969-973 [PMID: 7691675]
44 **Kessler S**, Campbell JR. Neuronal colonic dysplasia associated with short-segment Hirschsprung's disease. A possible cause of therapeutic failure. *Arch Pathol Lab Med* 1985; **109**: 532-533 [PMID: 3838882]
45 **Moore BG**, Singaram C, Eckhoff DE. Immunohistochemical evaluation of ultra short segment Hirschsprung's disease and literature review.Dis Colon Rectum, 1995 (In Press)
46 **Schofield DE**, Yunis EJ. Intestinal neuronal dysplasia. *J Pediatr Gastroenterol Nutr* 1991; **12**: 182-189 [PMID: 2051270 DOI: 10.1097/00005176-199102000-00008]
47 **Badner JA**, Sieber WK, Garver KL, Chakravarti A. A genetic study of Hirschsprung disease. *Am J Hum Genet* 1990; **46**: 568-580 [PMID: 2309705]
48 **Angrist M**, Kauffman E, Slaugenhaupt SA, Matise TC, Puffenberger EG, Washington SS, Lipson A, Cass DT, Reyna T, Weeks DE. A gene for Hirschsprung disease (megacolon) in the pericentromeric region of human chromosome 10. *Nat Genet* 1993; **4**: 351-356 [PMID: 8401581 DOI: 10.1038/ng0893-351]
49 **Romeo G**, Ronchetto P, Luo Y, Barone V, Seri M, Ceccherini I, Pasini B, Bocciardi R, Lerone M, Kääriäinen H. Point mutations affecting the tyrosine kinase domain of the RET proto-oncogene in Hirschsprung's disease. *Nature* 1994; **367**: 377-378 [PMID: 8114938 DOI: 10.1038/367377a0]
50 **Puffenberger EG**, Hosoda K, Washington SS, Nakao K, deWit D, Yanagisawa M, Chakravart A. A missense mutation of the endothelin-B receptor gene in multigenic Hirschsprung's disease. *Cell* 1994; **79**: 1257-1266 [PMID: 8001158 DOI: 10.1016/0092-8674(94)90016-7]
51 **de Oliveira RB**, Rezende Filho J, Dantas RO, Iazigi N. The spectrum of esophageal motor disorders in Chagas' disease. *Am J Gastroenterol* 1995; **90**: 1119-1124 [PMID: 7611209]
52 **Kirchhoff LV**. American trypanosomiasis (Chagas' disease)--a tropical disease now in the United States. *N Engl J Med* 1993; **329**: 639-644 [PMID: 8341339 DOI: 10.1056/NEJM199308263290909]
53 **Murray JA**, Ledlow A, Launspach J, Evans D, Loveday M, Conklin JL. The effects of recombinant human hemoglobin on esophageal motor functions in humans. *Gastroenterology* 1995; **109**: 1241-1248 [PMID: 7557091 DOI: 10.1016/0016-5085(95)90584-7]
54 **Quigley EM**. Symptoms and gastric function in dyspepsia--goodbye to gastroparesis? *Neurogastroenterol Motil* 1996; **8**: 273-275 [PMID: 8959732 DOI: 10.1111/j.1365-2982.1996.tb00266.x]
55 **Verne GN**, Sninsky CA. Chronic intestinal pseudo-obstruction. *Dig Dis* 1995; **13**: 163-181 [PMID: 8548980 DOI: 10.1159/000171499]
56 **Howe S**, Eaker EY, Sallustio JE, Peebles C, Tan EM, Williams RC. Antimyenteric neuronal antibodies in scleroderma. *J Clin Invest* 1994; **94**: 761-770 [PMID: 8040331 DOI: 10.1172/JCI117395]
57 **Colemont LJ**, Camilleri M. Chronic intestinal pseudo-obstruction: diagnosis and treatment. *Mayo Clin Proc* 1989; **64**: 60-70 [PMID: 2642997 DOI: 10.1016/S0025-6196(12)65304-X]
58 **Greydanus MP**, Camilleri M. Abnormal postcibal antral and small bowel motility due to neuropathy or myopathy in systemic sclerosis. *Gastroenterology* 1989; **96**: 110-115 [PMID: 2909417]
