Febrile children were most often treated with antibiotics (87%) and laboratory tests (53%). The incidence of bacterial meningitis, meningococcal sepsis, and death from infection was low. However, the presence of fever in children without an obvious source remains controversial. This study suggests that fever in pediatric primary care is a common presenting feature, and the management of febrile children requires a careful balance between ensuring adequate coverage and minimizing unnecessary testing and treatment.

The authors conclude that further research is needed to better understand the epidemiology and management of febrile illness in pediatric primary care settings. They recommend the use of empirical treatment strategies for febrile children without a source, with consideration for the potential risks and benefits of antibiotic use. The study highlights the importance of ongoing surveillance and research to improve the care of febrile children in primary care settings.
METHODS
We analyzed, in detail, the management of febrile episodes presenting to primary care sites for a random sample of 5000 children. To diagnose the frequency of the rare outcomes of meningitis and death from sepsis, we analyzed data from the entire cohort of 20,585 individuals.

Study Population and Data Sources
We performed a retrospective cohort study including all children 3 to 36 months old enrolled in 11 staff-model pediatric departments of Harvard Pilgrim Health Care between January 1, 1991 and December 31, 1994. Patients at these sites were treated by physicians or pediatric nurse practitioners. All sites offered on-site phlebotomy and laboratory testing. The pediatric population receiving care at these sites reflects the demographic characteristics of their communities. Thirty percent of patients were non-white and 13% were covered under Medicaid.

Frequency and Management of Febrile Episodes
We analyzed the febrile episodes of a computer-generated random sample of 5000 children. We calculated the number of days each child was covered by the health plan beginning on enrollment or the 91st day of life (whichever came later), and ending at disenrollment or their third birthday (whichever came first). Ambulatory clinical information was obtained from a computerized medical record system, which is the sole clinical record used in these practices for all clinical encounters, described in detail elsewhere. Providers select problem-based codes on a paper encounter form and add free text entries for details of history, examination, and treatment plan; these forms are then entered into the record by medical records department staff. This record captures vital signs on arrival (including temperature), laboratory tests, diagnoses, and medications prescribed in searchable fields. Diagnosis codes (International Classification of Diseases, Ninth Revision) for emergency department visits and hospitalizations were obtained from administrative claims files.

We identified all daytime, evening, and weekend visits (including urgent care) during which a temperature $\geq 38\text{\degree}C$ was measured in the office. We analyzed separately visits with a measured temperature of 38\text{\degree}C to 38.9\text{\degree}C and those with a temperature $\geq 39\text{\degree}C$. In order to analyze testing and treatment during initial visits for febrile illness separate from follow-up care, we defined initial visits with fever as those occurring at least 14 days after any preceding office visit (excluding well-child care). All visits during this subsequent 7 days were considered follow-up of the initial illness.

A "primary" diagnosis was assigned for each encounter by the clinician in 78% of visits. An additional 12% of visits had 2 or more diagnoses, only 1 of which was likely to be clinically related to the fever (eg, otitis media and diaper rash), and was assigned as primary. For the remaining 10% of cases, in which both diagnoses were possible causes of fever (eg, viral illness and otitis media), the diagnoses were reviewed by an investigator (J.A.F.) who gave priority to a potential bacterial source (eg, otitis media). In this retrospective study, we accepted clinicians’ diagnoses without independent confirmation by laboratory testing, because it is their final diagnoses that determine the distribution of diagnoses was similar among children with fever 38\text{\degree}C to 38.9\text{\degree}C, and 1552 had fevers $\geq 39\text{\degree}C$. There were a total of .84 (95% confidence interval [CI]: .82, .86) visits with fever $\geq 38\text{\degree}C$ per child-year, and .24 (95% CI: .22, .27) visits per child-year with fever $\geq 39\text{\degree}C$ (Fig 1). Of the 5508 visits, 3819 met our criteria for first contact for a febrile illness episode (ie, index visits). Of the index visits, 1069 (28%) were for fever $\geq 39\text{\degree}C$.

