ORIGINAL ARTICLE

Selective fluconazole prophylaxis in high-risk babies to reduce invasive fungal infection

Brian A McCrossan, Elaine McHenry, Fiona O'Neill, Grace Ong, David G Sweet

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See end of article for authors' affiliations

Correspondence to: Dr Brian A McCrossan, Regional Neonatal Intensive Care Unit, Royal Maternity Hospital, Grosvenor Road, Belfast BT12 6BJ, Northern Ireland, UK; brianmccrossan@doctors.org.uk

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Objectives: To evaluate the impact of selective fluconazole prophylaxis on incidence of invasive fungal infection and emergence of fluconazole resistance in neonatal intensive care.
Design: Retrospective study of very low birthweight (VLBW) babies (<1500 g birth weight) admitted to a neonatal intensive care unit (NICU) in the period 1 year before and after the implementation of an antifungal prophylaxis guideline.
Patients: VLBW babies with an additional risk factor: colonisation of *Candida* species from surface sites with a central venous catheter; third generation cephalosporin treatment; or total duration of antibiotic treatment >10 days.
Fluconazole protocol: Fluconazole 6 mg/kg for 3 weeks. Dose interval is every 72 h during the first 2 weeks of life. Thereafter, dose interval is reduced to every 48 h until 3 weeks old when daily fluconazole is given. Fluconazole is administered orally when enteral feeding achieved.
Results: 121 and 107 VLBW babies were admitted to the NICU in the year before and after the guideline was implemented, respectively. Data were available in 110 and 102 charts. 33/110 and 31/102 babies were eligible for fluconazole prophylaxis in the period before and after guideline implementation. 6/33 babies eligible for prophylaxis developed culture proven *Candida* sepsis before compared with no (0/31) babies after the guideline was implemented ($p = 0.03$). One baby (1/31) did develop probable *Candida* sepsis in the post guideline implementation period. During both study periods all *Candida* isolates remained fully susceptible to fluconazole.
Conclusions: Selective antifungal prophylaxis has reduced invasive fungal sepsis in one NICU without evidence of fluconazole resistance emerging.

Invasive fungal infection, most commonly due to *Candida* species, is increasingly common in preterm babies in neonatal intensive care.[1–6] The estimated incidence in very low birthweight (VLBW) babies is between 2% and 4%, but it may be as high as 10% in extremely low birthweight (ELBW) babies. Fungal sepsis has much higher mortality, 21–32%, than bacteraemia, and it is also associated with markedly higher rates of adverse neurodevelopmental outcomes.[6–10]

Fluconazole prophylaxis reduces the incidence and mortality from invasive fungal infection,[11–19] but widespread use of antifungals might increase the emergence of resistance.[3 10 20–23] Studies to date are too short to fully assess the potential for fluconazole resistance and there remain reservations about treating all babies to protect a few.[12] Fluconazole seems to be well tolerated in prophylactic doses,[11–19] but there are associations with rise in liver transaminases, cholestasis, toxic epidermal necrolysis and Steven–Johnson syndrome, and interactions with other medications.[2 13 24–26] Selective use of antifungal prophylaxis in the subset of VLBW babies at very high risk of fungaemia may be preferable to minimise the risk of adverse effects.[2 12] Although comparatively little data are available on selective antifungal prophylaxis, two recent studies reported reductions in invasive fungal infection with a fluconazole prophylaxis policy targeting VLBW babies with additional risk factors.[16 17] Recognised additional risk factors for acquiring fungal sepsis in preterm infants include third generation cephalosporin use, fungal colonisation, prolonged broad spectrum antibiotic use, parenteral nutrition with lipids, endotracheal intubation, male gender, central venous catheter use and number of days in situ, previous bacterial blood stream infections, postnatal steroids, gastrointestinal pathology, H_2-receptor antagonists, shock and coagulopathy.[2 25 27–30]

In October 2003, the neonatal intensive care unit (NICU) at the Royal Maternity Hospital, Belfast, developed a guideline for antifungal prophylaxis in VLBW babies with additional risk factors for fungal sepsis. We conducted this retrospective study to determine if the use of selective fluconazole prophylaxis was effective in reducing invasive fungal infection in high-risk babies. We also wanted to establish if there has been an increase in fluconazole resistance.