59 **Krishnamurthy S**, Kelly MM, Rohrmann CA, Schuffler MD. Jejunal diverticulosis. A heterogenous disorder caused by a variety of abnormalities of smooth muscle or myenteric plexus. *Gastroenterology* 1983; **85**: 538-547 [PMID: 6409704]
60 **Husebye E**, Hauer-Jensen M, Kjørstad K, Skar V. Severe late radiation enteropathy is characterized by impaired motility of proximal small intestine. *Dig Dis Sci* 1994; **39**: 2341-2349 [PMID: 7956601 DOI: 10.1007/BF02087648]
61 **Hashimoto Y**, Motoyoshi S, Maruyama H, Sakakida M, Yano T, Yamaguchi K, Goto K, Sugihara S, Takano S, Kambara T. The treatment of pheochromocytoma associated with pseudo-obstruction and perforation of the colon, hepatic failure, and DIC. *Jpn J Med* 1990; **29**: 341-346 [PMID: 1980322 DOI: 10.2169/internalmedicine1962.29.341]
62 **Ruchti C**, Eisele S, Kaufmann M. Fatal intestinal pseudo-obstruction in brown bowel syndrome. *Arch Pathol Lab Med* 1990; **114**: 76-80 [PMID: 2294870]
63 **Füger K**, Barnert J, Höpfner W, Wienbeck M. Intestinal pseudoobstruction as a feature of myotonic muscular dystrophy. *Z Gastroenterol* 1995; **33**: 534-538 [PMID: 8525657]
64 **Boige N**, Faure C, Cargill G, Mashako LM, Cordeiro-Ferreira G, Viarme F, Cezard JP, Navarro J. Manometrical evaluation in visceral neuropathies in children. *J Pediatr Gastroenterol Nutr* 1994; **19**: 71-77 [PMID: 7965481 DOI: 10.1097/00005176-199407000-00011]
65 **Husebye E**, Hauer-Jensen M, Kjørstad K, Skar V. Severe late radiation enteropathy is characterized by impaired motility of proximal small intestine. *Dig Dis Sci* 1994; **39**: 2341-2349 [PMID: 7956601 DOI: 10.1007/BF02087648]
66 **Cacoub P**, Benhamou Y, Barbet P, Piette JC, Le Cae A, Chaussade S, Cadranel JF, Callard P, Opolon P, Godeau P. Systemic lupus erythematosus and chronic intestinal pseudoobstruction. *J Rheumatol* 1993; **20**: 377-381 [PMID: 8474080]
67 **Sjogren RW**. Gastrointestinal motility disorders in scleroderma. *Arthritis Rheum* 1994; **37**: 1265-1282 [PMID: 7945489 DOI: 10.1002/art.1780370902]
68 **Cucchiara S**, Annese V, Minella R, Franco MT, Iervolino C, Emiliano M, Auricchio S. Antroduodenojejunal manometry in the diagnosis of chronic idiopathic intestinal pseudoobstruction in children. *J Pediatr Gastroenterol Nutr* 1994; **18**: 294-305 [PMID: 8057211 DOI: 10.1097/00005176-199404000-00008]
69 **Gerl A**, Storck M, Schalhorn A, Müller-Höcker J, Jauch KW, Schildberg FW, Wilmanns W. Paraneoplastic chronic intestinal pseudoobstruction as a rare complication of bronchial carcinoid. *Gut* 1992; **33**: 1000-1003 [PMID: 1644319 DOI: 10.1136/gut.33.7.1000]
70 **Bassotti G**, Pagliacci MC, Nicoletti I, Pelli MA, Morelli A. Intestinal pseudoobstruction secondary to hypothyroidism. Importance of small bowel manometry. *J Clin Gastroenterol* 1992; **14**: 56-58 [PMID: 1556409 DOI: 10.1097/00004836-199201000-00014]
71 **Fraser AG**, Arthur JF, Hamilton I. Intestinal pseudoobstruction secondary to amyloidosis responsive to cisapride. *Dig Dis Sci* 1991; **36**: 532-535 [PMID: 2007373 DOI: 10.1007/BF01298889]
