

DOI: 10.21767/2573-0282.100044

Aetiology of Febrile Illnesses Presenting to a District Hospital

Sahib El-Radhi^{1*} and Swatee Patel²¹Department of Computing and Mathematical Sciences, Consultant Paediatrician, Queen Mary's Hospital and University of Greenwich, UK²Department of Computing and Mathematical Sciences, Medical Statistician, Queen Mary's Hospital and University of Greenwich, UK***Corresponding author:** El-Radhi S, Department of Computing and Mathematical Sciences, Consultant Paediatrician, Queen Mary's Hospital and University of Greenwich, UK, Tel: 07768 357547; E-mail: sahib.el-radhi@hotmail.co.uk**Received date:** May 10, 2017; **Accepted date:** May 19, 2017; **Published date:** May 26, 2017**Citation:** El-Radhi S, Patel S (2017) Aetiology of Febrile Illnesses Presenting to a District Hospital. *Pediatric Infect Dis* 2: 44. doi: 10.21767/2573-0282.100044**Copyright:** © 2017 El-Radhi S, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Little attention has been given to the patterns of diseases in children admitted to a hospital. We retrospectively studied 874 children (477 male, 397 female) who were hospitalised consecutively during a ten months period to determine the incidence and types of their illness with an emphasis on patterns and causes of fever.

Respiratory symptoms of cough and wheezing were the single most common presenting cause of admission (20.3%). Fever (defined as one temperature record of >38.0°C or two successive record of 37.8°C) was the second most common presenting cause (15.8%) leading to admission, and within this group fever without focus was most common. Overall, fever was recorded in 35.9% of the study group. Urinary tract infection was the most common bacterial infection. Children with bacterial infections were usually febrile while the majority of those with presumed viral infections were afebrile. The mean body temperature in children with bacterial infections was significantly higher than in those with presumed viral infections. Overall, febrile children stayed significantly longer in hospital and underwent more laboratory tests compared with afebrile children. Although white blood count and C-reactive protein tended to be higher in bacterial than in presumed viral infections, both tests were sometimes normal in serious bacterial infections and abnormally high in presumed viral diseases. Mild hyponatraemia (<135 mmol/L) was a common laboratory finding in febrile illness, and severe hyponatraemia (<130 mmol/L), was more common in bacterial diseases.

It is concluded that febrile illnesses are common and only second to respiratory diseases as the leading cause of hospitalisation. Children with bacterial infection are usually febrile and those with high fever should be evaluated for serious bacterial diseases. Those children who present with fever without focus should be evaluated for an underlying urinary tract infection and bacteraemia.

Keywords: Febrile illnesses; Children; Bacterial infection; Asthma; Respiratory diseases

Introduction

Children with acute illnesses are predominately managed by primary care doctors and only a minority of them require admission to hospital. An increase in the paediatric medical admission rate has been noted for many years [1,2]. The proportion of children in the population who require admission to hospital has been shown to increase from 11% of children by the age of one year to 33% of children by the age of 4-5 years [3]. Reasons for that include an increased availability of beds resulting from shorter hospital stays and an increase in respiratory diseases, particularly asthma, in recent years [4,5].

Febrile illnesses have their highest incidence in early childhood, and fever is one of the leading causes of bringing children to hospital. Acute infectious diseases remain the most common causes of febrile illnesses worldwide. Although fever is often non-specific and benign, it may be the only sign of potentially severe infection. Therefore a thorough evaluation of a febrile child is essential, which includes determining the aetiology of fever. Despite the high prevalence of fever, little is known about the incidence of fever in paediatric diseases, causes and patterns of fever, or the percentage of febrile children admitted to hospital. There is also little information about the comparative length of stay in hospital of febrile and afebrile patients.

In addition to the clinical evaluation in hospitalised children, laboratory means are utilized to help determine the cause and the seriousness of their illnesses. These include urine culture, particularly in a febrile child, full blood count (FBC), C-reactive protein (CRP), electrolytes and urea (E & U) and blood culture.

The study was carried out to determine the most common causes of admission to our hospital, the incidence of fever in these diseases and the patterns of their febrile diseases. The data may help the hospital in developing guidelines to target the commonest paediatric problems.

Patients and Methods

The study population included all consecutive paediatric admissions over a period of 10 months. Children who were

admitted because of social indications and day cases for investigations were excluded.