METHODS

This retrospective study was conducted at a regional maternity unit. We included all babies <1500 g birth weight admitted to the Royal Maternity Neonatal Unit in Belfast, 1 year before and after 1 October 2003 when the guideline was implemented. Babies were excluded if they were admitted for short periods only (<48 h).

The antifungal prophylaxis guideline states that a VLBW baby should be *considered* for antifungal prophylaxis if they have any of the following additional risk factors:

- under treatment with a third generation cephalosporin;
- under treatment for more than 10 consecutive days with a systemic broad spectrum antibiotic;
- fungal colonisation from surface sites and a central venous catheter in situ.

Eligible babies were given antifungal prophylaxis at the discretion of the attending neonatologist. The fluconazole prophylaxis was given at any time during the admission and

Abbreviations: ELBW, extremely low birth weight; NICU, neonatal intensive care unit; VLBW, very low birth weight

there was no specific guidance regarding prophylaxis early in the infant's course. The prophylaxis regimen was fluconazole 6 mg/kg for 3 weeks. Dose interval was once every 72 h for the first 2 weeks of life. In babies aged between 2 weeks and 3 weeks, the dose interval was every 48 h. Babies more than 3 weeks of age were given daily fluconazole. Fluconazole was administered orally when enteral feeds were established. The guideline did not stipulate monitoring for adverse effects. This was left to the discretion of the attending neonatologist.

Data were collected on birth weight, estimated gestational age, identification of risk factors for fungal sepsis (in accordance with the NICU guideline), the number receiving prophylaxis, adherence to the dosing regimen and the incidence of fungal sepsis. The presence of other risk factors, not included in the guideline but identified in previous studies,[2 25 27–30] were also collected on eligible babies. The source, species and sensitivity patterns of *Candida* cultured was documented. Data were manually collected from the available medical records and the Belfast Link Laboratories microbiology database.

Culture proven *Candida* sepsis was defined as presence of a blood culture positive for *Candida* species or a clinically septicaemic baby with a urine culture or central line tip culture positive for *Candida* species. A diagnosis of probable *Candida* sepsis was made if the infant was clinically septicaemic with no positive cultures but there was additional evidence of fungi such as fungal balls on ultrasound scan. Clinical septicaemia was diagnosed by the attending neonatologist.

Antibiotic susceptibility testing for *Candida*

Antibiotic susceptibility of fungal isolates was tested using Sensititre Yeastone (TREK diagnostic systems, West Sussex, UK). The sensitivity range for *Candida* species for fluconazole were: sensitive, minimum inhibitory concentration (MIC) $\leqslant$8 μg/ml; intermediate, MIC 16–32 μg/ml; resistant $\geqslant$64 μg/ml.

Statistical analysis

The main outcome of interest was a positive diagnosis of invasive *Candida* infection. We analysed the data using the Fisher exact test. Group characteristics were compared by using either the Student t test or the Fisher exact test where appropriate on Windows SPSS (version 15.0).

Research ethics

Ethical approval was not required as this was a retrospective chart and computer records study, in keeping with our trust's research governance policy. The data collected did not affect patient care, was anonymous, and was securely collected and stored.

RESULTS

A total of 121 babies admitted to the NICU before the implementation of the guideline were eligible for inclusion in the study, and 110 charts were available for data collection. Five infants were excluded as they were admitted for less than 48 h before transfer for surgery. A total of 107 babies admitted to the NICU after the implementation of the guideline were eligible and 102 charts were available for data collection. None of these babies were excluded. Although a few records were missing, these did not include infants with *Candida* sepsis identified in the microbiology database. These babies had similar characteristics to the babies whose charts were available. None of the babies admitted before the implementation of the guideline received fluconazole prophylaxis. Among those admitted after the implementation of the guideline, 14 of the 31 eligible babies received prophylaxis. Eight of these 14 babies received the correct dose, interval and duration of treatment. In the remaining six there were minor errors in dosage (3/14) and duration of treatment (5/14).

