Management of the Febrile Child

Fever and the Pediatrician

- DS Smith 1970
- “...since the advent of modern clinical thermometry by Wunderlich in 1871, the ritual of temperature taking has been surpassed only by Alexander Graham Bell's invention in 1874 as the major curse of pediatrics.”
**Definition of Fever**

- **Traditional teaching**
  - 37.0°C (98.6°F)
- **Upper limit of normal for children**
  - 37.9°C (100.2°F)
- **Fever**
  - ≥ 38.0°C (100.4°F)

**Significant Fever - Related to Age of Infant**

- **< 3 months of age**
  - ≥ 38.0°C (100.4°F)
- **3 to 24 months**
  - ≥ 39.0°C (102.2°F)
How was the temperature taken?

- Accurate devices
  - Rectal thermometers
  - Oral thermometers
- Axillary, tympanic, skin devices are frequently unreliable
- History of fever is a fever

Antipyretics

- Alteration of acetaminophen and ibuprofen has not been proven to provide faster defervescence
- Combination did improve time without fever during the first 24 hours
- PARENTAL CONFUSION AND SUBSEQUENT OVERDOSE CAN LEAD TO TOXICITY
Defervescence

- There is no correlation between defervescence with antipyretics and incidence of serious infection
- Converse is also true

Children 0-24 months of Age
Concern for Significant Fevers

- Serious bacterial infections (SBI)
  - Bacteremia
  - Meningitis
  - Pneumonia
  - Urinary Tract Infection*
  - Soft tissue/ Bone/ Joint Infection
- Serious viral infections
  - HSV meningitis
Incidence of Serious Bacterial Infections (SBI)

- Wide range of incidences reported
  - 0-28 days
    - 9-13%
  - 2-3 months
    - 7.1%
  - 3 months to 2 years
    - 0.25-0.7%

Evaluation of febrile child

- History
  - Oral intake
  - Irritability and lethargy
  - Cough and tachypnea
  - Vomiting or diarrhea
  - Dysuria and incontinence
  - Underlying medical condition
### Physical examination

- Tachycardia, tachypnea or pulse oximetry
- Increased work of breathing and auscultation
- Oral lesions
- Abdominal tenderness
- Bone or joint pain
- Petechiae, cellulitis, exanthem

### Signs and Symptoms Predicting Severe Illness

- **Sensitivity**
  - 74%
- **Specificity**
  - 79%
Diagnostic Testing of Febrile Children

- CBC with differential
  - ANC
  - ABC
- ESR/ CRP/ procalcitonin (PCT)
- Blood culture
- Urinalysis
- Urine culture
- RVP/ PCR
- CSF analysis
- CXR

Blood Cultures

- Blood culture remains the GOLD STANDARD for diagnosis of bacteremia
- If drawing a CBC, obtain blood culture
Meningitis

- If considering the diagnosis of meningitis by history or physical examination
  - LP should always be performed
- If done, not obligated to proceed with antibiotics or admission

Lumbar Puncture

- Recommended on all febrile children
  - < 1 months of age
  - In all children less than 1 year of age who will be receiving parenteral antibiotics
- Remember Tube #4
  - Keep on ice
    - Viral PCR
CSF Normative Values

- Neonates age 0-28 days
  - WBC < 20/ mm³
- Young infants 29-60 days
  - WBC < 10/ mm³
- Older infants and children
  - WBC < 5/ mm³

CSF Pleocytosis

- PCR HSV 1/2
- PCR VZV
- PCR enterovirus (EVP)
“A single ‘best way’ just doesn’t emerge from the data available. What’s a pediatrician to do? Know the science of medicine, but also be ready to practice the art.”

- CBC/ diff
- Cultures of blood, urine, and CSF
- Tachypnea or leukocytosis (> 20,000/ microL) should have a chest radiograph
- Consider RVP or HSV work up
- Parenteral antibiotic therapy targeting the likely pathogens in the age group or obvious source
- Admit
Non-toxic Appearing Children

- Consider age
- Consider past medical history
- Consider physical exam
- Consider immunization status

SBI in Infants 0-3 months

- Gram positives:
  - Group B streptococcus
  - Enterococcus species
  - Staphylococcus aureus
  - Listeria monocytogenes
- Gram negatives:
  - Escherichia coli
  - Klebsiella species
  - Enterobacter cloacae
  - Salmonella species
Prevalence of SBI in Infants < 2 months of age

- Febrile neonates
  - SBI = 13%
- Febrile infants 1-2 months of age
  - SBI = 10%

Rochester Criteria for Infant at Low Risk for SBI (< 60 days old)

- Previously healthy infant without perinatal complications and with no previous Ab Rx
- Normal PE
- WBC count 5000-15000/ mm³
- Absolute band count < 1500/ mm³
- UA < 10 WBC/hpf on centrifuged cath specimen
**Variations of Rochester Criteria**