Figure 2 shows the diagnoses assigned at the initial visits. Fifty-six percent of febrile children with fever $\geq 39\text{\degree}C$ were diagnosed with a bacterial source for infection, 3% with a specific viral syndrome, and 32% with a nonspecific viral illness; the distribution of diagnoses was similar among children with fever 38\text{\degree}C to 38.9\text{\degree}C. The remaining children (5% of those with fever 38\text{\degree}C to 38.9\text{\degree}C and 9% with fever $\geq 39\text{\degree}C$) were explicitly designated "rule-out sepsis," “fever of unknown origin,” or “diagnosis deferred.” The most common diagnosis was otitis media, accounting for 48% of index encounters. An antibiotic was prescribed at 56% of index visits. Almost all (93%) children with a diagnosed bacterial infection were prescribed antibiotics, compared with 9% of those diagnosed with a viral illness.

Diagnostic testing and antibiotic treatment rates for febrile children without a bacterial or specific viral source are shown in Fig 3. WBC, blood cul-

Assessment of Population Outcomes
The claims files for the entire cohort (N = 20,585) were searched for International Classification of Diseases, Ninth Revision codes for meningitis and meningococcal disease. Cases specifically coded as bacterial meningitis, and meningitis cases hospitalized for $>4$ days, were confirmed by review of the ambulatory record to exclude nonbacterial meningitis and “rule out meningitis.” Hospitalizations ending in death with any diagnosis and ambulatory records containing the coded entry for a patient death from any cause were also reviewed. Cases were designated definite bacterial meningitis if there was a cerebrospinal fluid pleocytosis (>5 WBCs/mm$^3$) and a bacterial pathogen grown from a cerebrospinal fluid or blood culture. Patients treated with a full course of antibiotics for meningitis in the absence of a positive culture, often with previous oral antibiotic treatment, were considered to have presumed bacterial meningitis.

The ambulatory records of confirmed cases were reviewed by 2 investigators for evidence of an office visit for febrile illness in the week before hospitalization. Because our focus was the management of fever and treatment of occult bacteremia to prevent the development of serious bacterial infection, we excluded visits within 24 hours of hospital admission.

Data were analyzed using the SAS software (SAS version 6.12, SAS Institute, Cary, NC). Statistical comparisons were made using $\chi^2$ tests with Yates correction for 2 $\times$ 2 tables, and, where appropriate, $\chi^2$ tests for trend.20 The number of febrile visits and their management in the population were extrapolated from the diagnosis and management of index visits of the sample of 5000.

RESULTS
There were 20,585 eligible children in the full population. Of the random sample of 5000 children, 2411 (48%) were female and 13% were covered by Medicaid at some time during the study period. The subjects had a mean observation time of 1.3 years, and contributed a total of 6551 child-years.

Among the sample of 5000 children, we identified 5508 visits for febrile illness; of these, 3956 had documented temperatures of 38\text{\degree}C to 38.9\text{\degree}C, and 1552 had fevers $\geq 39\text{\degree}C$. There were a total of 84 (95% confidence interval [CI]: .82, .86) visits with fever $\geq 38\text{\degree}C$ per child-year, and .24 (95% CI: .22, .27) visits per child-year with fever $\geq 39\text{\degree}C$ (Fig 1). Of the 5508 visits, 3819 met our criteria for first contact for a febrile illness episode (ie, index visits). Of the index visits, 1069 (28%) were for fever $\geq 39\text{\degree}C$.

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Diagnostic testing and antibiotic treatment rates for febrile children without a bacterial or specific viral source are shown in Fig 3. WBC, blood cul-
tures, urine tests, and throat cultures were obtained significantly more frequently for fever $\geq 39^\circ C$ ($P < .01$). Among the subgroup with fever $\geq 39^\circ C$ and no evident bacterial or specific viral source, 159 (36%) of 440 received a WBC or blood culture, and 17% had a urine analysis or culture. Not surprisingly, younger infants were significantly more likely to receive diagnostic tests than older children (Fig 4) ($P < .01$ for each test, except no difference for radiographs, and increasing rates of throat culture with age $P < .05$). Over half of highly febrile infants 3 to 6 months of age received a WBC or blood culture, and 9% had a throat culture.

* Comparison of children with high fever and mild fever, $p < 0.01$.

Fig 3. Management of febrile children without an apparent bacterial or specific viral source.
culture. Of the 132 blood cultures obtained, 8 (6%, CI: 3%, 12%) were positive for bacterial pathogens, all *Streptococcus pneumoniae*.

