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In vivo imaging of intestinal helminths by capsule endoscopy

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ABSTRACT

This review examines the use of digestive endoscopy to visualize intestinal helminths. The infections caused by these parasites are responsible for high levels of morbidity and mortality. These helminths can be visualized using gastroduodenal endoscopy, endoscopic retrograde cholangiopancreatography, and colonoscopy. Endoscopic examination of the small bowel is limited by its considerable length and its distance from the mouth and anus. Since capsule endoscopy (CE) was first reported in 2000, it has been established as a noninvasive modality for the investigation of the gastrointestinal tract. CE is used as a first-line tool for imaging various small-bowel diseases, mainly obscure gastrointestinal bleeding and Crohn's disease. Since the Food and Drug Administration (FDA) approved CE in 2001, the indications for its use have expanded widely. For example, CE can be used to visualize the *in vivo* kinetics of intestinal helminths. If the current trends in technological development continue, CE will become more widely used to facilitate the diagnosis and treatment of helminth infections in the near future.

Contents

1. Introduction

Helminths, which are endemic in developing countries, places with poor sanitation, as well as in non-endemic areas because of immigration and travel, are among the most widespread infectious agents that affect human populations, particularly in the marginalized, low-income, and resource-constrained regions of the world. It is estimated that over one billion people in the developing countries are infected with one or more species of helminths [1,2]. The morbidity of helminthiasis induces a vicious circle of poverty, decreased productivity, and inadequate socioeconomic development [3]. Helminthiasis are also responsible for high levels of morbidity and mortality, including iron-deficiency anemia, seizures, portal hypertension, and chronic diarrhea [3–5].

Children exhibit especially high infection rates because they often play in close contact with the soil and frequently put their fingers in their mouths. Children are known to be more vulnerable to parasitic infection than adults because of their level of exposure to parasite eggs and cysts, level of hygiene, and level of immunity to infections [6–8]. Children are also vulnerable to serious complications of helminthic infection, such as malnutrition, anemia, and bowel obstruction, leading to cognitive deficits, difficulties in learning, and school absenteeism [9,10].

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2. Intestinal helminths

Helminths are multicellular worms. In their adult form, helminths cannot multiply in the human body. Intestinal helminths are usually transmitted through contact with infected feces (for example, through contaminated soil, food, or water). Human intestinal helminths, which range in size from 1 mm to several meters, are parasites that live in the human intestine, eat bowel contents, or suck blood from the intestinal wall. This leads to inflammation of the small intestine or colon, ulcers, anemia, and deficiencies in protein, iron, and vitamins (mainly A, C, and B12).

Technological advancements and the globalization of economic activity have led to the widespread movement of people and goods around the globe. These changes are associated with a recent increase in the incidence of intestinal helminth disease among the Japanese population. Arizono et al. reported a recent surge in the annual incidence rates of clinical cases of *Diphyllobothrium nihonkaiense* (*D. nihonkaiense*) in Japan [11]. The average incidence of tapeworm infections in Japan over the past 20 years was 0.32 cases per 100,000 individuals annually; in 2008, the rate was 1.0 case per 100,000 individuals. *D. nihonkaiense* infections are as prevalent in Japan as *D. latum* infections are in certain European countries [12]. Thus, we should note that intestinal helminth disease is an issue not only in developing countries, but also in more developed nations. Due to globalization of human activity, the potential sources of infection are distributed worldwide [13].

3. Screening and further examination for the presence of intestinal helminths

The CDC (Centers for Disease Control and Prevention) has stated that diagnosis of parasitic disease may be difficult, so the health care provider may order more than one kind of test. The CDC also implied that health care providers may order common parasite tests as follows: 1) A fecal (stool) exam, also called an ova and parasite test (stool O&P); 2) endoscopy; 3) blood tests (serology and blood smear); and 4) X-ray, magnetic resonance imaging (MRI), and computed tomography (CT) imaging.

Stool O&P is first used to find parasites that cause diarrhea, loose or watery stools, cramping, flatulence (gas), and other abdominal illnesses. The CDC recommends that 3 or more stool samples, collected on separate days, be examined. Stool O&P is an economical option and easier to implement on a wide-scale basis. Endoscopy is used when stool exams do not reveal the cause of the patient's symptoms [14]. No general serological test is available for diagnosis of intestinal helminth, except for special research laboratories [15].