72 **Husebye E**, Skar V, Høverstad T, Iversen T, Melby K. Abnormal intestinal motor patterns explain enteric colonization with gram-negative bacilli in late radiation enteropathy. *Gastroenterology* 1995; **109**: 1078-1089 [PMID: 7557072 DOI: 10.1016/0016-5085(95)90565-0]
73 **Quigley EMM**. Intestinal pseudo-obstruction. Champion MC, Orr WC. Evolving concepts in gastrointestinal motility. Oxford: Blackwell Science; 1996: 171-199
74 **Ferraz AA**, Cowles VE, Condon RE, Carilli S, Ezberci F, Frantzides CT, Schulte WJ. Nonopioid analgesics shorten the duration of postoperative ileus. *Am Surg* 1995; **61**: 1079-1083 [PMID: 7486451]
75 **Finan MA**, Barton DP, Fiorica JV, Hoffman MS, Roberts WS, Gleeson N, Cavanagh D. Ileus following gynecologic surgery: management with water-soluble hyperosmolar radiocontrast material. *South Med J* 1995; **88**: 539-542 [PMID: 7732443 DOI: 10.1097/00007611-199505000-00006]
76 **Morimoto H**, Cullen JJ, Messick JM, Kelly KA. Epidural analgesia shortens postoperative ileus after ileal pouch-anal canal anastomosis. *Am J Surg* 1995; **169**: 79-82; discussion 82-83 [PMID: 7818002 DOI: 10.1016/S0002-9610(99)80113-5]
77 **Cullen JJ**, Eagon JC, Kelly KA. Gastrointestinal peptide hormones during postoperative ileus. Effect of octreotide. *Dig Dis Sci* 1994; **39**: 1179-1184 [PMID: 7515341 DOI: 10.1007/BF02093781]
78 **Christenson JT**, SSchmuziger M, Maurice J, Simonet F, Velebit V. Postoperative visceral hypotension the common cause for gastrointestinal complications after cardiac surgery. *Thorac Cardiovasc Surg* 1994; **42**: 152-157 [PMID: 7940485 DOI: 10.1055/s-2007-1016478]
79 **Böhm B**, Milsom JW, Fazio VW. Postoperative intestinal motility following conventional and laparoscopic intestinal surgery. *Arch Surg* 1995; **130**: 415-419 [PMID: 7710343 DOI: 10.1001/archsurg.1995.01430040077017]
80 **Golzarian J**, Scott, Jr. HW, Richards WO. Hypermagnesemia-induced para-

lytic ileus.*Dig Dis Sci* 1994; **106**: 924-936
81 **Benson MJ**, Roberts JP, Wingate DL, Rogers J, Deeks JJ, Castillo FD, Williams NS. Small bowel motility following major intra-abdominal surgery: the effects of opiates and rectal cisapride. *Gastroenterology* 1994; **106**: 924-936 [PMID: 8143997]
82 **Plourde V**, Wong HC, Walsh JH, Raybould HE, Taché Y. CGRP antagonists and capsaicin on celiac ganglia partly prevent postoperative gastric ileus. *Peptides* 1993; **14**: 1225-1229 [PMID: 7510881 DOI: 10.1016/0196-9781(93)90180-O]
83 **Taché Y**, Mönnikes H, Bonaz B, Rivier J. Role of CRF in stress-related alterations of gastric and colonic motor function. *Ann N Y Acad Sci* 1993; **697**: 233-243 [PMID: 8257013 DOI: 10.1111/j.1749-6632.1993.tb49936.x]
84 **Bollinger SH**, Quigley EMM. Disordered gastrointestinal motility. Quigley EMM, Sorrell MF. The Gastrointestinal Surgical Patient Preoperative and Postoperative Care. Baltimore: Williams & Wilkins; 1994: 157-174
85 **Ludwig KA**, Frantzides CT, Carlson MA, Grade KL. Myoelectric motility patterns following open versus laparoscopic cholecystectomy. *J Laparoendosc Surg* 1993; **3**: 461-466 [PMID: 8251660 DOI: 10.1089/lps.1993.3.461]
86 **Schlemminger R**, Lottermoser S, Gieseler RK, Sostmann H, Nustede R, Köhler H, Schafmayer A. The adaptive response of the rat small intestine after resection and segmental transplantation during the early postoperative phase. *Res Exp Med* (Berl) 1993; **193**: 213-224 [PMID: 8235074]
