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## ARTICULO ESPECIAL

### Diagnosis, management and treatment of chronic Chagas' gastrointestinal disease in areas where Trypanosoma cruzi infection is not endemic

#### Diagnóstico, manejo y tratamiento de la afectación digestiva en la fase crónica de la enfermedad de Chagas en países no endémicos

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## 1 Introduction

3 Chagas disease, also known as American trypanosomiasis, is  
 4 a zoonosis that affects about 8–12 million people in Latin  
 5 America.<sup>1,2</sup> It is estimated that some 40 million people are  
 6 at risk of acquiring the infection.<sup>3</sup>

7 In its natural life cycle, *Trypanosoma cruzi* (*T. cruzi*) is  
 8 transmitted through triatomine vectors. Traditionally, Cha-  
 9 gas disease was regarded as being typical of poor rural  
 10 areas, though at present, increased migratory trends have  
 11 caused the disease to manifest in urban areas of endemic  
 12 countries,<sup>2,4</sup> as well as in countries that receive a growing  
 13 number of immigrants.<sup>5,6</sup> In such areas, where the vector is  
 14 lacking, *T. cruzi* can be transmitted through blood transfu-  
 15 sions and blood products,<sup>7</sup> organ and tissue transplants,<sup>8</sup> or  
 16 vertically from infected mothers to their offspring.<sup>9</sup>

17 Following an acute phase that usually goes unnoticed  
 18 because of its few or no symptoms, untreated Chagas  
 19 disease enters an initially asymptomatic chronic phase  
 20 known as the indeterminate form of the disease. After a  
 21 prolonged period of time (20–30 years), 20–30% of all  
 22 infected patients develop cardiac complications (cardiac  
 23 form), 15–20%<sup>10</sup> suffer digestive disorders (digestive form)  
 24 or both (mixed form), and under 5% develop the neurological  
 25 form of the disease. The rest of the patients continue to  
 26 present the indeterminate form of Chagas disease, with no  
 27 clinical manifestations at any point in life.<sup>11</sup> Digestive  
 28 manifestations are the second most common cause of  
 29 complications of Chagas disease, and although the mortality  
 30 rate is low, they can have a considerable impact upon  
 31 patient quality of life. The prevalence of such digestive  
 32 manifestations varies according to the geographical origin of  
 33 the patients. In this sense, they are more common in central  
 34 Brazil, less frequent in Bolivia, and practically non-existent  
 35 in countries north of the Amazon basin, Central America and  
 36 Mexico. In non-endemic areas, the prevalence of digestive  
 37 manifestations associated with the disease depends on the  
 38 origin of immigration. In Spain there have already been  
 39 reports of patients with Chagas disease and digestive  
 40 complications.<sup>12,13</sup>

41 As has been commented, the digestive complications of  
 42 Chagas disease are more common in the central and  
 43 southern regions of South America. Although all parts of  
 44 the digestive system may be affected, the alterations with  
 45 the greatest clinical expression correspond to the oesopha-  
 46 gus and colon. In endemic countries, megacolon is usually  
 47 the final manifestation, since onset of symptoms is slower  
 48 than in the case of oesophageal involvement.<sup>14</sup>

49 Spain is one of the countries that receive most immigrants  
 50 from Latin America. In 2001, Spain registered 49% of total  
 51 immigration from Latin American within Europe, followed by  
 52 Italy (13%), England (12%) and Germany (10%).<sup>15</sup> Immigration  
 53 from Ecuador was most significant in Spain, while in England  
 54 56% of the immigrants came from Jamaica, a non Chagas

(footnote continued)

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61 endemic area. These discrepancies can explain the differ-  
 62 ences in the epidemiology of Chagas disease in different  
 63 European countries, and they have already published data  
 64 on different aspects of the illness.<sup>16–18</sup> At present, Spain has  
 65 more than 2 million Latin American immigrants from  
 66 endemic areas.<sup>19</sup>