Queen Mary's hospital is a district general hospital situated in south-east London, which provides paediatric services for a population of approximately 100,000 children (1-16 years). The delivery rate is about 4,000 per annum. Between 70 and 150 children are admitted for acute illness under the care of paediatricians per month depending on the season, i.e. more admissions take place in winter months.

All children, referred by general practitioners or were self-referred, underwent a standard clinical evaluation in the Accident & Emergency Department, which included a complete history obtained from the child's carers, a physical examination and establishing a provisional diagnosis by the attending paediatrician. The child was then reviewed on the paediatric ward within a few hours by a middle-grade paediatrician and the above evaluation was repeated. All children were seen by a consultant paediatrician within 24 hours of the admission. Children were attended by a middle-grade paediatrician and/or consultant at the A & E Department if their condition so required.

The majority of diagnoses were made on clinical grounds (e.g. upper respiratory tract infection, URTI, tonsillitis, asthma) but some were only established by radiological or laboratory means (such as pneumonia, urinary tract infection, UTI, and bacteraemia). If there was no focus of infection in a febrile child, a diagnosis of fever without focus was made, which is defined as an acute febrile illness in which the aetiology of fever was not apparent after a careful history and physical examination [6]. A diagnosis of presumed viral infection (PVI) was made when bacterial infection (e.g. pneumonia) was excluded and all culture results were negative for bacterial growth such as UTI and bacteraemia [7]. Serious bacterial infections (SBI) include meningitis, pneumonia, urinary tract infection, cellulitis, osteomyelitis, bacteraemia.

A chief symptom was selected from the history, to reflect the main reason for bringing the child to hospital, e.g. wheezing/cough, vomiting, accident, skin rash or pyrexia. If there was more than one single complaint, the most serious symptom was selected. For example, when a child is admitted because of pyrexia and convulsion, the latter one was considered the chief complaint. Since a disease produces many symptoms the number of the presenting complaints may not reflect the true incidence of the disease.

All children were managed in accordance with our routine practice which is based on the hospital guidelines dealing with management of acute common paediatric diseases. The axillary temperature was recorded on admission and monitored at least 4 hourly. Fever was defined as a single temperature recording of $>38.0^{\circ}\text{C}$ or two successive recording of $>37.8^{\circ}\text{C}$ taken 4 hours apart during the first 24 hours of admission. Paracetamol 10-15 mg/kg was administered every 4 hours if there was fever. No routine investigations were carried out except for a urine sample for screening testing with dipsticks and for microscopy and culture and a stool culture from those children admitted because of gastroenteritis. Blood tests commonly performed,

usually together, were full blood count (FBC), C-reactive protein (CRP) and for electrolytes and urea. A white blood cell count (WBC) and a CRP >40 were considered abnormal (see later in Discussion). Blood culture was performed in all ill, febrile children. All febrile children without a focus were expected to undergo these blood tests. Other investigations were carried out as clinically indicated.

Antibiotics were used if there was evidence suggesting bacterial infection. Those febrile children with a focus of infection, e.g. otitis media or tonsillitis, were usually given antibiotics on admission. Those febrile children without focus were treated with antibiotics if they appeared ill, known to be immunocompromised, were less than one month of age or if the urine screening testing was positive for nitrate. Infants and young children between 1 and 36 months, who did not appear ill but whose screening blood tests (WBC, CRP) were abnormally high, were usually treated with antibiotics as well.

The timing of discharge was based on improvement of the condition and absence of fever in accordance with our usual practice. Following discharge, the case notes of the child were obtained and the case was enrolled into the study. Data were extracted from these notes and any missing information was obtained from the hospital laboratory's computerised record. The diagnosis at the time of discharge was the one taken for the study.

Results

During the study period, 874 children (477 male, 393 female) with a mean age of 39.67 months (standard deviation 47.54 months, range 3 days to 193 months) were admitted and studied retrospectively. Children were admitted for acute paediatric illnesses with a short history prior to hospitalisation. The duration of their stay in hospital ranged from one to 27 days, with a mean of 2.53 days.

