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## Chapter 5

### Maturation of the rectoanal inhibitory reflex in very premature infants

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# **Abstract**

## **Background**

Anorectal manometry using a micro-manometric sleeve assembly offers a noninvasive diagnostic test for identifying anorectal motor dysfunction in the neonate. We have previously shown that preterm infants with a postmenstrual age (PMA) > 30 weeks, and term infants exhibit a normal anal sphincter function.

## **Aim**

To characterize anal sphincter function in very premature infants  $\leq 30$  weeks PMA and to evaluate the time of maturation of the rectoanal inhibitory reflex (RAIR) using a sleeve catheter.

## **Methods**

Anorectal manometry was performed in 16 healthy neonates (9 female) with a mean PMA of 29 weeks (27-30 weeks) and a birth weight of 640 to 1590 g (median 1220 g) with a micromanometric assembly (od 2.0 mm). The assembly incorporated a 1.5-cm-long sleeve sensor for measurement of resting anal sphincter pressures and relaxation, and 4 side-holes recorded anal and rectal pressures. Rectal distension was performed with direct air insufflation to elicit the RAIR.

## **Results**

The mean anal sphincter pressure, rectal pressure, and anal sphincter oscillation frequency were  $24.5 \pm 11.4$  mmHg,  $6.5 \pm 4.8$  mmHg, and  $11.1 \pm 2.3$ /min, respectively. A normal RAIR could be elicited in 13 (81%) infants studied. In two infants the RAIR could not be elicited due to a low anal sphincter pressure of only 5 mmHg. In the other child, no RAIR was seen despite the repeated insufflation of at least 5 ml of air.

## **Conclusion**

The majority (81%) of premature infants older than 26 weeks' PMA have normal anorectal pressures and a normal RAIR.

## Introduction

Defecation problems in neonates are common. About 60% of infants less than 2500 g, and less than 37 weeks gestation, fail to pass meconium by 24 hours after birth<sup>1,2</sup>. Difficulties with bowel motility and delay in stooling commonly postpone the time of full enteral feeding in premature infants.

Anorectal manometry in the neonate offers a noninvasive diagnostic test for identifying anorectal motor dysfunction. Hirschsprung's disease can be diagnosed by anorectal manometry. Recently, sleeve manometry has been adapted and applied successfully to monitor the anorectal pressure profile in healthy preterm and term infants<sup>3</sup>. This study demonstrated that term and premature infants older than 30 weeks' postmenstrual age (PMA) have a normal anorectal pressure profile and rectoanal inhibitory reflex (RAIR) to rectal distension<sup>3</sup>. However, no studies have been performed in very premature infants using a sleeve catheter. Therefore, the aim of this study was to characterize anal sphincter function in very premature infants  $\leq 30$  weeks PMA and to evaluate the time of maturation of the rectoanal inhibitory reflex using a sleeve catheter.

## Methods

### Subjects

Studies were performed in 16 healthy preterm infants (nine girls, seven boys) ranging in PMA from 27-30 weeks (Table 1). Infant birth weight ranged from 640 to 1590 g (median, 1220 g), and weight at the time of study ranged from 690 to 1490 g (median, 1180 g). The time from birth to passage of the first stool ranged from 0 to 72 hours (median, 24 hours). Anorectal manometry was performed 3 to 23 days after birth (median, 7 days). No infants had any evidence of defecation problems, anorectal malformations, neurological dysfunction, or sepsis, and none were receiving prokinetic or oral/rectal laxative medication. Three infants were ventilated and two were receiving nasal continuous positive airway pressure at the time of measurement. The research Ethics Committee of the Emma Children's Hospital approved the study protocol, and written informed consent was obtained before each study.