<table>
<thead>
<tr>
<th>Type of Low-Risk Criteria</th>
<th>Differences From Original Rochester Criteria</th>
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<tbody>
<tr>
<td>Rochester 2</td>
<td>If diarrhea, ≤5–10 WBCs per high-power field in stool</td>
</tr>
<tr>
<td>Modified Rochester</td>
<td>Normal inflammatory markers (C-reactive protein levels or ESR)</td>
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<tr>
<td>Milwaukee</td>
<td>CSF: ≤10 WBCs per mm³; WBC count: ≤15,000 cells per mm³ (no band criteria); urinalysis: ≤5–10 WBCs per high-power field, no bacteria; urine dipstick: negative LE/nitrite</td>
</tr>
<tr>
<td>Philadelphia</td>
<td>Infant observation score: ≤10; WBC count: ≤15,000 cells per mm³ (no band criteria); urinalysis: ≤10 WBCs per high-power field, few or no bacteria; CSF: ≤8 WBCs per mm³, no bacteria, nonbloody</td>
</tr>
<tr>
<td>Philadelphia 2</td>
<td>WBC count: ≤15,000 cells per mm³; band/neutrophil ratio: ≤0.2; CSF: ≤8 WBCs per mm³, no bacteria, nonbloody</td>
</tr>
<tr>
<td>Boston</td>
<td>WBC count: ≤20,000 cells per mm³ (no band criteria); CSF: ≤10 WBCs per mm³; urinalysis: ≤10 WBCs per high-power field, no LE</td>
</tr>
<tr>
<td>Pittsburgh</td>
<td>Enhanced urinalysis: ≤9 WBCs per mm³, negative Gram stain results; CSF: ≤5 WBCs per mm³, negative Gram stain results (if ≤6 wk)</td>
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**Impression of sepsis**

"Not ill" or negative clinical impression of sepsis (history, physical examination, ESR of <30 mm/h, WBC count of <15,000 cells per mm³).

WBC indicates white blood cell; ESR, erythrocyte sedimentation rate; CSF, cerebrospinal fluid; LE, leukocyte esterase. The infant observation score includes 5 observations, that is, quality of cry, reaction to parent stimulation and state variation, color, hydration, and response to social overtures, each scored on a scale of 1 to 5.
0 to 90 Day Old Infant
Temp ≥ 38°C or 100.4°F

- CBC with diff
- Blood culture
- UA/ UCx
- RVP if indicated
- Stool leukocytes/culture/hemoccult if diarrhea
- CXR if respiratory symptoms or WBC > 20K

Limitation of Protocols

- Recent data has demonstrated that these criteria are not applicable to 0-1 month old infants and could result in 10% of neonates (0-28 days) with SBI being categorized as low-risk
- THEREFORE …
  - ALL CHILDREN UNDER ONE MONTH OF AGE MUST BE EVALUATED FURTHER
0 to 28 Day Old Neonate

- Perform LP
0 to 28 Day Old Neonate

- Start empiric antibiotics ASAP
  - Ampicillin/ Cefotaxime/ Acyclovir
  - Add Vancomycin for Staph coverage if CSF concerning for meningitis or ill appearing
0 to 28 Day Old Neonate
Broad Spectrum Abx Coverage

- Admit

Serious Viral Infections in Neonates

- HSV
- Varicella
- Influenza
- RSV
- Enterovirus
- Adenovirus
HSV Work Up Indications

- **Historical & clinical features**
  - Severe illness, hypothermia, lethargy, seizures, postnatal HSV contact, vesicular rash, interstitial pneumonitis
HSV Work Up

- Laboratory features
  - Thrombocytopenia
  - CSF pleocytosis/ RBC’s/ (-) Gram stain

- CSF HSV PCR
- HSV PCR skin lesions
- LFT’s

Geisinger Rapid Viral Panel

- Introduced by the Geisinger microbiology laboratory in 2010
- xTAG RVP assay PCR technique offers advantages over the method previously used for the detection of respiratory viruses
Geisinger Rapid Viral Panel

- Influenza A
- Influenza B
- RSV
- Parainfluenza types 1,2,3,4
- Human metapneumovirus
- Rhinovirus

- Adenovirus
- Coronaviruses: HKU1, NL63, 229E, OC43
- Bordetella pertussis
- Chlamydophila pneumoniae
- Mycoplasma pneumoniae

Concomitant Viral Infections

- Presence of URI symptoms does not rule in viral etiology
- Presence of URI symptoms does not rule out SBI
- Infants with “recognizable viral syndrome” have a lower risk of bacteremia
  - Bronchiolitis
  - Croup
  - Varicella
  - Stomatitis
Incidence of SBI is 1.1 to 7% among febrile infants with bronchiolitis vs. 10-17% in high risk febrile infants without bronchiolitis.

However, risk of SBI among neonates (1-28 days) was NOT altered by presence of RSV.