87 **Toledo C**, Salmerón JM, Rimola A, Navasa M, Arroyo V, Llach J, Ginès A, Ginès P, Rodés J. Spontaneous bacterial peritonitis in cirrhosis: predictive factors of infection resolution and survival in patients treated with cefotaxime. *Hepatology* 1993; **17**: 251-257 [PMID: 8428722 DOI: 10.1002/hep.1840170215]
88 **Ikehara O**. Vincristine-induced paralytic ileus: role of fiberoptic colonoscopy and prostaglandin F2 alpha. *Am J Gastroenterol* 1992; **87**: 207-210 [PMID: 1734699]
89 **Jambor CR**, Steedman DJ. Acute gastric dilation after trauma. *J R Coll Surg Edinb* 1991; **36**: 29-31 [PMID: 2037995]
90 **Frantzides CT**, Cowles V, Salaymeh B, Tekin E, Condon RE. Morphine effects on human colonic myoelectric activity in the postoperative period. *Am J Surg* 1992; **163**: 144-148; discussion 148-149 [PMID: 1733363 DOI: 10.1016/0002-9610(92)90267-U]
91 **Schippers E**, Hölscher AH, Bollschweiler E, Siewert JR. Return of interdigestive motor complex after abdominal surgery. End of postoperative ileus? *Dig Dis Sci* 1991; **36**: 621-626 [PMID: 2022164 DOI: 10.1007/BF01297029]
92 **Mitchell G**, Larochelle J, Lambert M, Michaud J, Grenier A, Ogier H, Gauthier M, Lacroix J, Vanasse M, Larbrisseau A. Neurologic crises in hereditary tyrosinemia. *N Engl J Med* 1990; **322**: 432-437 [PMID: 2153931 DOI: 10.1056/NEJM199002153220704]
93 **Tjon A Tham RT**, Vlasveld LT, Willemze R. Gastrointestinal complications of cytosine-arabinoside chemotherapy: findings on plain abdominal radiographs. *AJR Am J Roentgenol* 1990; **154**: 95-98 [PMID: 2104733 DOI: 10.2214/ajr.154.1.2104733]
94 **Livingston EH**, Passaro EP. Postoperative ileus. *Dig Dis Sci* 1990; **35**: 121-132 [PMID: 2403907 DOI: 10.1007/BF01537233]
95 **Stelzner M**, Phillips JD, Fonkalsrud EW. Acute ileus from steroid withdrawal simulating intestinal obstruction after surgery for ulcerative colitis. *Arch Surg* 1990; **125**: 914-917 [PMID: 2369317 DOI: 10.1001/archsurg.1990.01410190112018]
96 **Peschiera JL**, Beerman SP. Intestinal dysfunction associated with acute thoracolumbar fractures. *Orthop Rev* 1990; **19**: 284-288 [PMID: 2330226]
97 **Berkowitz N**, Schulman LL, McGregor C, Markowitz D. Gastroparesis after lung transplantation. Potential role in postoperative respiratory complications. *Chest* 1995; **108**: 1602-1607 [PMID: 7497768 DOI: 10.1378/chest.108.6.1602]
98 **Gaber AO**, Oxley D, Karas J, Cardoso S, Hathaway D, Shokouh-Amiri MH, Jensen SL, Abell TL. Changes in gastric emptying in recipients of successful combined pancreas-kidney transplants. *Dig Dis* 1991; **9**: 437-443 [PMID: 1804583 DOI: 10.1159/000171334]
99 **Van Thiel DH**, Gavaler JS, Schade RR, Chien MC, Starzl TE. Cytomegalovirus infection and gastric emptying. *Transplantation* 1992; **54**: 70-73 [PMID: 1321520 DOI: 10.1097/00007890-199207000-00012]
100 **Kadesky K**, Purdue GF, Hunt JL. Acute pseudo-obstruction in critically ill patients with burns. *J Burn Care Rehabil* 1995; **16**: 132-135 [PMID: 7775506 DOI: 10.1097/00004630-199503000-00007]