Endoscopy is one of the most fascinating and rapidly growing medical fields. Modern endoscopic procedures are used in the diagnosis and treatment of numerous pathologies of the digestive tract. For example, modern endoscopic tools such as upper endoscopy, endoscopic retrograde cholangiopancreatography (ERCP), and lower endoscopy have been used for the identification of intestinal helminths [16]. Fig. 1A–C shows endoscopic images from conventional endoscopy, such as an upper endoscopy [Fig. 1A], ERCP [Fig. 1B], and lower endoscopy [Fig. 1C]. Upper endoscopy may detect the presence of parasites, as patients with gastrointestinal helminths may present peptic ulcer-like symptoms or hematemesis [16]. ERCP is an effective diagnostic tool for demonstrating the presence of parasites in the biliary duct. ERCP is not used only for the diagnosis of biliary parasites, but also in therapy [16,17]. Lower endoscopy can be helpful to identify parasites of the lower gastrointestinal tract in cases of colitis, irritable bowel syndrome, colonic polyps or malignancy [18–21]. Table 1 summarizes intestinal helminths visualized by conventional endoscopy in Japan [16,22,23].

Radiography has acquired a role in the diagnosis of intestinal parasites, and in some instances, has assisted in their management with interventional procedures [24]. Fig. 1D and E shows fluoroscopic images of intestinal helminthic disease with contrast medium. Although fluoroscopy can non-invasively visualize intestinal helminths, these helminths could not be visualized under direct visual guidance. In addition, these helminths cannot be treated and removed directly, except in a few cases where the presence of the tapeworm was demonstrated as a radiolucent shadow, and those cases were completely treated with meglumine/diatrizoate sodium (Gastrografin) [25].

4. Traditional fiber endoscopy: its limitations and evolution

The first endoscope, introduced by Bruening in 1907, was a rigid instrument that enabled inspection of the upper gastrointestinal tract with the patient under general anesthesia [26]. Forty years later, the first flexible fiber-optic instrument enabled endoscopy to be performed under local anesthesia or light sedation. The introduction of flexible endoscopy in the early 1970s resulted in a great advancement in visualization techniques for alimentary tract imaging. However, the portion of the small bowel extending distally from Treitz's ligament to the terminal ileum remained a virtual endoscopic blind spot.

Until quite recently, the small bowel has been the most difficult part of gastrointestinal anatomy to examine. Historically, the small bowel was considered technically difficult to examine because of its length (3–5 meters), location, and tortuosity [27]. For example, barium radiography has traditionally been the primary method used to screen the small bowel, but the diagnostic value of this test is low for various specific lesions. Barium radiography of the small bowel is currently the primary radiographic means of diagnosing a small-bowel neoplasm and the best technique to locate small bowel lesions; however, its sensitivity is only 30–44% [28].

In 2001, a revolutionary type of fiber endoscopy was introduced: double-balloon endoscopy (DBE) [Fig. 1F] [29]. DBE enables the endoscopic examination and treatment of the entire small intestine. Besides the diagnostic advantages, the main advantage of DBE has been that it combines the ability to perform additional biopsies for histopathological evaluation together with the ability to perform therapeutic interventions during the same procedure. These DBE therapeutic options cover a whole range of widely used upper endoscopy and colonoscopy interventions, including electrocoagulation, argon plasma coagulation, polypectomy, balloon dilation of strictures, and retrieval of foreign bodies, including removal of retained wireless capsules. However, DBE is an invasive and time-consuming procedure, and there is a considerable risk of complications such as pancreatitis or perforations, especially in therapeutic procedures [30]. Nonetheless, the utility of DBE in the diagnosis of intestinal helminth disease has been established [31,32].

Fig. 1F shows the general appearance of a double-balloon endoscopy (DBE) device. It is performed using a 200 cm enteroscope equipped with a 140 cm overtube, which can be introduced per mouth or per anus. Pressure-sensitive latex balloons attached at the tip of both the scope and the overtube are inflated and deflated with air, thus allowing the advancement of the device along the small bowel loops [29]. Fig. 1G and H show a case of small intestine infection of *Strongyloides stercoralis* by DBE. As shown in Fig. 1G, DBE can visualize small intestine changes directly and can perform biopsies. In this case, this biopsy specimen revealed *S. stercoralis* infection [Fig. 1H].

5. Introduction of capsule endoscopy and its indications

Since capsule endoscopy (CE) was first reported in 2000, one year before the appearance of DBE [33], it has been established as a noninvasive modality for investigating the small intestinal tract. CE is used as a first-line tool for imaging various small-bowel diseases. Since its approval by the Food and Drug Administration (FDA) in 2001, the indications for its use have expanded widely. The most important indication for the use of CE remains obscure gastrointestinal bleeding (OGIB) after upper and lower gastrointestinal endoscopies have shown normal findings. Suspected Crohn's disease is also a well-accepted indication. There have been European, American, and British guidelines, among others, on the use of CE [34–38].

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