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# Contrast Enema for Neonatal Distal Bowel Obstruction: The Diagnostic and Pathological Yield

**Mark Fitzgerald[1,2,3*], Ajay Taranath[1], and Day Way Goh[1,4]**

[1]Women's & Children's Hospital, 72 King William Rd, Adelaide, 5000, South Australia, Australia

[2]Royal Darwin Hospital, 105 Rocklands Drive, Tiwi, 0810, Northern Territory, Australian

[3]Division of Surgery, Royal Darwin Hospital 105 Rocklands Drive, Tiwi, 0810, Northern Territory, Australian

[4]Discipline of Paediatrics, School of Medicine, University of Adelaide, Adelaide, South Australia, Australia

**[*]Corresponding author:**

Mark Fitzgerald,
Women's & Children's Hospital, 72 King William Rd, Adelaide, 5000, South Australia, Australia, Royal Darwin Hospital, 105 Rocklands Drive, Tiwi, 0810, Northern Territory, Australian and Division of Surgery, Royal Darwin Hospital 105 Rocklands Drive, Tiwi, 0810, Northern Territory, Australian

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Neonatal distal bowel obstruction; Contrast enema**;** Meconium ileus; Meconium plug syndrome; Hirschsprung's disease

**Abbreviations:**

CE: Contrast Enema; CF: Cystic Fibrosis; CMPI: Cow's Milk Protein Intolerance; DBO: Distal Bowel Obstruction; HD: Hirschsprung's Disease**;** MPS: Meconium Plug Syndrome**;** NEC: Necrotizing Enterocolitis

## 1. Abstract

### 1.1 Purpose

Neonatal distal bowel obstruction (DBO) can present a diagnostic challenge [1, 2] As different aetiologies have similar clinical manifestations with not all surgical intervention [2, 3]. Contrast enemas (CE) can help differentiate the aetiology avoiding the need for surgery [2-4]. We reviewed 20years of CE to evaluate their diagnostic and pathological yield in neonatal DBO.

### 1.2. Method

CE for DBO undertaken in neonate between 2001 and 2021 were reviewed with studies. Medical records for 98 patients (109 CE) were accessed to review the results, the definitive diagnosis, birth weight, gestation and age at time of CE.

### 1.3. Results

Meconium plug syndrome (MPS) (n=32) was the commonest radiological diagnosis followed by bowel atresia (n=20), Hirschsprung's disease (HD) (11) and meconium ileus (10). Of the CE 16% were normal, 14% were non diagnostic. One third of patients with a radiological diagnosis of MPS had a eventual definitive diagnosis that required surgical intervention, either HD, meconium ileus or SBO. The definitive diagnosis was most commonly MPS (n=29), followed by HD (21) and bowel atresia (16). There were no statistically significant differences in demographics among the definitive diagnoses.

### 1.4. Conclusion

CE in neonatal DBO has a high diagnostic and pathological yield aiding in determining which patients require surgery.

### 1.5. Level of Evidence

Level IV

### 1.6. Highlights

#### 1.6.1. What is Currently Known About This Topic?

Contrast enemas are commonly used to diagnose the aetiology of distal bowel obstruction in neonates. They can additionally be therapeutic in some conditions like meconium plug syndrome and meconium ileus. It has long been recognised that a proportion of patients with meconium plug syndrome will subsequently be diagnosed with Hirschsprung's disease.

### 1.6.2. What New Information Is Contained in This Article?

This article highlights that contrast enemas are useful in detecting Hirschsprung's disease in neonates with a distal bowel obstruction. It can detect alternative pathologies, thereby preventing unnecessary surgical intervention whilst confirming that Hirschsprung's disease should be considered in patients with meconium plug syndrome who have persistent obstructive symptoms.