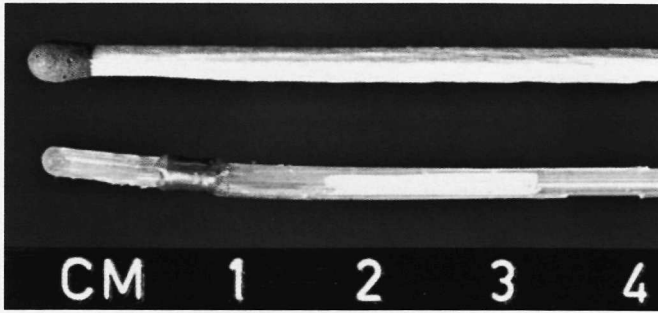
### Manometric Technique

Anorectal perfusion manometry was performed with a purpose-built silicone rubber micromanometric anorectal catheter (outer diameter, 2.0 mm). The design of the catheter was based on similar catheters used for measurement of anorectal motor function in children and adults but had a diameter smaller than a neonatal thermometer. The catheter incorporated a 1.5-cm-long sleeve sensor and an array of 3 side-holes spaced 0.5 cm apart for measurement of anal sphincter pressures and 1 side-hole located 0.5 cm proximal of the sleeve for measurement of basal pressure within the rectum (figure 1). All side-holes were perfused with sterile degassed water at a rate of 0.04 mL/min. An air channel was present on the tip of the catheter for air insufflation to distend the rectum.

**Table 1** Patient postmenstrual age (PMA) and parameters of anal sphincter function in 16 premature infants.

Parameters measured				Anorectal reflex	
PMA	Anal sphincter pressure (mmHg)	Baseline rectal pressure (mmHg)	Anal sphincter oscillation frequency (No./min)	No. of infants with normal RAIR	Threshold distention volume (mL)
29 (27-30)	24.5 ± 11.4	6.5 ± 4.8	11.1 ± 2.3	13 of 16	3.4 ± 1.6

*Results are expressed as mean ± 1SD*



**Figure 1** Photograph of anorectal manometry assembly incorporating 1.5-cm sleeve assembly.

Pressures were measured by pressure transducers situated in each perfusion line and connected to PC Polygraph HR preamplifiers (Synectics Medical, Stockholm, Sweden). The measured signals from the preamplifier were converted to digital values by an analog-digital converter and information was transmitted via a fiber optic cable to a personal computer. Before each measurement a calibration of the polygraph was performed.

### Protocol

Anorectal manometry was performed with the patient in the supine position. The catheter was positioned with the sleeve straddling the anal sphincter high-pressure zone and the air channel in the rectum. Bowel preparation or sedation was not necessary. With the catheter in position and after a 5-minute accommodation period, a baseline recording of anal sphincter pressure (ASP) and rectal pressure was made over a period of 2 to 3 minutes before an attempt was made to elicit the RAIR.

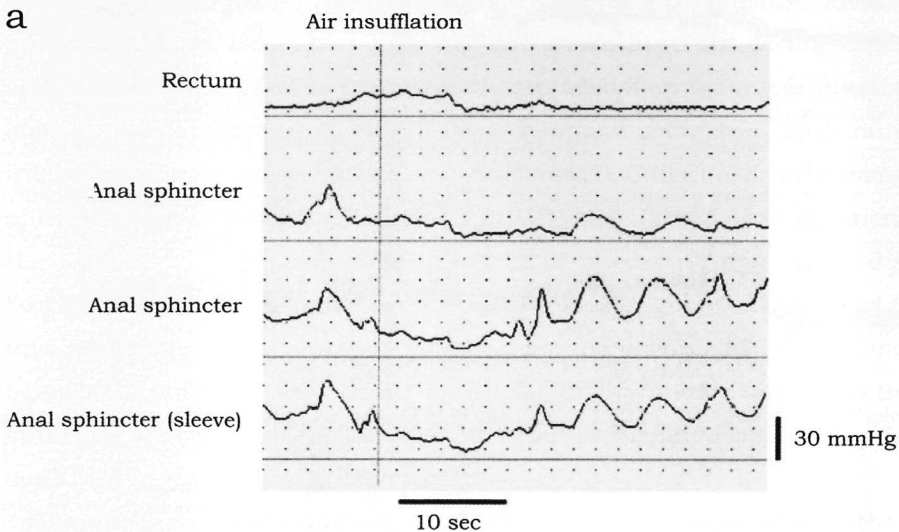
To elicit the RAIR, 1 to 5 mL of air was directly insufflated into the lumen of the rectum, this technique has previously been used by our group<sup>3</sup> in premature infants and has been found to be safe and effective. Balloon distension was not used in this study because it was considered inappropriate for these young infants. The initiation of the reflex was characterized by an anal sphincter pressure drop of at least 5 mmHg over a period of 2 to 5 seconds in association with cessation of rhythmic activity of the anal sphincter. The threshold air volume required to stimulate the RAIR was determined by increasing the volume of air injected in 1-mL increments in a stepwise fashion, to a maximum of 5 mL. Consecutive rectal distensions were performed at 1-minute intervals. When the threshold volume required to stimulate the reflex had been determined, 3 further distensions were performed. Recording sessions lasted an average of 30 minutes.