Incidence and mortality from invasive *Candida* infection

Following the introduction of the guideline, there was a significant reduction in culture proven invasive *Candida* infection in babies eligible for fluconazole prophylaxis (6% before and 0% after introduction of the guideline, p = 0.03). One baby admitted after the implementation of the guideline developed probable *Candida* sepsis. The diagnosis was made based on clinical septicaemia, ultrasound images suggestive of fungal balls in the renal tract and the steady improvement of the clinical course after administration of liposomal amphotericin B. No fungi were cultured from the urine or blood but fluconazole prophylaxis had been given. The reduction in invasive *Candida* infection (culture proven and probable) was not statistically significant. Table 1 shows the total number of babies who died and the mortality from *Candida* sepsis and other causes in the periods before and after the implementation of the guideline. Other causes of death included necrotising enterocolitis, bronchopulmonary dysplasia and intraventricular haemorrhage. A statistical analysis was undertaken to determine the effect of deaths from *Candida* sepsis on the mortality in the two groups (p = 0.2). The source and species of positive invasive *Candida* cultures is shown in table 2. All six babies with invasive *Candida* infection were ELBW and would have been eligible for prophylaxis if it have been available at that time.

We found significant differences between the infants who received fluconazole prophylaxis and those who were eligible but did not receive prophylaxis: infants receiving prophylaxis had a lower gestational age, two or more risk factors and more had received a third generation cephalosporin (see p values in

Table 1 Infant demographics, risk factors and incidence of *Candida* sepsis before and after the implementation of the antifungal prophylaxis guideline

	Before guideline implementation	After guideline implementation	p Value
Number of medical records available	110	102	–
Gestational age (weeks), median (range)	28 (24–36)	28 (23–34)	>0.9
Birth weight (g), median (range)	1040 (380–1495)	980 (429–1490)	0.3
Number eligible for prophylaxis, n/N (%)	33/110 (31)	31/102 (30)	>0.9
Cephalosporin use, n/N (%)	18/110 (16)	14/102 (14)	>0.9
Antibiotic >10 days, n/N (%)	23/110 (21)	19/102 (19)	>0.9
Fungal colonisation + central venous catheter, n/N (%)	6/110 (6)	6/102 (6)	>0.9
Culture proven *Candida* sepsis in eligible babies	6/33	0/31	**0.03**
Culture proven and probable *Candida* sepsis in eligible babies	6/33	1/31	0.1
Total died	7/33	3/31	0.2
Died *Candida* sepsis	4/33	0/31	0.11

Table 2 Description of cases of culture proven *Candida* sepsis before the prophylaxis era, including species, source and outcome

Case	Birth weight (g)	Gestational age (weeks)	Age at *Candida* sepsis (days)	Species	Source	Risk factors	Outcome
1	900	25	10	*C albicans*	Blood and CSU	Cephalosporin, >10/7 AB*, FC and CVC	Died, day 83
2	615	23	15	*C parapsilosis*	Blood	Cephalosporin	Died, day 28
3	752	25	28	*C parapsilosis* and *C albicans*	Blood and urine	Cephalosporin, >10/7 AB	Died, day 42
4	923	30	23	*C albicans*	Blood and urine	>10/7 AB	Alive, home day 57
5	630	24	20	*C parapsilosis*	Ascites	Cephalosporin	Alive, home day 170
6	660	24	19	*C albicans*	Urine	FC and CVC, >10/7 AB	Died, day 39

CSU, catheter specimen urine; CVC, central venous catheter; FC, fungal colonisation.
*10/7 AB, more than 10 days consecutive systemic antibiotics.

bold in table 3). There was also a tendency for ELBW babies to receive prophylaxis (table 3).

DISCUSSION

Here we have presented data on antifungal prophylaxis given to a subset of VLBW babies with recognised additional risk factors for fungal sepsis. The results for the entire group of babies eligible for fluconazole prophylaxis are shown, rather than the babies who were selected for treatment, as there were no suitable controls for the selected group. We found a significant reduction in culture proven *Candida* sepsis in a group of babies at particularly high risk, following the introduction of antifungal prophylaxis to a NICU. The retrospective nature of this study, relatively small numbers of eligible babies and low incidence of invasive *Candida* infection make this study underpowered to draw firm conclusions about the impact of selective fluconazole prophylaxis. Other limitations were the lack of controls and routine monitoring for adverse effects. However, the reduction in total cases of *Candida* sepsis (culture proven and probable) from 5% to 1% may be important, given the high morbidity and mortality associated with this condition.