## 2. Introduction

Distal bowel obstructions (DBO) in neonates can present a diagnostic challenge due to the various pathologies that require either surgical or non-surgical treatment [1-3]. The different aetiologies that necessitate surgical intervention, such as Hirschsprung's disease (HD), complicated meconium ileus and small or large bowel atresia, can manifest clinically in a similar fashion to those that can be managed non-operatively like meconium plug syndrome (MPS), uncomplicated meconium ileus, and small left colon syndrome [1, 3]. In neonates presenting with a DBO, a contrast enema (CE) can be used to differentiate the aetiology [3, 5, 6] and CE have been recognised as useful for determining the need for surgical exploration [2, 7]. However there remains some debate about its ability to accurately diagnose HD [1, 4]. One study reported a seven fold increase in false negatives of CE when attempting to diagnose HD in the neonatal period [4]. Another reported between 13-38% of patients labelled as having MPS following a CE were subsequently diagnosed with HD [1], indeed when the term "meconium plug syndrome" was first coined it was described as a mimic of HD [2, 7]. We reviewed the CE performed in a single centre over the past 20 years to evaluate the diagnostic yield of various pathologies in neonates with an unclear aetiology of a DBO.

## 3. Methods

Ethics approval was obtained (HREC/20/WCHN/158) and patient details were collected from the hospital's imaging database for all childern undergoing CE studies between January 2001 and March 2021. A total of 209 imaging studies were identified. All CE undertaken on patients over 28 days old were excluded (n=50). Patients who had a definitive diagnosis before the CE was undertaken were then excluded. This included those who had undergone a prior bowel surgery or rectal biopsy (n=37) as well as those with an anorectal malformation (n=5), abdominal wall defect (n=2) or isomerism (n=1). Five further patients were subsequently excluded as insufficient clinical information was retained within the institution. In total 109 CE for 98 separate patients were analysed from the 20-year period. The CE findings at the time of the scan were listed as the radiological diagnosis and recorded as one of the following: MPS, bowel atresia, HD, meconium ileus, SBO, or normal if no abnormalities were detected. CE that didn't ascribe a specific diagnosis, which listed several evenly positioned differentials or were terminated prior to a diagnosis being reached were recorded as non-diagnostic. The patient's definitive diagnosis was recorded as HD if confirmed histologically with a rectal biopsy whilst the definitive diagnosis for patients with a SBO or bowel atresia was made from the intraoperative findings or from pathology specimens collected at that time, patients with meconium ileus who required surgical intervention were confirmed in this manner. For patients who did not undergo a surgical intervention or a rectal biopsy the definitive diagnoses were those recorded at time of discharge. All patients had their electronic and paper clinical records accessed, with all pathology, imaging and operations reports examined. Follow up periods varyed between 20.6 months and 21.6 years with a mean of 10.6 years.