## Analysis of Manometric Records

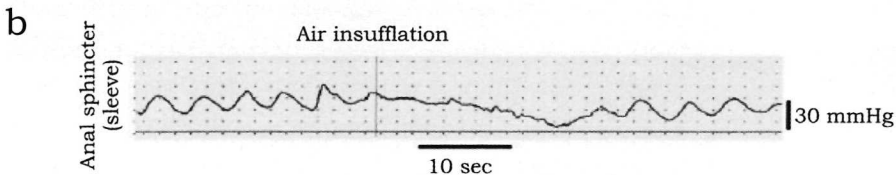
Baseline values for anorectal motor patterns were obtained by analysis of the manometric recording that immediately preceded attempts to elicit the RAIR. Mean resting anal sphincter pressure, anal sphincter oscillation frequency, and rectal pressure were measured during a period of at least 60 seconds. Anal sphincter pressure was defined by the nadir of the pressure oscillation wave. The anal sphincter oscillation frequency was demonstrated by measuring changes in anal canal pressure in basal unstimulated conditions and was defined as the number of oscillations in a period of 60 seconds. Group mean data are expressed as mean  $\pm$  SEM and were compared with analysis of variance statistics; inter-relationships between variables were established with Spearman rank correlation statistics. A  $P < 0.05$  was taken indicating statistical significance.

## Results

Anal sphincter tone was  $24.5 \pm 11.4$  mmHg (range, 5-46) and anal sphincter oscillations occurred at  $11.1 \pm 2.3$ /min (range 9-17; fig. 2). In 13 of the 16 infants (81%), a normal RAIR could be elicited at a threshold volume of  $3.4 \pm 1.6$  mL (range, 1-5). In two neonates (28 and 29 weeks' PMA) the RAIR could not be elicited due to a low anal sphincter pressure (5 mmHg), which made determination of the presence of the RAIR impossible using our criteria. In the other neonate (28 weeks PMA) who had a resting sphincter pressure of 46 mmHg, no RAIR was seen despite the repeated insufflation attempts to a maximum of 5 mL. The mean baseline rectal pressure before distension was 6.5 mmHg and during air insufflation the rectal pressure increased by 3.8 mmHg.

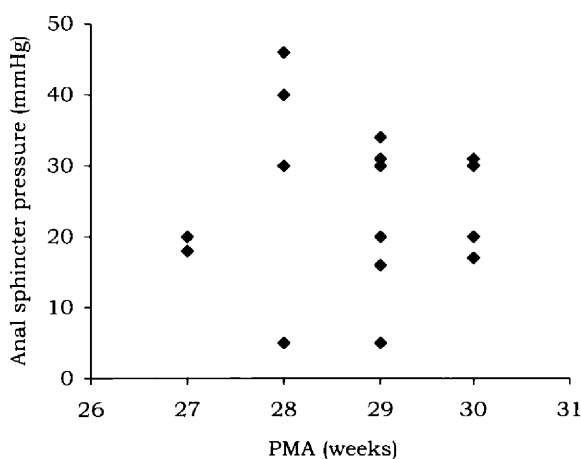


**Figure 2a** Anorectal pressure recordings showing elicitation of RAIR with air insufflation in premature infant 29 weeks' PMA.



**Figure 2b** Anorectal pressure recording showing anal sphincter oscillation frequency pattern interrupted by a RAIR in premature infant 29 weeks' PMA.