101 **Rex DK**. Acute colonic pseudo-obstruction (Ogilvie's syndrome). *Gastroenterologist* 1994; **2**: 233-238 [PMID: 7987621]
102 **Thessen CC**, Kreder KJ. Ogilvie's syndrome: a potential complication of vaginal surgery. *J Urol* 1993; **149**: 1541-1543 [PMID: 8501808]
103 **Jetmore AB**, Timmcke AE, Gathright JB, Hicks TC, Ray JE, Baker JW. Ogilvie's syndrome: colonoscopic decompression and analysis of predisposing factors. *Dis Colon Rectum* 1992; **35**: 1135-1142 [PMID: 1473414 DOI: 10.1007/BF02251964]
104 **Feldman RA**, Karl RC. Diagnosis and treatment of Ogilvie's syndrome after lumbar spinal surgery. Report of three cases. *J Neurosurg* 1992; **76**: 1012-1016 [PMID: 1588406 DOI: 10.3171/jns.1992.76.6.1012]
105 **Apostolakis ER**, Bircks W. Acute pseudo-obstruction of the colon (Ogilvie' s syndrome) following open heart surgery. *Thorac Cardiovasc Surg* 1990; **38**: 371-373 [PMID: 2291236 DOI: 10.1055/s-2007-1014054]
106 **Pai NB**, Murthy RS, Kumar HT, Gerst PH. Association of acute colonic pseudo-obstruction (Ogilvie's syndrome) with herpes zoster. *Am Surg* 1990; **56**: 691-694 [PMID: 2240863]
107 **Bortolotti M**, Mattioli S, Alampi G et al. Brainstern viral-like encephalitis as a possible cause of a gastroduodenal motility disorder: a case report. *J Gastrointest Motil*1989; **1**: 99
108 **Oh JJ**, Kim CH. Gastroparesis after a presumed viral illness: clinical and laboratory features and natural history. *Mayo Clin Proc* 1990; **65**: 636-642 [PMID: 2348727 DOI: 10.1016/S0025-6196(12)65125-8]
109 **Vassallo M**, Camilleri M, Caron BL, Low PA. Gastrointestinal motor dysfunction in acquired selective cholinergic dysautonomia associated with infectious mononucleosis. *Gastroenterology* 1991; **100**: 252-258 [PMID: 1983829]
110 **Déchelotte PJ**, Mulliez NM, Bouvier RJ, Vanlieféringhen PC, Lémery DJ. Pseudo-meconium ileus due to cytomegalovirus infection: a report of three cases. *Pediatr Pathol* 1992; **12**: 73-82 [PMID: 1313975 DOI: 10.3109/15513819209023282]
111 **Alampi G**, Bortolotti M, Mattioli S, Giangaspero F, Rossi L. Brain stem encephalitis in a patient with gastroduodenal and cardiovascular dysfunction: a case report. *Clin Neuropathol* 1990; **9**: 16-20 [PMID: 2306890]
112 **Nomdedéu JF**, Nomdedéu J, Martino R, Bordes R, Portorreal R, Sureda A, Domingo-Albós A, Rutllant M, Soler J. Ogilvie's syndrome from disseminated varicella-zoster infection and infarcted celiac ganglia. *J Clin Gastroenterol* 1995; **20**: 157-159 [PMID: 7769201 DOI: 10.1097/00004836-199503000-00020]
113 **Mathias JR**, Baskin GS, Reeves-Darby VG, Clench MH, Smith LL, Calhoon JH. Chronic intestinal pseudoobstruction in a patient with heart-lung transplant. Therapeutic effect of leuprolide acetate. *Dig Dis Sci* 1992; **37**: 1761-1768 [PMID: 1330462 DOI: 10.1007/BF01299872]
114 **Hart RG**, Kanter MC. Acute autonomic neuropathy. Two cases and a clinical review. *Arch Intern Med* 1990; **150**: 2373-2376 [PMID: 2241448 DOI: 10.1001/archinte.1990.00390220109022]