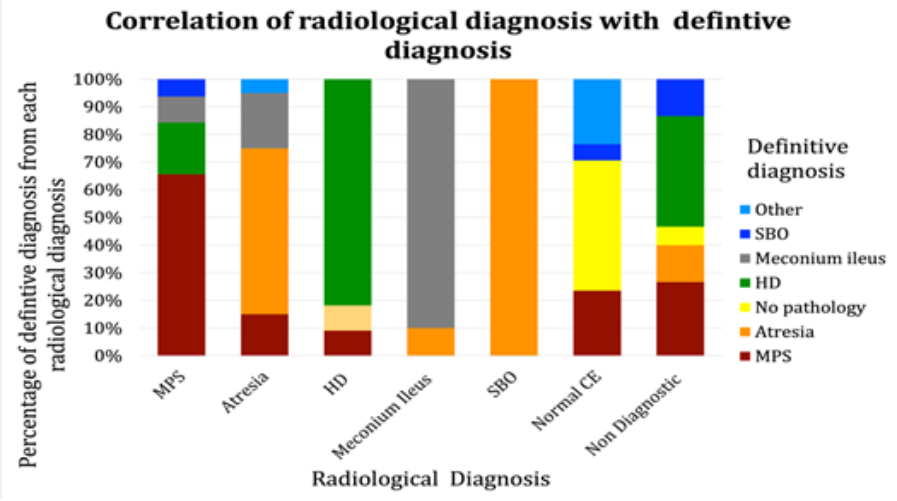
## 4. Results

In total 109 CE were included from a total of 98 patients, 51 males and 47 females. Nine patients underwent two CE and one patient underwent three imaging studies within the neonatal period. In the 98 different patients the final definitive diagnosis was MPS in 29 patients, HD in 21 patients, a small or large bowel atresia in 16 patients, meconium ileus in 13 patients whilst 10 had no underlying pathology and four had SBO from congenital adhesions. The remaining five were recorded as 'other' with two patients having cow's milk protein intolerance (CMPI), one with necrotising enterocolitis (NEC), one had adynamic bowel with no other cause found (HD was excluded on biopsy) and the final patient had no diagnosis determined at the time of their death from an genetic seizure disorder. The demographics of the patients are summarised in Table 1 and broken down by definitive diagnosis. There were no statistical differences among the definitive diagnoses for maternal age, gestation at birth, age at time of CE or birth weight. Males were more commonly diagnosed with a surgical pathology like HD (16:5, M:F) or atresia (11:5, M:F). Of the 109 CE performed the most common *radiological diagnosis* was MPS (n=32) followed by bowel atresia (n=20), HD (n=11) meconium ileus (n=10) and SBO (n=4). The remaining CE were either radiologically normal (n=17) or non-diagnostic (n=15). Table 2 outlines the patient's initial radiological diagnosis following their CE versus their subsequent definitive diagnosis. Figure 1 demonstrates the definitive diagnosis. Patients with a radiological diagnosis of MPS had no alternative diagnosis elicited pathologically in 21 of the 32 (66%) and were discharged with a definitive diagnosis of MPS. The remaining 11 patients had alternative definitive diagnoses of HD (6/32, 19%), meconium ileus (3/32, 9%) and SBO (2/32, 6%). Two thirds of patients with a radiological diagnosis of MPS but with a definitive diagnosis of HD had HD recorded as a less likely differential diagnosis at the time of the CE report. Most of the patients with a radiological diagnosis of MPS underwent a rectal biopsy (20/32) with six returning positive for HD, one was non- diagnostic and not repeated with the remainder of biopsies able to exclude HD. Expressed as a percentage of each radiological diagnosis. compared to females. Females were more commonly found to have MPS (10:19 M:F) or meconium ileus (4:9 M:F). Patients with