A Cochrane meta-analysis concluded that fluconazole prophylaxis for all VLBW or ELBW babies considerably reduces the incidence of fungal sepsis.[11 12] More recent studies have included additional risk factors. Bertini *et al* observed a marked reduction in invasive candidiasis (7.6% to 0%) when fluconazole prophylaxis was given to VLBW babies with central venous catheters in situ (38% of all VLBW babies in the study period).[17] Uko *et al* reported similar results when a shorter course of lower-dose fluconazole prophylaxis (3 mg/kg) was given to VLBW babies receiving systemic antibiotics for more than 3 days (51% of all VLBW babies in the study period).[18] All of the studies quoted report similar reductions in the incidence of *Candida* sepsis; however, none adopted a risk-based policy as selective as this guideline (14% of all VLBW babies in the study period).

To achieve greater selection of babies at highest risk of fungal sepsis our guideline only included what are considered the most important risk factors: cephalosporin treatment, fungal colonisation, prolonged antibiotic use and the presence of a central venous catheter.[11 25 29 30] H_2-receptor antagonists and postnatal dexamethasone are rarely used in our unit and were not included in the guideline. The guideline was not designed to be prescriptive and a large proportion of eligible babies in our NICU were considered not to require antifungal prophylaxis by the attending neonatologist. For example, two VLBW infants were started on a cephalosporin for suspected necrotising enterocolitis, but this was discontinued after 48 h once the clinical picture made this improbable. Eleven babies were eligible because of prolonged antibiotic use as their only risk factor. None of these babies received prophylaxis. It is difficult to comment on the decisions of individuals in a retrospective study. However, in practice, fluconazole prophylaxis was administered to infants with lower birth weights, with two or more risk factors and, in particular, those receiving a third generation cephalosporin.

It is possible that other factors may have influenced the decrease in invasive fungal infection. Although there was no change in infection control policy in the NICU, an audit of blood stream infections in this unit during the same period showed a modest 26% reduction in laboratory-confirmed blood stream infections but no reduction in those not confirmed by

Table 3 Infant demographics and risk factors following the implementation of the antifungal prophylaxis guideline

	Received fluconazole prophylaxis	Eligible but no fluconazole prophylaxis	p Value
Birth weight (g), median (range)	800 (475–1150)	1030 (540–1493)	0.1
Number <1000 g birth weight, n/N (%)	12/14 (86)	9/17 (53)	0.07
Gestational age (weeks), median (range)	25 (24–31)	27 (25–32)	**0.01**
DOL fluconazole prophylaxis started, median (range)	15 (6–108)	N/A	–
Weight (g) when prophylaxis started, median (range)	910 (475–2080)	N/A	–
Cephalosporin, n/N (%)	12/14 (86)	4/17 (24)	**0.001**
Cephalosporin >48 h, n/N (%)	12/14 (86)	2/17 (12)	**<0.001**
>10 days antibiotics, n/N (%)	8/14 (57)	14/17 (82)	0.2
Candida colonisation and CVC in situ, n/N (%)	5/14 (36)	2/17 (12)	0.2
⩾2 Risk factors, n/N (%)	11/14 (79)	3/17 (18)	**0.001**
CoNS bacteraemia, n/N (%)	7/14 (50)	11/17 (65)	0.5
Other bacteraemia, n/N (%)	4/14 (29)	3/17 (18)	0.7
Necrotising enterocolitis, n/N (%)	5/14 (36)	2/17 (12)	0.2
Other gastrointestinal pathology, n/N (%)	0 (0)	0 (0)	–
Patent ductus arteriosus, n/N (%)	8/14 (57)	10/17 (59)	>0.9

DOL, day of life; CoNS, coagulase-negative staphylococci.

What is already known on this topic

- Fluconazole prophylaxis reduces the incidence of invasive fungal infection and mortality in very low birthweight babies.
- There are concerns that widespread use may lead to fluconazole resistance in *Candida* species.