The ten most common presenting problems leading to admission and the main diagnoses of these symptoms are shown in Table 1. Children with a leading symptom that required admission but their total number was below 20 were not included in the analysis. These totalled 130 children who were admitted for uncommon diagnoses including excessive crying, headaches, diabetes etc. Therefore, the total number of the children with the ten leading symptoms was 744 (874 minus 130; 85.1%). No deaths occurred among the 874 patients.

Wheezing/cough ($n=177$; 20.3% of all admissions). This was the most common presenting symptom leading to hospital admission. Of the 177, 115 (67.6%) were asthmatics. All asthmatic patients presented with wheezing and cough. The highest number of admissions was in September ($n=34$; 29%).

Thirty two children with cough/wheezing who were less than one year of age had virus-induced wheeze (viral-induced wheeze or wheezy bronchitis). Twenty nine with the same symptoms were diagnosed with bronchiolitis. Altogether there were 74 children with bronchiolitis, of which 45 (74 minus 29) who were brought to the hospital for causes other than cough/wheezing

such feeding difficulties, choking, or apnoea. There was one child with pneumonia who presented with wheezing.

Fever

(n=138; 15.8%) was the second most common symptom after wheezing and is discussed in detail below.

Diarrhoea, with or without vomiting

(n=110; 12.6). All children presented with diarrhoea were diagnosed as gastroenteritis. A stool sample from eight children was positive for Rotavirus antigen and another four were positive for salmonella. Stool samples from other children showed no abnormalities.

Fits

(n=82; 9.4%). Fifty seven children were diagnosed as having febrile convulsion and all were feverish on admission. Twenty three children of the remaining 25 had either first afebrile convulsion or recurrent afebrile convulsions (epilepsy); one had a fit due to breath holding attack and one had pseudo-seizure.

Accidents

(n=58; 6.6%). Trauma, mainly head injury, has led to 35 admissions. Accidental ingestion of tablets and overdose intending to cause self-harm, led to 19 admissions. Other causes of accidents include alcohol intake in two, scald in one and drowning in one. All the 58 children survived without complications.

Rash

(n=56; 6.4%). In 29 children a presumed viral aetiology was the final diagnosis and this was the most common single cause of those children admitted with a rash. Other causes were cellulitis (n=8); idiopathic thrombocytopenic purpura (n=3); Henöch Schönlein purpura (n=3); urticaria (n=3); meningococemia (n=2), erythema multiforme (n=2); eczema (n=2); staphylococcal scalded skin syndrome (n=1); impetigo (n=1); varicella (n=1); drug-induced (n=1).

Vomiting

(n=45; 5.1%). No cause was found (possible viral-induced) in 15 cases. Other causes include gastro-oesophageal reflux (n=12), associated with an upper respiratory tract infection (n=7), pyloric stenosis (n=8), appendicitis (n=6) and feeding problems (n=1).

Abdominal pain

(n=31; 5.1%). Causes include a non-specific diagnosis of abdominal pain (psychogenic) (n=14), appendicitis (n=6), mesenteric adenitis (n=5), constipation (n=4), abdominal migraine (n=1), intussusception (n=1).

Stridor/croupy

(n=27; 3.1%). Was always due to acute laryngotracheobronchitis and was considered viral in aetiology in all cases.

Feeding problems

(n=20; 2.3%). The leading cause was bronchiolitis (n=15). Other causes were choking during feeding (n=2), cerebral palsy (n=2) and of unknown aetiology (n=1).

Fever

There were 138 (15.8%) children who were admitted with fever as the principal reason for the admission (Table 1). Altogether there were 314 of the 874 children (35.9%) whose illnesses were associated with fever. The remaining 560 children were afebrile on presentation and none developed subsequently fever while in hospital.

The mean age of the febrile group (39.15 months) was slightly lower than that of the afebrile group (39.76 months) and was statistically insignificant: $p=0.84$, 95% confidence interval: -5.4691 to 7.0532). Their mean body temperature was 38.71°C (range 37.8 to 41°C). The duration of fever after admission ranged from 0.5 to 5 days (mean 1.52 days). The mean length of hospital stay was significantly higher in the febrile group (range 1 to 14 days, mean 2.87 days) compared to that of the afebrile group (range 1 to 27 days, mean 2.3 days): $p=0.001$, 95% confidence interval -0.76 to -0.19.

Table 1: Number of the ten leading symptoms and their diagnoses of 744 children admitted.