67 Chagas disease is an emergent disease in Spain,<sup>5</sup> and  
 68 poses different challenges for the Spanish healthcare  
 69 system.<sup>20</sup> One such challenge is adequate management  
 70 and treatment of the patients that develop complications of  
 71 the disease. In line with the consensus document on the  
 72 management of the cardiac complications of Chagas disease  
 73 auspiced by the Sociedad Española de Medicina Tropical y  
 74 Salud Internacional (SEMETS),<sup>21</sup> the present document  
 75 addresses the diagnosis, management and treatment of  
 76 the digestive manifestations of the disease in the Spanish  
 77 setting.

## 81 Pathogenesis of digestive involvement in Chagas 82 disease

83 The pathogenesis of the disease is subject to controversy,  
 84 though current knowledge points to the existence of mixed  
 85 mechanisms with direct participation by the parasite<sup>22,23</sup>  
 86 and associated autoimmune phenomena<sup>24,25</sup> involving mi-  
 87 crovascular alterations and autonomous denervation.<sup>26–29</sup>

88 Thus, the acute phase of Chagas disease is characterized  
 89 by direct parasite invasion of the muscle tissue of the  
 90 digestive system, with lymphocytic infiltrates (ganglionitis)  
 91 and degenerative neuronal lesions.<sup>30</sup>

92 However, the pathogenesis of the digestive involvement  
 93 has been most studied in the chronic form of the disease.  
 94 The fundamental damage that occurs as a result of  
 95 peristaltic dysfunction and that ultimately results in mega-  
 96 visceral presentations is the destruction of the neurons of  
 97 the enteric nervous system.<sup>31</sup> Neuronal damage is variable in  
 98 each case, and can affect all sections of the digestive tract.

99 A recent study in patients with megacolon suggests that  
 100 such neuronal destruction may be selective, fundamentally  
 101 affecting the nitric oxide (NO) and vasoactive intestinal  
 102 peptide (VIP) producing neurons that are involved in smooth  
 103 muscle relaxation.<sup>32</sup> In cases of megacolon and megaeso-  
 104 phagus, an important reduction in the number of interstitial  
 105 cells of Cajal has also been demonstrated.<sup>33,34</sup> These cells play  
 106 an important role in the modulation of digestive tube motility;  
 107 as a result, their destruction could constitute a key element in  
 108 the pathogenesis of the digestive changes of Chagas disease.

109 From the histological perspective, and in addition to  
 110 neuronal reduction, patients with Chagas disease and  
 111 megacolon present focal areas of fibrosis in the smooth  
 112 muscle and myenteric plexuses, together with lymphocytic  
 113 infiltrates at submucosal, myenteric plexus and smooth  
 114 muscle level. Probably as a compensating mechanism,  
 115 muscle wall hypertrophy is observed. Such hypertrophy  
 116 becomes less apparent in very advanced forms of the  
 117 disease.<sup>35</sup>

118 The ultimate outcome of the motor disorders, with  
 119 sphincter discoordination and increased intraluminal pres-  
 120 sure, is progressive dilatation and a reduction of organ  
 121 contractile capacity. In addition, the *muscularis mucosa* can  
 122 become hypertrophic, and there have been reports of

hyperplastic and dysplastic alterations of the oesophageal epithelium favouring an increase in the number of cases of carcinoma.<sup>36</sup>

Although the oesophagus and colon (particularly the rectum, sigmoid colon and descending colon) are the portions of the digestive tube with the most evident clinical manifestations, all gastrointestinal segments can be affected. At gastric level there have been reports of altered myoelectrical activity (gastric dysrhythmias), alterations in gastric emptying and distension, hypoperistalsis,<sup>37</sup> hypotonus, hypochlorhydria and eventually pyloric hypertrophy – though gastric dilatation is not frequent. Involvement of the small bowel has also been documented (Chagas enteropathy), manifesting either with or without dilatation.<sup>38</sup>