What this study adds

- Fluconazole prophylaxis may reduce the incidence of invasive fungal infection when given to a subgroup of babies at particularly high risk of invasive fungal infection.

the laboratory. In addition, prevention of horizontal transmission of *Candida* by hand infection control measures has had only limited success in decreasing *Candida* colonisation and sepsis in neonates.[31 32]

Fluconazole prophylaxis gives rise to concerns that species which are inherently resistant to fluconazole will be selected out, or that there will be a gradual increase in resistance among previously sensitive strains. A strain of *C parapsilosis*, less susceptible to fluconazole, has been identified as causing blood stream infections in a NICU where fluconazole prophylaxis has been practised for 10 years.[33] Azole resistance in *Candida albicans* has also been reported, and *Candida* resistance has been found in preterm animals.[34 35] However, similar to most previous studies,[11–17] we found no evidence of the emergence of fluconazole-resistant strains, and all isolated *Candida* remained fully susceptible to fluconazole. As the study period was short it will be necessary to continue surveillance with these issues in mind.

In conclusion, the incidence of *Candida* sepsis in the NICU noticeably decreased in the 12 months following the introduction of an antifungal prophylaxis guideline, using fluconazole, targeted at a subset of VLBW babies at higher risk of invasive fungal infection. This study highlights the practicalities of implementing a fluconazole prophylaxis policy that attempts to appropriately identify those infants at greatest risk, while not exposing infants at lesser risk to a potentially harmful medication. Our results suggest that this risk-based approach correctly identifies those infants most likely to benefit from fluconazole prophylaxis. Achieving the correct balance has implications for cost effectiveness, emergence of resistant species and reducing exposure to potentially harmful medications. We are unable to prove any causal relationship due to the lack of power and retrospective nature of this study. However, a multicentre randomised controlled trial would elucidate the importance of particular risk factors in the development of fungal sepsis and the role of antifungal prophylaxis.

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Authors' affiliations
Brian A McCrossan, David G Sweet, Regional Neonatal Intensive Care Unit, Royal Maternity Hospital, Belfast, Northern Ireland, UK
Elaine McHenry, Grace Ong, Department of Microbiology, Royal Victoria Hospital, Belfast, Northern Ireland, UK
Fiona O'Neill, Department of Pharmacy, Royal Victoria Hospital, Belfast, Northern Ireland, UK