115 **Gesser RM**, Valyi-Nagy T, Fraser NW, Altschuler SM. Oral inoculation of SCID mice with an attenuated herpes simplex virus-1 strain causes persistent enteric nervous system infection and gastric ulcers without direct mucosal infection. *Lab Invest* 1995; **73**: 880-889 [PMID: 8558851]
116 **Gesser RM**, Valyi-Nagy T, Altschuler SM, Fraser NW. Oral-oesophageal inoculation of mice with herpes simplex virus type 1 causes latent infection of the vagal sensory ganglia (nodose ganglia). *J Gen Virol* 1994; **75 (Pt 9)**: 2379-2386 [PMID: 8077936 DOI: 10.1099/0022-1317-75-9-2379]
117 **Mathan MM**, Chandy G, Mathan VI. Ultrastructural changes in the upper small intestinal mucosa in patients with cholera. *Gastroenterology* 1995; **109**: 422-430 [PMID: 7615191 DOI: 10.1016/0016-5085(95)90329-1]
118 **Hirose R**, Taguchi T, Hirata Y, Yamada T, Nada O, Suita S. Immunohistochemical demonstration of enteric nervous distribution after syngeneic small bowel transplantation in rats. *Surgery* 1995; **117**: 560-569 [PMID: 7740428 DOI: 10.1016/S0039-6060(05)80256-9]
119 **Geboes K**. Immunopathological studies of the small intestinal intramural nervous system and of intramural vessels in Crohn's disease. *Verh K Acad Geneeskd Belg* 1993; **55**: 267-301; discussion 301-303 [PMID: 8128776]
120 **Rao SS**, Read NW, Brown C, Bruce C, Holdsworth CD. Studies on the mechanism of bowel disturbance in ulcerative colitis. *Gastroenterology* 1987; **93**: 934-940 [PMID: 3653643]
121 **Jacobson K**, McHugh K, Collins SM. Experimental colitis alters myenteric nerve function at inflamed and noninflamed sites in the rat. *Gastroenterology* 1995; **109**: 718-722 [PMID: 7657099 DOI: 10.1016/0016-5085(95)90378-X]
122 **Vermillion DL**, Collins SM. Increased responsiveness of jejunal longitudinal muscle in Trichinella-infected rats. *Am J Physiol* 1988; **254**: G124-G129 [PMID: 3337232]
123 **Vermillion DL**, Ernst PB, Collins SM. T-lymphocyte modulation of intestinal muscle function in the Trichinella-infected rat. *Gastroenterology* 1991; **101**: 31-38 [PMID: 1646141]
124 **Rühl A**, Hurst S, Collins SM. Synergism between interleukins 1 beta and 6 on noradrenergic nerves in rat myenteric plexus. *Gastroenterology* 1994; **107**: 993-1001 [PMID: 7926489]
125 **Rühl A**, Berezin I, Collins SM. Involvement of eicosanoids and macrophage-like cells in cytokine-mediated changes in rat myenteric nerves. *Gastroenterology* 1995; **109**: 1852-1862 [PMID: 7498650 DOI: 10.1016/0016-5085(95)90752-1]
126 **Hogaboam CM**, Snider DP, Collins SM. Activation of T lymphocytes by syngeneic murine intestinal smooth muscle cells. *Gastroenterology* 1996; **110**: 1456-1466 [PMID: 8613051 DOI: 10.1053/gast.1996.v110.pm8613051]
127 **Heeckt PF**, Halfter WM, Schraut WH, Lee KK, Bauer AJ. Small bowel transplantation and chronic rejection alter rat intestinal smooth muscle structure and function. *Surgery* 1993; **114**: 449-456; discussion 456-457 [PMID: 8342147]
128 **Koch TR**, Carney JA, Go VL, Szurszewski JH. Altered inhibitory innervation of circular smooth muscle in Crohn's colitis. Association with decreased vasoactive intestinal polypeptide levels. *Gastroenterology* 1990; **98**: 1437-1444 [PMID: 2338187]

E- Editor: Li RF

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com