Involvement of the small intestine may favour the development of bacterial overgrowth, pseudo-obstructive syndromes and dyspeptic syndrome.<sup>35</sup> Patients with gastric or small intestine involvement normally also present oesophageal or colon involvement.<sup>35,38</sup>

### Diagnosis of chronic infection due to *T. cruzi*

The diagnosis of Chagas disease has already been addressed in the first consensus document<sup>5</sup> and in other reviews.<sup>39</sup> In addition to the considerations of the mentioned consensus document, and in the context of the study of the digestive manifestations of chronic Chagas disease, it is advisable to screen for *Trypanosoma cruzi* in all patients coming from Latin America and presenting with constipation, dysphagia or any of the digestive symptoms attributable to the disease. Mention will only be made here of the fact that the diagnosis is based on two criteria:

- Compatible epidemiological antecedents.
- Serological tests. In order to accept infection, the patient must yield two positive results with two serological techniques involving the use of different antigens. In the event of doubts or discrepancies between them, a third technique is indicated.

### Study of the digestive system in a patient with *T. cruzi* infection

#### Medical History

The aim is to detect symptoms indicative of probable digestive involvement. To this effect, attention should focus on the associated signs and symptoms reflected in Table 1. When compiling the medical history, a number of aspects must be taken into account:

1. Coexisting heart disease may be found in up to 30% of all patients.<sup>40</sup>
2. Patients may also present digestive disorders unrelated to Chagas disease.
3. There may be variations in the way in which the symptoms are described, due to the different cultural origins of the patients.

**Table 1** Chagas disease. Signs and symptoms of digestive involvement

– Symptoms associated with oesophageal alterations:	65
● Dysphagia: patient questioning should analyze the characteristics of dysphagia	67
○ Dysphagia in relation to solids / liquids.	69
○ Changes with heat / cold.	71
○ Location of dysphagia.	73
● Regurgitation: generally liquids with food remnants	75
○ Active, after ingestion, with contraction of abdominal muscles.	77
○ Passive, in advanced cases, generally in decubitus, with possible episodes of aspiration pneumonia.	79
● Retrosternal chest pain: improves with fluid ingestion.	81
● Odynophagia.	83
● Nocturnal cough.	85
● Sialorrhoea.	87
● Parotid gland hypertrophy.	89
– Symptoms associated with gastric / duodenal alterations:	91
● Dyspepsia.	93
● Pyrosis.	95
● Bloating	97
● Satiety sensation.	99
● Epigastric pain, not always present, predominantly in the immediate postprandial period.	101
– Symptoms associated with colon alterations:	103
● Constipation.	105
● Diarrhoea: number of movements/day.	107
● Changes in bowel habit.	109
● Straining at stool.	111
● Incomplete evacuation sensation.	113

4. Anxiety associated with the immigration process may be related to some symptoms or may condition them.
5. Patients should be questioned about their current dietary habits. Immigration causes many Latin American immigrants to change their diets in comparison with what they were used to eating in their home countries. There are basically two reasons for this: economic and market-related (i.e., certain foods typically found in Latin American countries are difficult to find in Spain). These changes in diet can in turn induce changes in bowel habit, and may modify the symptoms related with Chagas disease.<sup>41</sup>
6. Drug treatment. It is important to know whether the patient is taking certain drugs that can intensify or lessen the digestive symptoms (e.g., codeine, laxatives, psychoactive drugs, etc.).<sup>42</sup>
7. As in all clinical histories, it is important to establish previous illness, as this will help us to correlate the symptoms to other disorders. The geographical origin of the patient must be established, in view of the different incidences of the digestive manifestations according to

the place of origin.

8. Nutritional evaluation (Table 2) in patients with Chagas disease is of great importance for a number of reasons. Firstly, and given the possible existence of cardiovascular involvement, the early diagnosis and management of vascular risk factors is particularly relevant. On the other hand, altered nutritional status is a marker of potential digestive involvement.

### Physical examination

A complete physical examination (including body weight and body mass index (BMI)) is required.