Anal sphincter pressure (ASP) was lower in very premature infants compared to older (premature) infants. However, no significant correlation was found between ASP and PMA (figure 3). In addition, neither rectal pressure nor rectal wave frequency showed any age correlation. Gestational age, postnatal age, and time delay from birth to passage of first stool did not correlate with any parameters of anorectal function. Ventilation or nasal CPAP did not influence either sphincter pressure ( 23.0 mmHg vs 25.2 mmHg, ns) or wave frequency (13.5/min vs 10.2/min, ns) compared to children who were not receiving this therapy.



**Figure 3** Scatter plot of the correlation between PMA and anal sphincter pressure.

## Discussion

In this study, we evaluated the anal sphincter function in healthy very premature infants  $\leq 30$  weeks' postmenstrual age (PMA) and the time of maturation of the rectoanal inhibitory reflex (RAIR) using a sleeve catheter. Our recordings showed normal anorectal pressures and a normal RAIR in most premature infants despite significant prematurity.

Earlier studies evaluating anorectal motor function in premature infants have produced inconsistent data<sup>4-6</sup>. These conflicting data may be the result of the use of side hole sensors for pressure measurement in the anal canal. Side hole sensors can be easily displaced from the anal sphincter high-pressure zone during air insufflation or with body movement<sup>7</sup>. As previously shown in premature and healthy infants, children and adults, displacement can be avoided by using a sleeve sensor, which allows for sphincter movement and pressure measurement over the length of the sleeve<sup>3</sup>.

Table 2 compares the findings of the current study with those of our previous study in older preterm infants of 31 to 38 weeks' PMA, using the same manometric technique. These data indicate that despite what appears to be normal anorectal function in the majority of infants, very premature infants in general have a lower resting anal sphincter pressure, are less likely to exhibit a normal anorectal inhibitory reflex and require greater rectal stimulus to elicit the RAIR. Hence, there does appear to be some evidence of anorectal functional immaturity in some very premature infants. Nevertheless, as all of the infants defecated normally, the level of immaturity does not appear to be of any pathological significance.

**Table 2** Parameters of anal sphincter function in premature infants; comparison with previously published data from older infants.

Parameter	Current Study (N = 16)	Benninga et al., 2001 <sup>3</sup> (N = 22)	
PMA (wk)	27-30	31-33	34-38
Distention stimulus	Air insufflation	Air insufflation	Balloon
Anal sphincter pressure (mmHg)	24.5 $\pm$ 11.4*	31.6 $\pm$ 13.0*	49.3 $\pm$ 10.9*
Anal sphincter oscillation frequency (n/min)	11.1 $\pm$ 2.3	10.3 $\pm$ 1.4	10.3 $\pm$ 1.8
Normal RAIR	81%	92%	100%
Threshold volume (mL)	3.4 $\pm$ 1.6	2.8 $\pm$ 1.8	2.1 $\pm$ 0.6

\*  $P < 0.001$ , one-way anova. Results are expressed as mean  $\pm$  1SD

In the current study, we could not demonstrate a RAIR in three infants. Two of them showed a low anal sphincter pressure of 5 mmHg and one child showed a normal anal sphincter pressure of 46 mmHg. In one child with a low anal sphincter pressure, we were able to perform a follow up manometry at 12 months of age, which confirmed normal anorectal function. In the other two infants, parents did not consent to a second anorectal manometry, however both had no clinical evidence of abnormal defecation patterns suggesting normal anorectal function. These follow-up observations suggest that absence of a normal RAIR was more likely due to delayed maturation of anorectal function, rather than any underlying motility disorder.

In contrast with a comparable study in older neonates, no correlation was found between resting anal sphincter pressure and PMA<sup>3</sup>. The reason for this is unclear.

An anorectal micromanometric sleeve catheter is suitable for use in evaluating anorectal pressures in very premature neonates down to 26 weeks' gestation. In these infants normal anorectal function is usually seen; however, the RAIR is less reliably elicited and requires a greater threshold stimulus than older preterm infants. This study indicates that a micromanometric anorectal sleeve assembly can detect a RAIR in very premature infants. We believe that manometry can be used to reliably assess anorectal function and possibly exclude Hirschsprung's disease, however, as in term infants; a rectal biopsy is needed to confirm the diagnosis of Hirschsprung's disease in infants who do not demonstrate the RAIR.

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