a radiological diagnosis of MPS had no alternative diagnosis elicited pathologically in 21 of the 32 (66%) and were discharged with a definitive diagnosis of MPS. The remaining 11 patients had alternative definitive diagnoses of HD (6/32, 19%), meconium ileus (3/32, 9%) and SBO (2/32, 6%). Two thirds of patients with a radiological diagnosis of MPS but with a definitive diagnosis of HD had HD recorded as a less likely differential diagnosis at the time of the CE report. Most of the patients with a radiological diagnosis of MPS underwent a rectal biopsy (20/32) with six returning positive for HD, one was non- diagnostic and not repeated with the remainder of biopsies able to exclude HD. All 11 patients with a CE suggestive of HD subsequently underwent a rectal biopsy with nine confirming HD histologically (82%). Of the two that were negative one was discharged with no underlying pathology; they were labelled as 'adynamic bowel' whilst the other was diagnosed with MPS. Two of these 11 were discharged before undergoing a rectal biopsy and both were labelled with MPS in their initial discharge summary. The first, a boy born at 31 weeks weighing 1.92kg, underwent his CE on day 17 which had a calibre change between the rectum and sigmoid consistent with HD. He was actively followed up by the surgical team and electively admitted at three months of age due to ongoing constipation. A rectal biopsy at this point demonstrated HD. The second, a boy also was born at 36 weeks' gestation weighing 2.97kg, underwent a CE on day three which revealed a dilated tortuous sigmoid colon with dilation extending proxiamlly. He was readmitted with enterocolitis at four months of age and during this admission underwent a biopsy that demonstrated HD. Both of these are considered to be a delayed diagnosis of HD. Of the 17 CE that demonstrated no radiological abnormalities only one had a pathology that required surgical intervention. This was a girl born at 26 weeks gestation who underwent a CE on Day 28. She had a congenital adhesion SBO requiring surgical intervention before subsequently developing NEC on two separate occasions each requiring a laparotomy. She succumbed during the second episode of NEC. Of the remaining normal CE eight had no underlying pathology (four of these had rectal biopsies to exclude HD), four had MPS (one of which had a normal biopsy) and two had CMPI. Two patients never received a definitive diagnosis, one was labelled as an adynamic bowel, with normal rectal biopsy, whilst the other died from an underlying genetic seizure disorder without reaching a diagnosis for their bowel dysfunction. In total 15 CE (in 14 patient) were classified as a non-diagnostic study with only one patient undergoing a second CE (this repeat CE was also non diagnostic). Of the 15 non diagnostic CE three were unable to visualise the entire colon, five listed two or more main differentials whilst seven had abnormal features on CE however these were not attributable to a specific pathology. Of the 15 non-diagnostic CE the subsequent definitive diagnosis was atresia in two patients, MPS in four patients (three of these patients had rectal biopsies which were normal), one patient had no underlying pathology, whilst the patient undergoing two non-diagnostic CE had a SBO. The remaining six patients had HD proven on biopsy. Of the patients with non- diagnostic CE rectal biopsies were performed in nine patients with three biopsies detecting ganglion cells, while six had biopsies confirming HD. Of the patients with HD confirmed histologically after a non-diagnostic CE three had features of suggestive of HD with HD recorded as a differential diagnosis, one patient's CE was terminated early due to clinical instability and one had a colic-colic intussusception that prevented adequate assessment. The radiological diagnosis was recorded as bowel atresia (small or large) in 20 CE with 12 patients having this confirmed operatively. Meconium ileus was later diagnosed in four of the 20 patients, with two testing positive for cystic fibrosis (CF). The two patients (Identical twin girls of Vietnamese descent) without CF who had meconium ileus both, after their CE, underwent a laparotomy, enterotomy and enterostomy to remove obstructing inspissated meconium. Of the remaining patients MPS was the definitive diagnosis in three patients whilst one patient underwent a laparotomy for suspected atresia and was found to have NEC with a patent continuous lumen. In total 55 rectal biopsies were performed on 51 patients with four patients undergoing two biopsies. HD was diagnosed in 21 patients (41%) whilst 29 patients (57%) had a biopsy that excluded HD, one biopsy was non diagnostic and not repeated after 15 years (Figure 2). Shows the breakdown of the definitive diagnosis for patients with a negative rectal biopsy and the initial radiological diagnosis of patients who were diagnosed with HD on a rectal biopsy). Four patients underwent a repeat biopsy with the repeat biopsy demonstrated HD in three patients. The fourth had a biopsy at one week of age demonstrating eosinophilic proctitis and a repeat biopsy at the age of 10 years which excluded HD. One patient had an inconclusive result on biopsy that was not repeated in 15 years of follow up. All but two cases of HD were diagnosed in the immediate period after the CE while two had delayed diagnosis. The vast majority of biopsies were done within a week of the CE (n=47, 85%), whilst three were performed after one week but within 30 days of the CE (5%) and four biopsies (7%) were done on three patients between one month and one year after the CE, the last was done at age 10 as mentioned above (2%). The three patients having a rectal biopsy between one month and one year after the CE all had HD. The first of these three patients had a biopsy two days after the CE that demonstrated HD and this was repeated at eight months for confirmation immediately prior to their definitive surgery. The second required two biopsies (83 and 91 days after CE) to reach the diagnosis of HD whilst the third had HD confirmed with one biopsy 111 days after their CE.