Salivary gland hypertrophy and sialorrhoea may be present as manifestations of oesophageal disorders.

The abdominal exploration should be thorough, including the evaluation of tympanism and abdominal distension and/or asymmetry. In advanced phases it is possible to detect enlarged organs, with palpation of some distended portion of the colon.

### Complementary tests

#### Electrocardiogram (ECG)

All patients diagnosed with Chagas disease should undergo an ECG study even if no cardiological symptoms have been reported. The ECG tracing may help identify early cardiological alterations or may suggest that certain patient symptoms are of coronary – not digestive – origin.<sup>43</sup>

A 12-lead ECG tracing is to be obtained, including at least a 30-second lead DII recording.

#### Radiological study

All patients diagnosed with Chagas disease should undergo a posteroanterior and lateral projection chest X-ray study, in order to detect cardiomegalia (despite the low sensitivity in diagnosing Chagas cardiopathy) and mediastinal alterations secondary to megaoesophagus.

All subjects with upper and/or lower digestive tract symptoms should undergo an oesophagogram and barium enema (Annex A). Any of the organs that comprise the digestive system may be affected; consequently, radiological alterations may be evidenced at any level.<sup>14</sup> The complete radiological study (colon and oesophagus) may be carried out on the same visit – in which case the first step should involve a barium enema.

Given the existence of digestive tract alterations in up to 11% of all asymptomatic patients,<sup>14</sup> radiological evaluation is recommended in all patients with *T. cruzi* infection.

#### Diagnosis of *Helicobacter pylori* infection

Although the relationship between non-ulcerative dyspepsia and *H. pylori* infection is the subject of controversy,<sup>44–46</sup> all the national<sup>47</sup> and international consensus documents<sup>48</sup> consider the “test and treat” strategy to be indicated from the cost-effectiveness perspective in adult patients with non-investigated dyspepsia under 45–50 years of age without clinical alarm signs or symptoms. Since the prevalence of *H. pylori* infection in this population is moderate to high,<sup>49–53</sup> we recommend the evaluation of such infection in all patients presenting dyspepsia, pyrosis, or signs of postprandial abdominal distension. It is advisable to confirm *H. pylori* eradication at least four weeks after the end of treatment.<sup>54</sup>

There are different techniques for diagnosing *Helicobacter pylori* infection; of the existing options, we recommend the breath test with <sup>13</sup>C-urea, since it is noninvasive and offers high sensitivity and specificity,<sup>55,56</sup> provided the technique is available.

#### Study of parasites in stools

The digestive symptoms attributable to Chagas disease can also be caused by other intestinal parasitoses, with a high prevalence among patients from Latin America. Serial evaluations of parasites in stools are advised, based on three samples on alternate days, and including a fresh sample analysis.

**Table 2** Evaluation of nutritional condition based on anthropometric parameters and plasma protein measurements

A. (BMI) Body Mass Index: weight (kg)/height <sup>2</sup> (m)				
BMI (kg/m <sup>2</sup> )	Nutritional condition			
< 19.9	Malnutrition			
20–25	Normal			
25–29.9	Overweight			
30–34.9	Grade I obesity			
35–39.9	Grade II obesity			
> 40	Grade III obesity			
B. Determination of plasma proteins				
	Normal	Mild depletion	Moderate depletion	Severe depletion
Albumin (g/dl)	3.5–4.5	2.8–3.5	2.1–2.7	< 2.1
Transferrin (mg/dl)	250–350	150–250	100–150	< 100
Prealbumin (mg/dl)	18–28	15–18	10–15	< 10

## Oesophageal manometry

Chagas oesophageal disease is manometrically characterized by changes in oesophageal body peristalsis and lower oesophageal sphincter (LES) relaxation. These alterations are variable, and range from nonspecific motor disturbances to diffuse oesophageal spasms and even manifestations analogous to those of idiopathic achalasia.