Chief complaints	No	%	Most common diagnosis
Wheezing/cough	177	20.3	Asthma, URTI, bronchiolitis
Fever	138	15.8	Fever without focus, URTI
Diarrhoea	110	12.6	Gastroenteritis
Fits	82	9.4	Febrile convulsion
Accidents	58	6.6	Trauma
Rash	56	6.4	Presumed viral
Vomiting	45	5.1	Non-specific, possible viral
Abdominal pain	31	3.5	Non-specific, functional
Croup/stridor	27	3.1	Viral croup
Feeding problems	20	2.3	Bronchiolitis, URTI
Total number	744		

The number of children with presumed viral or proven or probable bacterial infections is shown in Table 2 562 were considered to have viral infection (Group 1) and 88 to have bacterial infections (Group 2). The number of children in the two groups was 650, representing 67.5% of the total number of

children admitted. Of the 562 children of Group 1, 206 (36.6%) were feverish and only 20 of them (9.7%) had a high fever of $>40^{\circ}\text{C}$. Of the 88 children in Group 2, 82 (93.1%) were feverish and 28 of them (34.1%) had a high fever of $>40^{\circ}\text{C}$. The mean temperature of Group 1 was 38.5°C (standard deviation 0.9). The mean temperature of Group 2 was 39.2°C (standard deviation

0.8). The difference between the two means of temperature is highly significant ($p < 0.0005$; 95% confidence interval for the mean difference is 0.40 to 0.89). The overall incidence of serious bacterial infection was 60. Urinary tract infection was the most common bacterial infection diagnosed in 22 of 88 patients with bacterial infection.

Table 2: All children considered to have infections, those with fever, and those with fever of $>40^{\circ}\text{C}$ caused by presumed viral infection (Group1=562) and in those with proven or probably be caused by bacterial infection (Group 2=88); URTI=upper respiratory tract infection; GE=gastroenteritis; FC=febrile seizure.

Group- 1				Group-2			
Disease	No of febrile children	mean c $>40^{\circ}\text{C}$	No of (No)	Disease	No of febrile children	mean c $>40^{\circ}\text{C}$	No of (No)
Asthma n=115	22	38.3	0	UTI (n=22)	21	39.2	6
URTI N=106	24	38.7	4	Pneumonia (n=18)	18	39.6	11
GE (n=104)	24	38.3	1	Tonsillitis (n=20)	16	39	4
Bronchiolitis (n=74)	19	38.4	1	Bacteraemia (n=10)	10	39.2	1
FC (n=57)	57	39.0	7	Cellulitis (n=7)	6	39	2
PVI (n=32)	32	38.8	5	Otitis media (n=4)	4	39.2	0
Viral-induced wheeze (n=22)	4	38.4	0	GE (n=4)	4	39.1	1
Croup (n=27)	11	38.7	1	Bacterial Meningitis (n=3)	3	40	3
Rash-presumed viral (n=23)	11	38.8	1				
Viral meningitis (n=2)	2	38.2	0				
No: 562	206		20	88	82		28

There were 64 children with fever without focus who had three principal causes: a presumed virus infection (PVI, n=32), with negative urine and blood cultures; 22 children had UTI, all except two, were due to *E. coli* infection. The remaining ten cases had bacteraemia according to blood culture results (4 *St. pneumoniae*; 3 *meningococci*; 2 *E. coli* and one *streptococci*). Table 3 shows the results of common laboratory investigations (WBC, CRP and sodium levels) in the two groups. About 40% (304 out of 744) of children underwent blood tests, which were performed for 44.8% of febrile and 23% of afebrile children. Overall, there was a tendency for both screening tests to be mildly increased in febrile presumed viral infections and significantly so in bacterial infections. The mean WBC was ≥ 15.000 and CRP >40 in those with bacterial infection (Group 2).

In those afebrile children of Group 1, hyponatraemia was found in 23% (23 of 99 blood tests) of which 2 (10%) were severe. The incidence of hyponatraemia in those febrile children of the same group increased to 44.8% (56 of 125 blood tests) of which 14 was severe. The difference between the two proportions (23% versus 44.8%) is highly significant (the 95% confidence intervals are 0.108, 0.368, $p < 0.0005$). The highest incidence of hyponatraemia was detected in children with bacterial infection: 65% (52 of 80 blood tests) of which 14 were severe. There is a statistically significant difference between

overall incidence of low sodium in the three groups (the 95% confidence intervals are 0.36.4, 0.584, $p < 0.0005$).