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REFERENCES

1 **Koskoff EH**, Buescher ES, Karlowiicz MG. Candidaemia in a neonatal intensive care unit: trends during fifteen years and clinical features of 111 cases. *Pediatr Infect Dis J* 1998;**17**:504–8.
2 **Neely MN**, Schreiber JR. Fluconazole prophylaxis in the very low birth weight infant: not ready for prime time. *Pediatrics* 2001;**107**:404–5.
3 **Moreira MEL**. Controversies about the management of invasive fungal infections in very low birth weight infants. *J Pediatr (Rio J)* 2005;**81**(1 Suppl):S52–8.
4 **Makhoul IR**, Kassis I, Smolkin T, *et al*. Review of 49 neonates with acquired fungal sepsis: further characterization. *Pediatrics* 2001;**107**:61–6.
5 **Stoll BJ**, Gordon T, Korones SB, *et al*. Late-onset sepsis in very low birth weight neonates: a report from the National Institute of Child Health and Human Development Neonatal Research Network. *J Pediatr* 1996;**129**:63–71.
6 **Stoll BJ**, Hansen N, Fanaroff AA, *et al*. Late-onset sepsis in very low birthweight neonates: the experience of the NICHD Neonatal Research Network. *Pediatrics* 2002;**110**:285–91.
7 **Friedman S**, Richardson SE, Jacobs SE, *et al*. Systemic candida infection in extremely low birth weight infants: short term morbidity and long term neurodevelopmental outcome. *Pediatr Infect Dis J* 2000;**19**:499–504.
8 **Lee BE**, Cheung P, Robinson JL, *et al*. Comparative study of mortality and morbidity in premature infants (birth weight <1250 g) with candidemia or candidal meningitis. *Clin Infect Dis* 1998;**27**:559–65.
9 **Harris MC**, Pereira GR, Myers MD, *et al*. Candidal arthritis in infants previously treated for systemic candidiasis during the newborn period: report of three cases. *Pediatr Emerg Care* 2000;**16**:249–51.
10 **Benjamin DK Jr**, Stoll BJ, Fanaroff AA, et al; National Institute of Child Health and Human Development Neonatal Research Network.. Neonatal candidiasis among extremely low birth weight infants: risk factors, mortality rates, and neurodevelopmental outcomes at 18 to 22 months. *Pediatrics* 2006;**117**:84–92.
11 **Benjamin DK**, DeLong ER, Steinbach WJ, *et al*. Empirical therapy for neonatal candidemia in very low birth weight infants. *Pediatrics* 2003;**112**:543–7.
12 **McGuire W**, Clerihew L, Austin N. Prophylactic intravenous antifungal agents to prevent mortality and morbidity in very low birth weight infants. *Cochrane Database Syst Rev* 2004;**1**:CD003478.
13 **Kaufman D**, Boyle R, Donowitz, et al. Fluconazole prophylaxis against fungal infection in preterm infants. *N Engl J Med* 2002;**346**:1913–4.
14 **Kaufman D**, Boyle R, Hazen KC, *et al*. Twice weekly fluconazole prophylaxis for prevention of invasive candida infection in high-risk infants of <1000 grams birth weight. *J Pediatr* 2005;**147**:172–9.
15 **Healy CM**, Baker CJ, Zaccaria E, *et al*. Impact of fluconazole prophylaxis on incidence and outcome of invasive candidiasis in a neonatal intensive care unit. *J Pediatr* 2005;**147**:166–71.
16 **Manzoni P**, Ariso R, Mostert M, *et al*. Prophylactic fluconazole is effective in preventing fungal colonization and fungal systemic infections in preterm neonates: a single-center, 6 year, retrospective cohort study. *Pediatrics* 2006;**117**:e22–32.
17 **Bertini G**, Perugi S, Dani C, *et al*. Fluconazole prophylaxis prevents invasive fungal infection in high-risk, very low birth weight infants. *J Pediatr* 2005;**147**:162–5.
18 **Uko S**, Soghier LM, Vega M, *et al*. Targeted short-term fluconazole prophylaxis among very low birth weight and extremely low birth weight infants. *Pediatrics* 2006;**117**:1243–52.
19 **Benjamin DK Jr**, McKinney RE, Benjamin D, *et al*. When to suspect fungal infection in neonates: a clinical comparison of candida albicans and candida parapsilosis fungaemia with coagulase-negative staphylococcal bacteraemia. *Pediatrics* 2000;**106**:712–8.
20 **Kaufman D**. Strategies for prevention of neonatal invasive candidiasis. *Semin Perinatol* 2003;**27**:414–24.
21 **Sims ME**, Yoo Y, You H, *et al*. Prophylactic oral nystatin and fungal infections in very-low-birthweight infants. *Am J Perinatol* 1988;**5**:33–6.
22 **Nguyen MH**, Peacock JE Jr, Morris AJ, *et al*. The changing face of candidemia: emergence of non-Candida albicans species and antifungal resistance. *Am J Med* 1996;**100**:617–23.
23 **Lewis RE**, Klepser ME. The changing face of nosocomial candidemia: epidemiology, resistance, and drug therapy. *Am J Health Syst Pharm* 1999;**56**:525–33.
24 **Pfaller MA**, Lockhart SR, Pujol C, *et al*. Hospital specificity, region specificity, and fluconazole resistance of Candida albicans bloodstream isolates. *J Clin Microbiol* 1998;**36**:1518–29.
25 **Saiman L**, Ludington E, Pfaller M, et al; National Epidemiology of Mycosis Survey study group. Risk factors for candidemia in neonatal intensive care unit patients. *Pediatr Infect Dis J* 2000;**19**:319–24.
26 **Aghai ZH**, Mudduluru M, Nakhla TA, *et al*. Fluconazole prophylaxis in extremely low birth weight infants: association with cholestasis. *J Perinatol* 2006;**26**:550–5.
27 **Feja KN**, Wu F, Roberts K, *et al*. Risk factors for candidemia in critically ill infants: a matched case-control study. *J Pediatr* 2005;**147**:156–61.
28 **Kicklighter SD**, Springer SC, Cox T, *et al*. Fluconazole for prophylaxis against candidal rectal colonization in the very low birth weight infant. *Pediatrics* 2001;**107**:293–8.
29 **Karlowicz MG**, Rowen JL, Barnes-Eley ML, *et al*. The role of birth weight and gestational age in distinguishing extremely low birth weight infants at high risk of developing candidaemia from infants at low risk: a multi center study. *Pediatr Res* 2002;**51**:301A.