Table 1 shows the rates of follow-up during the 7 days after an initial febrile visit, stratified by initial antibiotic treatment. A total of 43% of children had medical contact as either an in-person visit or by telephone. Of the 1154 children with a follow-up visit, 121 had a WBC performed, 67 had a blood culture drawn, and 60 had their urine screened. In total, 449 children (12%) were prescribed a new antibiotic at follow-up: 223 received a first prescription for the illness and 226 had their antibiotic switched. Children treated with an antibiotic at the first encounter were less likely to return for follow-up. This was true for children initially presenting with temperatures of 38°C to 38.9°C (27% vs 32%; *P* ≤ .01) as well as febrile children who had a temperature of ≥39°C at the index visit (29% vs 38%; *P* < .01).

One hundred fifty (4%) of the 3819 febrile visits were associated with an emergency department visit within the next week. Eighty-two patients were seen in the emergency department on the same day as the office visit and were likely to have been sent to the hospital directly from the office or within hours of being seen. For the remainder, the most common emergency department diagnoses, which accounted for 62% of visits, were pyrexia of unknown origin, otitis media, viral infection, pneumonia, and bronchiolitis. Ten of these patients were hospitalized with diagnoses of pneumonia (4), septicemia (3), urinary tract infection (2), and cellulitis (1).

In the full cohort of 20 585 children, we identified 14 who were treated for definite (9) or pre-

**TABLE 1.** Follow-up Management Within 7 Days for Febrile Children

<table>
<thead>
<tr>
<th>All Febrile Children</th>
<th>Temperature 38°C to 38.9°C at Initial Presentation</th>
<th>Temperature ≥39°C at Initial Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Antibiotic Prescribed at First Visit (N = 3819) (%)</td>
<td>No Antibiotic Prescribed at First Visit (N = 3819) (%)</td>
</tr>
<tr>
<td>In-person follow-up</td>
<td>1154 (30)</td>
<td>422 (27)*</td>
</tr>
<tr>
<td>Telephone follow-up</td>
<td>895 (23)</td>
<td>305 (20)*</td>
</tr>
<tr>
<td>ANY follow-up†</td>
<td>1630 (43)</td>
<td>592 (38)*</td>
</tr>
<tr>
<td>Diagnostic testing at follow-up:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White blood cell count</td>
<td>121 (3)</td>
<td>30 (2)</td>
</tr>
<tr>
<td>Blood culture</td>
<td>67 (2)</td>
<td>10 (1)</td>
</tr>
<tr>
<td>Urine screen</td>
<td>60 (2)</td>
<td>10 (1)</td>
</tr>
<tr>
<td>Radiograph</td>
<td>49 (1)</td>
<td>19 (1)</td>
</tr>
<tr>
<td>Throat culture</td>
<td>36 (1)</td>
<td>3 (0)</td>
</tr>
<tr>
<td>Antibiotic prescribed at follow-up:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any antibiotic</td>
<td>449 (12)</td>
<td></td>
</tr>
<tr>
<td>Antibiotic switched</td>
<td>226 (6)</td>
<td>161 (10)</td>
</tr>
<tr>
<td>Antibiotic prescribed for those not initially treated</td>
<td>223 (6)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

* Comparison of children 38°C to 38.9°C who were and were not prescribed an antibiotic at first visit, *P* ≤ 0.01.

† Comparison of children ≥39°C who were and were not prescribed an antibiotic at first visit, *P* ≤ 0.01.

‡ Number of “ANY follow-up” is smaller than the sum of in person and telephone because some patients received both.
SUMMARY OF THE CLINICAL CASES

- **Case 1**: 10-year-old boy presented with a temperature of 39.6°C and was diagnosed with H. influenzae meningitis, which was treated with an oral antibiotic for otitis media. No pathogen was identified.
- **Case 2**: 20-month-old boy presented with a temperature of 40.6°C and was treated with an oral antibiotic for otitis media. There was no preceding office visit.
- **Case 3**: A 5-year-old boy presented with a temperature of 39.4°C and was diagnosed with bronchiolitis and had no testing or treatment. No pathogen was identified.
- **Case 4**: A 3-year-old boy presented with a temperature of 39°C and was treated with an oral antibiotic for otitis media. There was no preceding office visit.
- **Case 5**: A 1-year-old boy presented with a temperature of 39.6°C and was treated with an oral antibiotic for meningitis. There was no previous febrile visit (not including care in the emergency department).