We recommend manometry for all those patients who, even in the presence of a normal oesophagogram, present oesophageal symptoms and in whom there are diagnostic doubts that condition the perceived quality of life.

In the case of non-advanced disease (0–II), variants of normal behaviour can be observed, such as partial LES relaxation and intermittent and/or segmental aperistalsis. In the case of severe disease (III–IV), complete aperistalsis with low oesophageal body pressure values are observed.<sup>57</sup>

In addition, manometry may be useful for evaluating the response to different treatments.

## Endoscopy

Endoscopy is indicated in selected cases of chronic Chagas disease:

- In the presence of megaesophagus, to assess the condition of the oesophageal mucosa.
- When underlying oesophageal/colon disease is suspected due to the existence of other signs or symptoms reported by the patient or established from the family history, with the criteria applied to the general population (Table 3).

- Removal of an impacted foreign body, particularly in megaesophagus stages III–IV.
- Fitting of a nasogastric feeding tube, in cases of advanced oesophageal disease.

## Management of the patient infected with *T. cruzi* and with suspected digestive involvement

It is estimated that each year between 2–5% of all patients with the indeterminate form of Chagas disease evolve towards chronic cardiac or digestive forms of the illness<sup>10</sup>.

### Asymptomatic patient

Although the patient shows no digestive symptoms, a guided medical history will be carried out on each of the yearly visits. Body weight will be taken and nutritional condition evaluated.

### Symptomatic patient

#### With normal complementary test findings

Once all the test results have been obtained and are found to be within normal limits, the following is recommended even if the patient continues to present symptoms:

1. Evaluation of some other possible underlying diseases (anxiety, digestive disorders of some other aetiology, etc.).
2. Start symptomatic treatment.

**Table 3** Indications of upper digestive tract endoscopy (modified from the clinical guidelines of the Asociación Española de Gastroenterología)

Organ	Indications
Oesophagus	<ul style="list-style-type: none"> <li>● Study of gastrooesophageal reflux</li> <li>● Portal hypertension</li> <li>● Achalasia</li> <li>● Suspected neoplasm</li> <li>● Oesophageal dilatations</li> <li>● Extraction of foreign bodies</li> <li>● Peptic acid disease</li> </ul>
	<ul style="list-style-type: none"> <li>● Hiatal hernia</li> <li>● Oesophageal stenosis (dysphagia or odynophagia)</li> <li>● Barrett oesophagus</li> <li>● Toxic substances ingestion (acid or alkaline)</li> <li>● Varicose vein sclerotherapy</li> <li>● Polypectomy</li> <li>● Study of retrosternal pain</li> </ul>
	<ul style="list-style-type: none"> <li>● Dyspepsia unresponsive to clinical management in patients over 45 years of age</li> <li>● Atrophic gastritis</li> <li>● Persistent nausea and vomiting</li> </ul>
Stomach	<ul style="list-style-type: none"> <li>● Suspected neoplasm</li> <li>● Control of digestive bleeding</li> <li>● Polypectomy</li> <li>● Percutaneous gastrostomy</li> </ul>
Duodenum	<ul style="list-style-type: none"> <li>● Polypectomy</li> <li>● Malabsorption syndrome (biopsies)</li> <li>● Control of bleeding lesion</li> </ul>
	<ul style="list-style-type: none"> <li>● Duodenal ulcer and duodenitis</li> </ul>

### With altered complementary test findings

*Megaesophagus.* The management of megaesophagus depends on the degree of oesophageal disease (Table 4), the nutritional condition of the patient and the existing comorbidities. Clinical or surgical options are available, as well as tube and/or balloon dilatation measures.

There are no specific treatments capable of restoring oesophageal function, though partial recovery of oesophageal peristalsis can be observed following clinical, endoscopic or surgical management. The therapeutic measures are the same as those applied in cases of idiopathic achalasia, and are basically destined to reduce lower oesophageal sphincter (LES) pressure (cardia). The management option should be based on the general patient characteristics, the symptoms, and the degree of radiological and manometric involvement.