Two patients had initially been thought to have MPS but were subsequently found to have HD on biopsy. Both patients were discharged with a radiological diagnosis of MPS but had features reported on their CE that suggested a possible differential diagno-

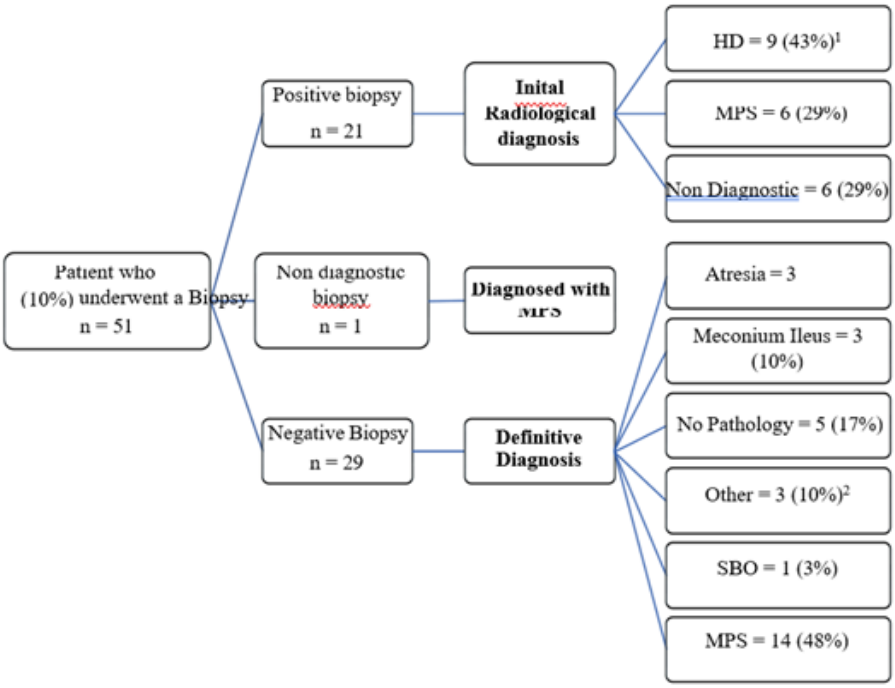
sis of HD. The first of these two was actively followed up by the surgical team and readmitted electively at about 12 weeks of age for biopsy that was repeated nine days later as it was non diagnostic, the second biopsy demonstrated HD. The second patient, however, was not followed up but re-presented to hospital at 16 weeks of age with enterocolitis and subsequently diagnosed as HD on rectal biopsy.




CE Contrast Enema, MPS Meconium Plug Syndrome, SBO Small Bowel Obstruction, HD Hirschsprung's Disease.

**Figure 1:** Correlation of initial Radiological Diagnosis with subsequent Definitive Diagnosis.

This table highlights the definitive diagnosis as percentage of the different radiological diagnosis assigned at the time of the CE. CE demonstrating MPS were correct in nearly two thirds of patients whilst the corroboration of CE with biopsies for HD was 82%. Neonates with a CE without pathological features were found to have a pathology that required surgical intervention in only 5% of cases.




[1]This includes the two delayed biopsies.

[2]One had NEC, one had CMPI whilst the final one never had a diagnosis reached

HD = Hirschsprung's Disease, MPS = Meconium Plug Syndrome, SBO = Small Bowel Obstruction, NEC = necrotising enterocolitis, CMPI = Cow's milk protein intolerance.

**Figure 2.** Outcomes for patients who underwent a rectal biopsy.

For patients that underwent a rectal biopsy that was positive for HD (n=21) the initial radiological diagnosis was HD in 43% of cases and MPS in 29% of cases whilst the CE was non diagnostic in 29% of cases. For patients who underwent a biopsy that was negative for HD (n=29) 50% had MPS whilst 15% had an atresia and 15% had no underlying pathology. The remaining 20% were split between meconium ileus (10%), SBO (3%), and other pathologies (10%). One patient had a non-diagnostic rectal biopsy that was not repeated in 15 years of follow up and was diagnosised with MPS.