**Note**: The rate of culture-positive meningitis in our population, 33/100 000 (95% CI: 15, 36) was consistent with the 15/100 000 reported by national surveillance programs. In 2015, 10 of the 15 cases (67%) cases treated as meningitis or who had fatal sepsis had no previous febrile visit (not including care within 24 hours of admission). Four of the remaining 5 were treated according to guideline recom-
mandations, leaving only 1 who would have received different care based on strict adherence to the guideline. The fact that 3 children who subsequently developed meningitis had only mild fever at their previous visit suggests that a single temperature ≥39°C documented in the office may not be a sensitive criterion for who may develop meningitis. However, testing all children with fevers ≥38°C would dramatically increase the number of episodes treated or tested.

These data should be interpreted in light of several caveats. We chose to measure only rates of meningitis, meningococcemia, and death from sepsis because they are the most severe potential sequelae of untreated bacteremia. We believe that it is concern for these life-threatening infections that have been the primary drivers of recommendations for testing and treatment of children with fever without a clear source. Other serious bacterial infections including osteomyelitis, septic arthritis, and others would be important to include in a comprehensive analysis of the sequelae of bacteremia. Also, we identified cases of possible or probable meningitis, relying on hospital claims for this diagnosis with confirmation by very “liberal” criteria. We chose to err on the side of maximizing the rate of possible meningitis cases to test the upper bound of the usefulness of an aggressive approach to testing or treating all highly febrile children.

Finally, we excluded patients admitted to the hospital within 24 hours of the only primary care visit. We did this because we sought data on the outcomes of treatment of fever without a source to prevent sequelae of bacteremia, rather than on the accurate diagnosis and management of children who present to their primary care site with signs and symptoms of meningitis or sepsis.

The use of automated managed care data allows analysis of treatment patterns and outcomes in defined populations of children, and calculation of rates of both rare and common events. Ascertainment of the use of medical care services from office visits to hospitalizations is nearly complete, and the denominator of covered children can be calculated precisely based on registration data. Although using such cohorts differs from studying geographically defined populations, managed care systems are an important source of data for epidemiologic and health services research. The generalizability of conclusions from such work depends on the representativeness of the managed care population with regard to the broader community. Likewise, additional research is required to determine if the practices of clinicians in these settings reflect those of local peers practicing in other systems of care.

The practice guideline for febrile children published in Pediatrics in 1993 was a consensus statement of recognized experts, but was not endorsed by the American Academy of Pediatrics or Red Book Committee. In the practices we studied, the majority of febrile children were diagnosed with a bacterial source and treated with an antibiotic; of those who fit the criteria for the guideline, 36% received recommended laboratory testing. Strict adherence to the recommendations would have resulted in 1570 additional tests performed in our population. Whether a change in practice toward more aggressive screening for bacteremia is warranted remains an important question whose answer depends on the effectiveness, costs, and discomforts of testing and treatment, the morbidity and costs of meningitis and other serious infections, and the preferences of families. Further work on specific epidemiologic and clinical criteria for improved diagnosis of viral illness may identify a group of children at sufficiently low risk of bacteremia to obviate the need for further testing. In addition, clinical history including the height and duration of fever at home may be informative.

We support the continuing attempts to improve the management of children with fever in primary care settings based on the best available evidence. The benefits and potential disadvantages of increased screening and treatment of febrile episodes in primary care settings beyond the rates observed here are uncertain. However, it is unlikely that more aggressive management will substantially decrease population-based rates of meningitis or sepsis in this age group. Because meningitis and bacterial sepsis are rare, continued monitoring of management and outcomes in large, defined populations will be necessary to further refine guidelines for children with fever.

ACKNOWLEDGMENTS

This study was supported by the Harvard Pilgrim Health Care Foundation. Additional institutional support for this work was provided by the CVS Foundation.

We thank Gary Fleisher, MD, for his helpful comments on earlier drafts of this manuscript, and our colleague, Irina Miroshnik, for her contributions to this analysis.

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Jonathan A. Finkelstein, Cindy L. Christiansen and Richard Platt

PEDIATRICS 2000;105;260

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