Nitrates (isosorbide dinitrate, 2.5-5 mg po, 5 minutes before meals) and nifedipine (10<sup>o</sup> mg po 45 min before meals),<sup>58</sup> induce LES relaxation and can be used in some cases. However, these measures are not always effective, undesirable effects are frequent, and their action tends to subside over time (tachyphylaxis); such drugs are therefore only recommended as temporary treatment whilst waiting for definitive management.

The two most widely used treatment options are pneumatic balloon dilatation (presently performed via endoscopy),<sup>59</sup> and laparoscopic myotomy (Heller technique). In advanced cases, or in the presence of relapse, the Serradoria surgical technique or oesophagectomy is performed. Cardiomyectomy with Pinotti funduplicature may be used as a surgical alternative.<sup>60,61</sup>

Although all of these procedures have advantages and inconveniences, their overall efficacy is similar. It is therefore advisable to use the technique with which the centre has most experience.

Endoscopic botulin toxin injection in the sphincter region is able to reduce the symptoms in patients with idiopathic achalasia and Chagas megaesophagus. The main inconvenience of this treatment is the limited duration of the effect obtained (months). As a result, it would be indicated in patients with oesophageal involvement and a high surgical risk or serious concomitant diseases.

*Megacolon.* The management of megacolon basically depends on the degree of constipation (defined according to the Rome III criteria), the degree of colon dilatation/

lengthening, the nutritional condition of the patient and the existing comorbidities. Clinical (symptomatic) or surgical treatment options are available. It is important to mention that patients with megacolon can present without constipation, and that the first manifestation of the disease may be a complication (e.g., volvulus).

The literature offers no established classification of the degrees of colon involvement. A sigmoid colon or descending colon diameter of over 6.5 cm is considered pathological from the radiological perspective, and defines megacolon. However, a range of colonic changes have been described in patients with Chagas disease and constipation (Table 5).

The literature likewise offers no consensus regarding the surgical management of choice for Chagas megacolon. At present, some specialized centres advocate technical variants of the classical procedure of Duhamel-Haddad<sup>62</sup> (rectosigmoidectomy with retrocecal interpositioning) or rectosigmoidectomy with end-to-side low colorectal anastomosis. Recently a new procedure has been described consisting of rectosigmoidectomy with ileal loop interpositioning.<sup>63</sup> To date, this technique has been used via the laparoscopic approach in a single published experience in Spain<sup>12</sup>.

Treatment and management of colon involvement according to the degree of involvement.

Groups 0-1

- Initial hygiene – dietary measures for all patients.
  - Abundant fluid intake: at least two litres of water a day.
  - Limitation of astringent foods, and provision of a fibre-rich diet.

**Table 5** Classification by groups of patients with chagasic colon disease

<b>Group 0:</b> No alterations in barium enema	99
<b>Group 1:</b> Patients with dolichocolon	101
<b>Group 2:</b> Dolichomegacolon:	103
● Descending colon > 6.5 cm in diameter	105
● Ascending colon > 8 cm in diameter	107
● Caecum > 12 cm in diameter	109

**Table 4** Classification of chagasic oesophageal disease<sup>72</sup>

<b>Group 0:</b> Asymptomatic cases without radiological alterations, showing some degree of denervation as established by pharmacological methods. Air in gastric fundus.	113
<b>Group I:</b> Oesophagus with apparently normal calibre in radiological study. Slow transit, with minor retention on X-rays one minute after ingestion of contrast. The contrast medium forms a small residual column, levelled at the upper extremity and perpendicular to the walls of the oesophagus. Air in gastric fundus.	115
<b>Group II:</b> Oesophagus with small-moderate increase in calibre. Appreciable contrast retention. Presence of residual column of variable height. Frequent presence of tertiary waves, with or without lower oesophageal hypotonus. Absence of air in gastric fundus.	119
<b>Group III:</b> Oesophagus with large increase in diameter. Reduced motor activity. Lower oesophageal hypotonus. Important contrast retention. Absence of air in gastric fundus.	121
<b>Group IV:</b> Dolichomegaoesophagus. Oesophagus with great retention capacity, atonic, elongated. Absence of air in gastric fundus	123