**Table 1:** Demographic data of all cases according to definitive diagnosis: The definitive diagnoses were assessed for the gender of the child, their age at the time of the CE, gestation at time of delivery, the birth weight of the child and the age of the mother at the time of delivery. Each is expressed as the mean plus or minus one standard deviation. There were no statistical differences among the groups in terms of age at CE, gestation, birth weight or maternal age. Males were more commonly diagnosed with a surgical pathology like HD (16:5, M:F) or atresia (11:5, M:F) compared to females. Females were more commonly found to have MPS (10:19 M:F) or meconium ileus (4:9 M:F).

| Definitive Diagnosis | Patients (% of total) | Gender (M:F) | Age at CE (days) | Gestation (weeks) | Weight (grams) | Maternal Age (years) |
|---|---|---|---|---|---|---|
| **Total Patients** | 98 | 51:47 | 4.9 ± 5.86 | 36.4 ±3.32 | 2863 ± 802.6 | 31.4 ± 5.48 |
| **MPS** | 29 (30%) | 10:19 | 3.1 ± 2.19 | 36.3 ± 2.33 | 2942 ± 785.9 | 31.0 ± 5.50 |
| **HD** | 21 (21%) | 16:05 | 4.2 ± 4.17 | 38.3 ± 2.43 | 3294 ± 605.3 | 32.3 ± 5.09 |
| **Bowel Atresia** | 16 (16%) | 11:05 | 2.0 ± 1.08 | 37.1 ± 2.83 | 3127 ± 564.8 | 31.0 ± 6.05 |
| **Meconium Ileus** | 13 (13%) | 04:09 | 4.9 ± 6.00 | 34.88 ± 4.47 | 2329 ± 851.2 | 34.9 ± 4.47 |
| **No pathology present** | 10 (10%) | 05:05 | 10.8 ± 7.88 | 37.0 ± 2.38 | 2716 ± 811.0 | 32.6 ± 3.72 |
| **Other**[1] | 5 (5%) | 03:02 | 12.4 ± 10.65 | 32.6 ± 4.24 | 1884 ± 812.5 | 25.5 ± 8.33 |
| **SBO** | 4 (4%) | 02:02 | 12.2 ± 10.69 | 32.3 ± 3.24 | 2343 ± 320.8 | 28.5 ± 3.75 |

[1]Other definitive diagnosis included Necrotising enterocolitis (n=1), Cow's milk protein intolerance (2), and no clear aetiology identified (2)
M Male, F Female, CE contrast enema, MPS Meconium plug syndrome, HD Hirschsprung's disease, SBO Small bowel obstruction.

**Table 2:** Comparison of radiological diagnosis versus definitive diagnosis.
The initial findings of the 109 CE (radiological diagnosis) are listed in rows with the columns corresponding to the underlying pathology of the patient (definitive diagnosis) undergoing the CE.
The cells with a percentage listed in brackets represent the number and percentage of radiological diagnoses from the CE that concurred with the definitive diagnosis, either from pathological sampling or at the time of discharge. CE that demonstrated MPS were correct in two out of three patients whilst 82% of CE suggestive of HD were proven correct on histological sampling. Other represents those with CMPI,
NEC, abnormal motility, and patients whom no definitive diagnosis was reached.

| | | Definitive Diagnosis[1] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Radiological Diagnosis** | **Total** | **MPS** | **Atresia** | **No pathology** | **HD** | **Meconium ileus** | **SBO** | **Other** |
| MPS | 32 | 21 (66%) | - | - | 6 | 3 | 2 | - |
| Atresia | 20 | 3 | 12 (60%) | - | - | 4 | - | 1 |
| Normal Study | 17 | 4 | 0 | 8 (48%) | - | - | 1 | 4 |
| HD | 11 | 1 | - | 1 | 9 (82%) | - | - | - |
| Meconium Ileus | 10 | - | 1 | - | - | 9 (90%) | - | - |
| SBO | 4 | - | 4 | - | - | - | 0 | - |
| Non Diagnostic | 15 | 4 | 2 | 1 | 6 | - | 2 | - |

CE Contrast Enema, MPS Meconium Plug Syndrome, SBO small bowel obstruction, HD Hirschsprung's Disease, NEC Necrotising Enterocolitis, CMPI Cow's milk protein intolerance
[1]the sum of the individual Definitive diagnosis here exceed the the total number of patients as the patients who underwent multiple contrast enema had the radiological diagnosis of each individual imaging study compared to the patients definitive diagnosis.