Table 3: laboratory blood tests performed in the febrile and afebrile children of Group 1 with presumed viral infections and Group 2 with bacterial infections.

	No of blood tests	WBC	CRP (Mg/L)	Hyponatraemia (severe)
Afebrile presumed viral (No: 562)	99	12.8 (4.5-29.0)	12 (0-72)	23 (2)
Febrile presumed viral (No: 206)	125	13 (3.5-30.0)	29 (0-142)	56 (14)
Bacterial No: (88)	80	17.7 (4.5-34.0)	89 (2-348)	52 (14)
Total blood tests	304			

Discussion

The study showed that the majority of children were admitted to the hospital with a small number of diagnoses. The first four

presenting symptoms (cough/wheezing, fever, diarrhoea and fits) leading to admission (Table 1). Accounted for 58% of all admission. The study also showed that respiratory symptoms of wheezing and cough were the leading cause of hospital admission and that asthma was the most common diagnosis. This finding is in agreement with other studies [8,9] that asthma was the single most common cause for admission. A study from Australia reported that asthma remained the second most common cause for admission to the paediatric hospital [10]. Epidemiological studies have shown that the prevalence of asthma in children has increased steadily over the past few decades, even taking into account differences in diagnostic criteria [11]. The cumulative incidence of wheezing illness was reported to be 24% in children by the age of 16 years [12]. As the prevalence of asthma in children continues to increase annually by around 5%, asthma is likely to remain one of the most common paediatric problems facing paediatricians. The increase was not only due to an increase in its prevalence, but also due to changes in the thresholds for admission [13]. However, the increase of admission due to asthma is not reported universally as some authors reported a decreased rate of hospitalisation for children with asthma, generally attributed to the increasing use of inhaled steroids, which are known to reduce the frequency of exacerbation and hospitalisation [14].

Fever is recognised as a cardinal sign of illness, particularly of infections. As some of the febrile illnesses are serious, accurate measurement of body temperature is important in detecting the illness and monitoring its treatment. Febrile illnesses are common and among the leading causes of bringing children to hospitals. In this study fever was the second most common leading cause for admission (15.8%). This is in agreement with another study, which reported similar incidence of fever leading to an admission [10]. The overall measurements of fever were recorded in 314 of the total 874 (35.9%) children, which actually exceeded the incidence of wheezing of 20.7%. The reason why only 138 (15.8%) and not all 314 (35.9%) presented with fever as the leading cause for admission was probably because of so many paediatric illnesses (e.g. convulsion, gastroenteritis) are associated with fever. Once, for example, convulsion occurs, it becomes more important than fever as the leading cause for the admission. In addition, parents of children with respiratory or gastrointestinal symptoms are more likely to seek medical attention if the children are also febrile [15]. Furthermore, fever may not have been measured by the parents and only recognised on admission. In total, 44 children were brought to our hospital for reasons other than fever but were found to be feverish in the hospital.

Diseases caused by possible viral infections such as URTI, bronchiolitis and presumed viral infection (PVI) were significantly more common than those caused by bacterial infections (502 *versus* 88, Table 2). This is not unexpected since infections causing fever in children are mostly caused by viruses.

Serious bacterial infections (n=57) occurred in 57 of the 874 children (6.5%) and in 18.1% of all febrile children. McCarthy [16] reported an almost identical result of 18% in a retrospective review of 1169 children with fever attending the emergency room. As almost all children with SBI presented with fever, the

presence of this sign, particularly high fever, appears to be an important marker for considering the possibility of SBI, and appropriate investigations and treatment should be initiated promptly.

Fever without focus of infection was the single most common finding in children presented with fever (64=46.3% of all causes of fever). A slightly lower incidence of 41.5% was reported from Australia [17]. Of those children without a focus of infection, a possible viral infection was assumed to be present in 50% following negative blood and urine cultures. Although there may be an overlap in the clinical appearance between those children with a viral infection and those with urinary tract infection and bacteraemia, careful history, physical examination and laboratory screening tests can usually lead to the correct diagnosis. Several authors [18] have suggested multiple observation items (how ill the child looks) as predictors of bacterial illness such as bacteraemia.