- Definition of times for bowel movement, taking care not to delay defecation in case of need.
- Increased gentle daily physical exercise: favour walking and minimize sedentary lifestyle.
- Clinical treatment: in patients with constipation who do not respond to hygiene – dietary measures.
  - Laxatives, particularly osmotic agents: mineral oil, milk of magnesia, lactulose, macrogol.
    - Attempts should be made to minimize their use.
  - Cleansing enemas if the mentioned laxatives prove ineffective. The use of glycerine is suggested.

#### Group 2

- Hygiene – dietary measures and clinical treatment with the same indications as in patients belonging to groups 0-1.
- Surgery: in patients of this group presenting symptoms refractory to the above management measures, in the absence of surgical contraindications.
  - Sigmoidectomy and low colorectal anastomosis.
  - Rectosigmoidectomy with ileal loop interpositioning.
  - Rectosigmoidectomy with retrorectal colon descent (Duhamel-Haddad surgery).<sup>63</sup>

Annex B addresses management of the complications of megacolon.

*Chagas enteropathy.* In megaduodenum, surgery is only indicated if the patient shows unequivocal evidence of duodenal stasis. The most common procedure is duodenojejunal anastomosis close to the duodenojejunal flexure.<sup>64</sup> In cases of megajejunum or megaileum, partial enterectomy is only indicated if the affected sections are not very extensive.<sup>65</sup> In situations of extensive involvement, clinical management is indicated with continuous gastric aspiration, correction of dehydration and electrolyte imbalances, and the provision of parenteral nutrition.

The diagnostic technique of choice for establishing bacteriological overgrowth is the exhaled hydrogen test following the administration of glucose.<sup>66</sup> If testing proves positive, non-absorbable antibiotic use (rifaximin) for two weeks is recommended.

*H. pylori infection.* If the breath test proves positive, eradicating treatment is indicated, with control testing starting four weeks after the end of treatment<sup>47,48</sup>.

If the symptoms persist despite efficacy of the mentioned treatment, symptomatic management with proton pump inhibitors is indicated, together with fibrogastroscopy to discard underlying pathology.

*Parasites in stools.* Specific treatment should be provided, depending on the diagnosed parasite, in accordance with the national and international guidelines.<sup>67,68</sup>

### Etiological treatment of patients with chronic Chagas disease

At present, two drugs have been approved for the treatment of Chagas disease. The dose of benznidazole (5 mg/kg/day) and nifurtimox (10 mg/kg/day), and the recommended treatment duration (60 days) have experienced no changes

since publication of the first consensus document in Spain. Benznidazole is recommended as first choice treatment, since it offers a lesser incidence of side effects.<sup>69</sup>

The healing rate in the chronic phase of Chagas disease is estimated to be 8–25% (in observations of up to 8 years after the end of treatment),<sup>70</sup> though recent studies in patients in the chronic indeterminate phase (group 0 of the Kuschnir classification, 64% of the included patients) or with Chagas myocardiopathy and no signs of heart failure (groups I and II of the classification of Kuschnir) report reduction in disease progression and even regression to earlier stages of heart disease after treatment with benznidazole.<sup>71</sup> No similar studies in patients with digestive involvement are available.

According to the consensus documents of 2005<sup>5</sup> and 2007<sup>21</sup>, specific treatment of patients with *T. cruzi* infection is recommended. Treatment is also advised in subjects with early onset digestive disease, establishing patient–physician agreement with due information on the potential appearance of side effects and on the effectiveness of therapy as established by previous experience.

