

# Clinical Examinations of the Rectoanal Inhibitory Reflex Correlated with Anography Findings, Histopathological Findings, and Clinical Outcomes

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## Abstract

The diagnostic method for Hirschsprung's disease (HD) involves rectal biopsy to determine the presence of histopathological findings for aganglionosis. Contrast enema (CE) and anorectal manometry help to support the indication for biopsies. Patients with HD lack a rectoanal inhibitory reflex (RAIR) that can be studied using manometry, ultrasound, or a modified contrast enema (CE), which provokes the RAIR with an injection of cold fluid. A question that arises is whether the RAIR also could be visualized with only a specific clinical examination.

**Objective:** The purpose of the study was to test the hypothesis that the RAIR could be seen with a cold fluid injection into the rectum to identify children without HD and thus to avoid additional investigations involving a CE or rectal biopsy.

**Materials and method:** In a prospective study all children who were suspected to have HD and who had clinical symptoms were examined using modified CEs. In children in whom the RAIR was found with a modified CE but who still had constipation, further examinations including biopsy were necessary. These children were examined under general anesthesia. Cold water was injected in the rectum to induce and register the RAIR, and a rectal biopsy was conducted. The results were correlated with the modified CE results, histopathological findings from the rectal biopsy, and clinical follow-up outcomes.

**Results:** The clinical cold fluid examination was not comparable with the modified CE for demonstrating a RAIR in children without HD ( $p < 0.001$ ) and did not correlate with the rectal biopsy ( $p < 0.001$ ). Thus, the proportion of unnecessary x-ray examinations, as well as the number of rectal biopsies, could not be reduced with a clinical examination using cold water only.

**Conclusion:** The findings demonstrated that an examination using cold water was not a reliable method for evoking the RAIR.

**Keywords:** Hirschsprung's disease; Aganglionosis; Diagnostic; Rectoanal inhibitory reflex (RAIR); Radiology; Modified contrast enema; Clinical examination; Neonatal surgery

## Introduction

Hirschsprung's disease (HD) is a clinicopathological entity caused by a developmental disorder of the enteric nervous system. HD occurs in 1 out of 5000 live births, and 80–90% of cases are diagnosed during the neonatal period [1,2]. The important diagnostic features of HD include the combination of aganglionosis with hypertrophic nerve trunks along a variable portion of the distal intestine [3-5]. This leads to the pathognomonic absence of the rectoanal inhibitory reflex (RAIR) [6]. The lack of peristaltic wave progression in the aganglionic segment of the involved intestine, as well as the absence of or abnormal internal anal sphincter relaxation is a hallmark of HD [7].

Traditional contrast enema (CE) has a place in the diagnosis of HD but is not essential for confirming the diagnosis. CE can usually detect or indicate the transition zone, which can be used to decide whether a transanal, trans-abdominal laparoscopic, or an open surgical approach should be used [8].

Anorectal manometry was used earlier in combination with rectal biopsy and CE and was the preferred method for evaluating patients with suspected HD [2,9]. Manometry is not necessary to diagnose HD but adds a diagnostic value to determine the RAIR, thus sometimes identifies children who do not have HD [8]. Manometry has been used to measure the intra-anal pressure during provocation, thus demonstrating the presence or absence of the RAIR [10].

Ultrasonography has also been reported as a method to visualize the RAIR in children with suspected HD [11]. Newer methods include a modified cold CE in which a radiographic investigation simultaneously

as the CE is given can reveal the RAIR as well as visualize the contracted bowel segment, and the transition zone [12].

The diagnosis is then finally verified histopathologically using a rectal biopsy taken 1–3 cm above the dentate line [13], revealing the combination of aganglionosis and hypertrophic nerve trunks in patients with HD. In our pediatric surgical and pediatric radiology departments, the unanesthetized children who had both an ultrasound probe placed in the perineum, along with a rectal tube, were difficult to place in a dorsal lithotomy position, so this examination was not clinically relevant.

The detection of the RAIR with manometry can be uncertain, as even small involuntary catheter movements could cause a false recording of a decrease in intra-anal pressure. Therefore, at our pediatric surgery center, manometry was performed under general anesthesia in conjunction with a rectal biopsy. However, anorectal manometry has now been replaced by a radiological method for visualizing the RAIR using a modified CE [11,12]. With a modified CE, a cold contrast agent

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is injected into the rectum that provokes the RAIR. The movement of rectal contents into and out of the anal canal can be simultaneously observed. At the same time, the dilatation of the internal anal sphincter (IAS) can be measured using real-time sonograms and a modified CE.

It is tempting to consider that the RAIR could be visualized during a child's clinical examination using a modified CE [12]. The aim of this study was to evaluate the application of clinical cold fluid examination using only saline to observe the existence of the RAIR.

## Materials and Methods

**Study population:** In a prospective study, we investigated children with severe constipation and a tentative HD diagnosis. All the children were initially examined using a modified CE examination [12]. If this was either inconclusive or HD was not suspected, the children were included in this study.

Following the clinical routines of our center, the children then underwent a rectal biopsy under general anesthesia with Propofol®, Sevoflurane®, and nitrous oxide®. The children received ventilation using a laryngeal mask airway (Unique; Laryngeal Mask Company, Ltd, Mahe, Seychelles).