Furthermore, this study shows that the mean body temperature and the number of fevers of >40°C were higher in children with proven bacterial infection (bacteraemia, UTI, meningitis) and probably bacterial infections (pneumonia, tonsillitis, otitis media) than in those with presumed viral infections (Table 2). These findings are in agreement with reports [19] showing that a high degree of fever closely correlates with the rate of serious bacterial infection, including meningitis, bacteraemia, UTI and salmonella enteritis. Bacteraemia and pneumonia in particular have been reported to be a common diagnosis in highly febrile children [20,21].

Fever is usually the result of immune mechanisms involving the production of potent pyrogens such as interleukin-1 and interleukin-6. Although a high degree of fever may accompany bacterial or viral infection, endogenous pyrogens, such as tumour necrosis factor-alpha and interleukin-6 were found to be significantly higher in patients with bacterial infection, such as pneumonia and UTI, than in those with viral infections [22]. Reduced production of another pyrogen, interferon-gamma, was reported in children with asthma and bronchiolitis [23]. This finding may explain the low rate of fever associated with lower respiratory tract diseases [24].

Children with fever, whether due to viral or bacterial infection, underwent more blood tests those who were afebrile (Table 3). The indication to perform blood tests in admitted febrile children is not clear-cut and many of these tests may be unnecessary, particularly in a child with presumed viral infection such URTI or bronchiolitis. White blood cell count (WBC) and CRP are unlikely to be helpful for the management of these diseases. These illnesses are known to be caused primarily by viral infection and the treatment is usually symptomatic without the need to use antibiotics. Similarly, febrile children who look ill, with or without established diagnosis of serious bacterial infection (SBI) should receive antibiotics empirically irrespective of the result of the WBC or CRP. On the other hand, those children who do not appear ill with suspected SBI or without a focus of infection, high CRP and WBC can predict the presence of bacterial infection, such as urinary tract infection (UTI) or bacteraemia. The performance of these two tests appears to be of great value in distinguishing viral from bacterial infections.

These results are in agreement with those of several studies [25-27] which have evaluated the use of these non-specific tests of WBC and CRP, and concluded that WBC >15,000 and CRP >50 are useful tests to predict serious illness.

During acute febrile diseases disturbance of water and electrolytes balance occurs frequently, particularly in regard to hyponatraemia [28]. Our results showed that hyponatraemia may occur in both afebrile and febrile presumed viral and bacterial infections. However, mild and severe hyponatraemia was more common in children who were febrile (56 of 125 blood tests=44.8%) with presumed viral infection compared to those who were afebrile (23 of 99 blood tests=23%), and significantly more common in those with bacterial infection (52 of 80 blood tests=65%) (Table 3). There was little difference of severe hyponatraemia between febrile of presumed viral and bacterial infections. These changes may be the result of an increased arginine vasopressin (AVP) hormone concentration as part of an endogenous antipyretic activity of this hormone during febrile illnesses.

One of the criticisms of this study is that diseases were grouped under presumed viral infection (PVI) but without providing a proof of the viral aetiology. In addition, although the aetiology of asthma is multi-factorial, the disease was added to the viral infection group because viruses are the most frequent precipitating factors associated with acute childhood wheeze [29], and upper respiratory tract viruses were associated with 78% of asthma exacerbation in children [30]. Similarly, although viral infection is a common cause of tonsillitis and otitis media [31,32], these were included in the bacterial infection group. These children appeared unwell with tonsillar exudate in cases of tonsillitis, and inflamed tympanic membrane in case of otitis media, and were without significant signs of URTI supporting bacterial aetiology.

In conclusion, fever is a very common complaint among children and is the second leading cause for hospital admission. Although fever is mostly trivial and self-limited symptom caused by viral infection, it is sometimes a marker for serious bacterial infections. Therefore, a febrile child has to be carefully evaluated to differentiate these two groups. History and physical examination, taking into consideration the degree of fever, are usually sufficient to reach a diagnosis. Appropriate laboratory investigations are indicated in children with suspected serious bacterial infections and in those presenting without a focus. Urinary tract infection and bacteraemia are common underlying disorders in children who present with fever without a focus of infection.

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