### Final considerations

Chagas disease is to be suspected in all patients with a compatible epidemiological history and symptoms suggestive of digestive involvement. The low specificity of the digestive symptoms and the scant knowledge of the latter in the Spanish setting make it necessary to increase awareness of the diagnostic and management protocols for these patients, with a view to improving knowledge of the disease among the healthcare professionals in charge of detecting and managing the illness.

Most patients with digestive involvement can be diagnosed and treated in non-specialized centres, though in situations of first line treatment failure, diagnostic uncertainties, or the need for complex complementary techniques, referral is advised to a specialist in gastrointestinal diseases and to a centre specialized in imported diseases.

In any case, patient referral does not imply obviation on the part of the primary care physician (i.e., the professional who initially sees the patient) of the need to compile a good medical history, conduct a clinical exploration with correct cardiological and digestive evaluation, and obtain a conventional ECG tracing and chest X-ray study before referring the patient.

### Conflict of interest

All the authors declare that there are no conflicts of interest.

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## Annex A. Rezende and Ximenes techniques for barium contrast radiological study in patients with suspected chagasic digestive disease

### Oesophagogram (Rezende technique<sup>73</sup>)

- In evolved cases, prior tube cleansing of the oesophagus is indicated to remove food remains.
- Patient in the standing position, in right anterior oblique projection.
- Administer contrast until a column of sufficient height is obtained to ensure passage to the stomach, allowing visualization of the shape of the oesophagus, its diameter, wall contours and kinetic activity.
- X-rays of this area are to be obtained at the time of contrast administration and after 60 seconds.

### Barium enema (Ximenes technique<sup>73</sup>)

- The study is to be made without prior preparation.
  - Initial plain abdominal X-rays.
  - Introduction of 300 ml of barium contrast diluted in 1,200 ml of water to form 1,500 ml of suspension.
  - The patient is to remain in the right lateral position for 5 minutes.
  - Three radiological projections are indicated after contrast administration: dorsal decubitus, ventral decubitus and lateral. The focus-film distance should be one meter.

## Annex B. Management of the complications of megacolon

### a) Fecaloma

- Proctolysis with liquid vaseline through a rectal tube: 300 ml in slow drip, followed by saline cleansing enemas.
- Manual removal.

### b) Sigmoid volvulus

- Endoscopic reduction.
- Surgery, if endoscopic resolution is not possible.

### c) Perforation

- Early surgical intervention.

## CUADRO A. Técnicas de Rezende y Ximenes para la realización de estudio radiológico baritado en pacientes con sospecha de afectación digestiva chagásica

### Esofagograma ( Técnica de Rezende<sup>73</sup>)

- En casos evolucionados, se debe realizar lavado previo de esófago con sonda para la retirada de residuos alimentarios.
- Paciente en bipedestación, en posición oblicua anterior derecha.
- Introducir contraste hasta que exista una columna con altura suficiente para producir el paso a estómago, de forma que permita observar la forma del esófago, diámetro, contorno de las paredes y la actividad cinética del mismo.
- Se realizarán radiografías de esta zona en el momento de la toma del contraste y a los 60 segundos de la ingestión del mismo

### Enema opaco (Técnica de Ximenes<sup>75</sup>)

- El estudio se ha de realizar sin preparación previa.
- Radiografía simple de abdomen inicial
- Introducción de 300 ml de bario diluidos en 1200 ml de agua formando 1500 ml de suspensión
- Mantener al paciente durante 5 minutos en posición lateral derecha.
- Realización de tres proyecciones radiológicas tras la inserción de contraste: decúbito dorsal, decúbito ventral y lateral. La distancia foco-film ha de ser de 1 metro

## CUADRO B. Manejo de las complicaciones del megacolon

### a) Fecaloma

- Proctolisis con vaselina líquida a través de sonda rectal: 300 cc a goteo lento seguido de enemas de limpieza con solución salina.
- Extracción manual.

### b) Vólvulo de sigma

- Reducción endoscópica
- Tratamiento quirúrgico, si no es posible resolución endoscópica.

### c) Perforación

- Tratamiento quirúrgico precoz.

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