During the examination, the children were placed in a dorsal lithotomy position with their knees flexed to 90°. Under general anesthesia, the children were examined to attempt to provoke a RAIR. A thin catheter was advanced into the central part of the rectal ampulla. Two sequential, quick (< 5 s) 20-mL injections of cold saline (16°C) were administered into the rectum and the perineum was observed for a RAIR or any reaction in the perineum. Within 24 h of the examination, none of the included children had been administered an enema or undergone a digital rectal examination or disimpaction. No patients were excluded from this study. Finally, we conducted a clinical follow-up of the children.

## Statistical Consideration

The sample size was calculated for 2 samples using percentage values [14].

An alpha error level or confidence level of 5% was used, corresponding to a 95% confidence interval. This means the probability of incorrectly rejecting the null hypothesis that there is no difference in the percentage values.

A beta error level or statistical power of 50% was used. This means the probability of incorrectly failing to reject the null hypothesis that there is no difference in the percentage values or assuming no difference when a real difference exists.

The percentage of 99% was used in the group excluded from the aganglionic diagnosis if a modified CE was used and a histopathological finding from a rectal biopsy was determined.

The percentage of 70% was expected from the study group. The calculation provided a sample size of 8 for both samples.

While conducting the study, the statistics were calculated after every sample was collected to minimize the number of included children. Fisher's 2-tailed exact test was used to evaluate the null hypothesis. All statistical analyses were performed following the advice of a statistician. SPSS Statistics was used for the statistical calculations. A p-value of <0.05 was considered statistically significant.

## Ethical Considerations

Intention to treat was the main analytical strategy and utilized

	Radiologic examination	Clinical examination	P value*
RAIR +	9	0	
RAIR -	0	9	< 0,001

\* Fisher Exact Probability Test: 2-tailed

**Table 1:** Radiological examination findings, using a modified contrast enema, as compared with clinical examination findings, in an attempt to disclose the rectoanal inhibitory reflex (RAIR). All the rectal biopsies showed normal anatomical findings without aganglionosis or hypertrophic nerve trunks. A clinical follow-up with a median duration of 27 months (range, 3-70 months) verified that all the examined children had constipation that was treatable with laxatives and diet, and HD was no longer suspected.

for all patients. The regional research ethics committee approved this study (registration number, 2010/49). The data were anonymized prior to performing the calculations and are presented in such a way that it is impossible to identify any single patient; therefore, it was not necessary to obtain approval from the individual patient's guardians. All evaluations, treatments, and procedures described in this report were standard of care and were conducted at a tertiary center for pediatric surgery. No protocols were exercised that would have required appropriate informed consent or approval of an institutional review board.

## Results

Nine children were included, 5 girls and 4 boys (median age, 2 months; range, 4 days–2. 6 years); 6 were younger than 1 year of age, and 1 was between 1 and 2 years of age.

A cold fluid, saline, was administered rectally during a clinical examination under general anesthesia but did not provoke a RAIR. Thus, the described clinical examination did not provoke a RAIR in any child.

For all the children included, the modified CE had previously revealed a RAIR, but this could not be re-established using only cold water ( $p < 0.001$ ) (Table 1).

All rectal biopsies revealed normal anatomical findings without aganglionosis or hypertrophic nerve trunks. Those findings correlated with the modified CE ( $p = 1$ ) but did not correlate with the cold water examination, as no RAIR could be detected ( $p < 0.001$ ).

During a median duration of 27 months (range, 3-70 months), the clinical follow-up verified that all the examined children had constipation that was amendable to treatment with only laxatives and diet, and none were suspected to have HD.

## Discussion

This attempt to simplify the investigation for a RAIR in children was unsuccessful. The results showed that a RAIR could not be evoked with cold saline under general anesthesia. We are not aware of any similar study reported in medical literature.

The RAIR was expected because all the children had normal RAIRs previously documented using modified CE and had rectal biopsies without pathology. However, the clinical examination with cold saline could not provoke the RAIR in any child. Therefore, it was not comparable to the modified CE or rectal biopsy. Furthermore, a clinical follow-up would disclose if the child's constipation could be successfully treated using only a laxative, thus excluding HD. In other words, the proportion of unnecessary x-ray examinations, as well as the number of rectal biopsies, could not be markedly reduced using a clinical examination only.

In this study, a clinical examination was performed on children under general anesthesia prior to a rectal biopsy. General anesthesia was considered necessary for obtaining the biopsy samples. Furthermore, it was advantageous for the clinical examination because it eliminated disturbances and any measurement artifacts caused by a child's voluntary movements. Experiences from examinations of adults indicated that a sonography examination for the RAIR was well tolerated, without any adverse effects without anesthesia [15]. Previous experience [11] showed that the visualization of the RAIR with sonography for children suspected of having HD was possible and not hampered by general anesthetic drugs. However, the RAIR has been visualized using a modified contrast X-ray in children who were awake [12].

It remains to be demonstrated whether a RAIR could be provoked with only cold saline in children without general anesthesia. This would also be beneficial, as it would eliminate the risk of general anesthesia.

In summary, the results of this pilot study on children with constipation indicated that a clinical examination for the RAIR was not comparable to a modified CE or the histopathological findings from a rectal biopsy. The proportion of unnecessary x-ray examinations, as well as the number of rectal biopsies, could not be reduced using a clinical examination alone. Thus, the hypothesis that the RAIR could be clinically visualized with only cold water under general anesthesia was rejected.

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