30 **Manzoni P**, Farina D, Leonessa M, *et al.* Risk factors for progression to invasive fungal infection in preterm neonates with fungal colonization. *Pediatrics* 2006;**118**:2359–64.
31 **Pfaller MA**. Epidemiology and control of fungal infections. *Clin Infect Dis* 1994;**19**(Suppl 1):S8–13.
32 **Saiman L**, Ludington E, Dawson JD, *et al.* Risk factors for Candida species colonization of neonatal intensive care unit patients. *Pediatr Infect Dis J* 2001;**20**:1119–24.
33 **Sarvikivi E**, Lyytikainen O, Soll DR, *et al.* Emergence of fluconazole resistance in a Candida parapsilosis strain that caused infections in a neonatal intensive care unit. *J Clin Microbiol* 2005;**43**:2729–35.
34 **Giusiano G**, Mangiaterra M, Rojas F, *et al.* Azole resistance in neonatal intensive care units in Argentina. *J Chemother* 2005;**17**:347–50.
35 **Yoder BA**, Sutton DA, Winter V, *et al.* Resistant Candida parapsilosis associated with long term fluconazole prophylaxis in an animal model. *Pediatr Infect Dis J* 2004;**23**:687–8.

IMAGES IN NEONATAL MEDICINE

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Ultrasound guided percutaneous relief of tension pneumomediastinum in a 1-day-old newborn

A 35-week gestational age baby with antenatal diagnosis of probable infantile polycystic kidney disease born via normal vaginal delivery required immediate intubation and ventilation in the delivery room. On admission, the baby's blood pressure was normal (mean of 42 mm Hg) and pulse oximetry read 96% on 100% Fio_2. An *x* ray showed moderate pneumomediastinum. Within 2 h the baby's blood pressure mean dropped to the low 30s, the pulse oximetry reading dropped to the high 70s, the heart rate increased to 180 and the baby's perfusion was diminished. A repeat *x* ray (fig 1) showed a large pneumomediastinum with displacement of the heart to the right. Needle aspiration was unsuccessful. A 12 F chest tube was inserted through a subxiphoid incision into the anterior mediastinum under ultrasound guidance. The baby's blood pressure mean increased to the low 60s, the pulse oximetry reading returned to greater than 90%, the heart rate returned to normal and the baby's perfusion improved. A chest *x* ray (fig 2) showed the pneumomediastinum to be remarkably relieved.

In hospitalised patients, the main cause of pneumomediastinum is mechanical ventilation with high peak airway pressure and positive end expiratory pressure.[1] Although most cases of pneumomediastinum can be managed conservatively,[2] if there is continuous leakage of air in the mediastinal soft tissue, tension pneumomediastinum may occur and result in compromised venous return, which may evolve into a life-threatening condition.[1 3 4] Cases of tension pneumomediastinum relieved by using CT or fluoroscopic guidance have been reported.[1 5] In our case, we used ultrasound guidance during the procedure. This technique provides a rapid and simple method of management in critically ill patients.

Ibrahim S I Mohamed
Division of Neonatology, Department of Pediatrics, University of Montréal, Sainte-Justine Hospital, Montréal, Quebec, Canada
Yi-Horng Lee, Sani Z Yamout
Department of Pediatric Surgery, State University of New York at Buffalo, Women and Children's Hospital of Buffalo, Buffalo, New York, USA
Sami Fakir
Department of Pediatric Radiology, State University of New York at Buffalo, Women and Children's Hospital of Buffalo, Buffalo, New York, USA
Anne Marie Reynolds
Division of Neonatology, Department of Pediatrics, State University of New York at Buffalo, Women and Children's Hospital of Buffalo, Buffalo, New York, USA