## 5. Discussion

The meconium plug syndrome was first described by Clatworthy et al in 1956 as a DBO in neonates associated with pellets of meconium in the colon, the passage of which sometimes relieved the obstruction [2]. They reviewed their original case series a decade later with additional patients included and noted that a substantial proportion of these cases went on to be diagnosed with Hirschsprung's disease or meconium ileus [7]. The role of a CE in the neonatal period is to help determine the cause of a DBO and identify pathologies that need surgical intervention [2, 3, 7]. Its role in preventing a laparotomy for MPS was first reported over 60 years ago [2, 7]. Some recent studies have challenged this and report a decreasing role for CE both in treatment [3, 8, 9] and as the initial investigation for neonatal DBO [4, 10]. Additionally it has been reported that neonatal CE have high false negative rates [4] as well as false positive rates for diagnosing HD [10]. While

several studies have shown that CE is inferior to anorectal manometry and rectal biopsies in the diagnosis of HD [10] CE can demonstrate features of HD and provide information about the level of transition in HD [11]. In this study we only encountered two false positives (1.8%) for HD on CE and two patients (1.8%) had delayed diagnosis of HD which were detected at 15 and 18 weeks old. In neonatal DBO CE can be difficult to interpret as different pathologies can result in similar radiological appearance [1–3]. Both meconium ileus and distal small bowel atresia can result in a microcolon through failure of meconium to pass through the colon [8]. Additionally whilst meconium plugs are typically present in MPS they are not specific for MPS [8]. Despite this the yield of the CE in detecting neonates who required operative management was high in this study. Only 12 of the 109 (11%) CE failed to detect a pathology that subsequently required surgical intervention with one study being reported as a normal study and the remainder as MPS; The majority (n=9) of these CE were done within the first four days of life. The patients with a non-diagnostic study went on to be diagnosed with HD in six cases, SBO in three and meconium Ileus in three. In this study, of the 32 patients with a radiological diagnosis of MPS six had a definitive diagnosis of HD. This represents nearly 19% of cases which is consistent with other studies [1, 11]. In all six of these cases a rectal biopsy was done within three days. Each of these six had clinical features of ongoing obstruction post CE to warrant a rectal biopsy. Moreover, in this study only two patients out of 109 CE (1.8%) had a delay in detecting HD, this compares with 14% reported previously [1]. In the original 1966 follow up case series by Ellis at al they described two of 30 cases (6.7%) that were diagnosed with HD at a later date due to intermittent bowel obstructions [7]. These cases highlight that patients with a diagnosis of MPS should be followed closely. In these patients the threshold for undertaking a rectal biopsy should be low [1, 11, 12], particularly if they continue to have episodes of obstruction or constipation [2, 7].

Beyond detecting HD another recent study showed that contrast enema have sufficiently high specificities and sensitivities to exclude surgical pathologies more generally [13], and provide alternative diagnoses in neonatal DBO [3, 8, 9]. In this series 20 CE were suggestive of atresia with 12 of these confirmed intraoperatively, four being meconium ileus requiring intervention and only four having an alternative diagnosis that didn't require surgical intervention. Additionally, four CE reported findings consistent with a small bowel obstruction all of which were found to have obstructions from an atresia intraoperatively, three had jejunal atresia and one had an atresia of the transverse colon.

## 6. Conclusion

Contrast enema in the setting of neonatal distal bowel obstruction has a high diagnostic yield and can help determine which patients require surgical intervention. There should be a low threshold for proceeding to rectal biopsy for those with a radiological diagnosis of meconium plug syndrome in the presence of ongoing obstruction or incomplete resolution of symptoms.

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