Correspondence to: Dr Anne Marie Reynolds, Division of Neonatology, Department of Pediatrics, State University of New York at Buffalo, Women and Children's Hospital of Buffalo, Buffalo, New York, USA, 219 Bryant Street, Buffalo, New York, 14222, USA; areynolds@upa.chob.edu

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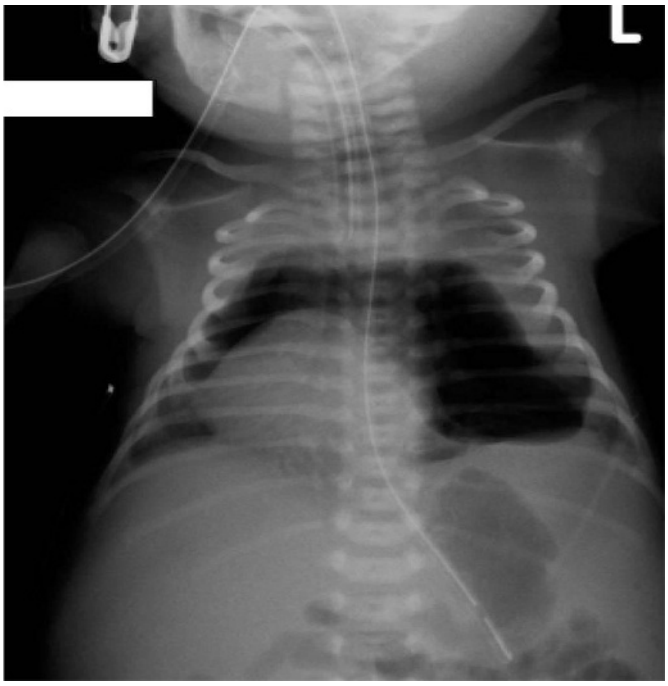

Figure 1 Large pneumomediastinum with displacement of the cardiac silhouette to the right. Diffuse patchy densities of both upper lobes due to passive atelectasis.

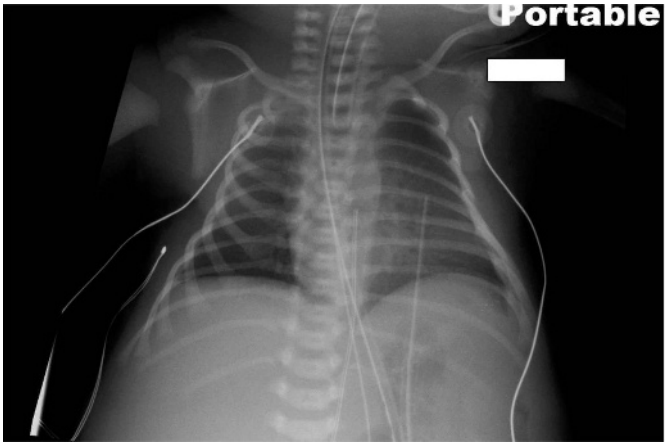

Figure 2 Insertion of mediastinal tube with marked decrease in pneumomediastinum. Improvement of aeration of upper lobes. An endotracheal tube and an umbilical artery catheter are in good position. The umbilical vein catheter is high and was adjusted.

References

1 **Dondelinger RF**, Coulon M, Kurdziel JC, *et al.* Tension mediastinal emphysema: emergency percutaneous drainage with CT guidance. *Eur J Radiol* 1992;**15**:7–10.
2 **Morrow G**, Hope JW, Boggs TR Jr. Pneumomediastinum, a silent lesion in the newborn. *J Pediatrics* 1967;**70**:554–60.
3 **Turlapati KM**, Spear RM, Peterson BM. Mediastinal tube placement in children with pneumomediastinum: hemodynamic changes and description of technique. *Crit Care Med* 1996;**24**:1257–60.
4 **Moore JT**, Wayne ER, Hanson J. Malignant pneumomediastinum: successful tube mediastinostomy in the neonate. *Am J Surg* 1987;**154**:688–91.
5 **Chau HH**, Kwok PC, Lai AK, *et al.* Percutaneous relief of tension pneumomediastinum in a child. *Cardiovasc Intervent Radiol* 2003;**26**:561–3.