Need full evaluation.
### 29 to 60 Day Old Infant
#### Low Risk Clinical Criteria

- Full term (≥ 37 weeks gestation)
- No prolonged NICU stay
- No chronic medical problems
- No systemic antibiotics within 72 hours
- Well appearing and easily consolable
- No serious focal source

### 61 to 90 Day Old Infant
#### Low Risk Clinical Criteria

- No chronic medical problems
- No systemic antibiotics within 72 hours
- Well appearing and easily consolable
- No serious focal source
29 to 90 Day Old Infant Laboratory Work Up

- Same initial work up as 0-28 old neonate
  - CBC with diff
  - Blood culture
  - UA/UCx
  - RVP if indicated
  - Stool leukocytes/Cx/Hemoccult if diarrhea
  - CXR if respiratory symptoms or WBC > 20K
29 to 90 Day Old Infant
Low Risk Laboratory Criteria

- CBC
  - WBC 5,000 to 15,000/ mm³
  - Absolute band count ≤ 1,500/ mm³
- UA
  - ≤ 10 WBC/hpf
  - Negative esterase and nitrites
- CXR negative if obtained
- Stool ≤ 5 WBC/hpf or hemoccult negative
29 to 90 Day Old Infant
Low Risk Discharge Criteria

- Feeding well
- No social/family concerns
- Reliable follow up in 12-24 hours
- Outpatient plan accepted by PCP and family

MAY BE DISCHARGED HOME
29 to 60 Day Old Infant
Low Risk Clinical Criteria NOT SATISFIED
Low Risk Clinical Criteria NOT SATISFIED

- LP

- Antibiotics ASAP
  - Ampicillin and Cefotaxime
    - Add Vancomycin if LP abnormal
  - Acyclovir if HSV work up indicated

- Admit
  - Regardless of LP results

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61 to 90 Day Old Infant
Low Risk Clinical Criteria NOT SATISFIED
Low Risk Clinical Criteria NOT SATISFIED

- Limited data

- One prospective study with infants 57-89 days of age days showed no increased SBI incidence than those 57-180 days

- THEREFORE… disposition remains controversial
61 to 90 Day Old Infant
Low Risk Clinical Criteria NOT SATISFIED
Low Risk Clinical Criteria NOT SATISFIED

- LP still recommended
- BUT disposition dependent on LP
  - LP normal
    - Discharge with 24 hour follow-up if discharge criteria meet on IM/IV Ceftriaxone
  - LP abnormal
    - Start antibiotics ASAP
      - Ceftriaxone/ Vancomycin
      - Admit

“Classic Predictors of Bacteremia”

- Risk of bacteremia exceeded over 10%
  - Age 3 to 24 months
  - Fever ≥ 39° C
  - WBC ≥ 15,000/ microL
**Diagnostic Testing**

**CBC with differential**

- 5 fold higher risk of bacterial infection if WBC > 15,000
- WBC < 5,000 also carries an increased risk

**Pneumonia**

- Most children with fever and pneumonia have some abnormality on PE
  - Tachypnea
  - Abnormal auscultation
  - Nasal flaring
- However, a reliable physical examination in a young child can be a challenge
**WBC Counts**

- In a prospective study, radiographic pneumonia was found in **20 to 30%** of highly febrile young children (< 5 years) without clinical evidence of pneumonia, but with a **WBC ≥ 20,000/ microL**

- **WBC > 25,000**
  - Most common diagnosis was pneumonia
  - Second most common is viral syndrome

**CXR**

- Order CXR if WBC > 20,000 even in the absence of physical findings

- Otherwise, unless signs of lower respiratory disease, CXR is not part of the routine work up
### Inflammatory Makers

- Multicenter, prospective observational study of 6579 children, 3-36 months of age, with FWS ≥ 39°C
- ANC ≥ 10,000/ mm³
- ABC ≥ 1,500/ mm³
  - Sensitivity 76%
  - Specificity 78%

### Inflammatory Mediators

- CRP
  - Wide range of sensitivity and specificity that vary by cutoff levels
  - 12 hour delay from onset of fever
- Procalcitonin
  - More rapid rise than CRP
  - Preliminary data suggest greater sensitivity and specificity for SBI than WBC, ANC, CRP
Occult Bacteremia in Infants (3-24 months)
preHIB/Pneumococcal Immunizations

- S. pneumonia (80%)
  - 13 vaccine serotypes
  - Nonvaccine serotypes
- H. influenza Type B (20%)
- N. meningitidis
- Others

3 to 6 Month Old Infant
Fever ≥ 39°C or 102.2°F

- We need to worry about the “old players” in this incompletely immunized group
  - Haemophilus influenza type B
  - Streptococcus pneumoniae
Immunization Status

- **“Complete” immunization**
  - Primary series of 2-3 immunizations for HIB3/HIB4
  - Primary series of 3 immunizations for PCV13

- **Incomplete immunization**
  - < 6 months of age
  - NOT received the primary series of 3 PCV13 and 2-3 HIB immunizations

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**3-6 Month Old Infant**
Fever ≥ 39°C or 102.2°F

**Clinical Criteria**
- No Meningitis
- No systemic abx w/ ± 12h
- Well appearing
- No serious fecal source

**Laboratory Criteria**
- UA ≤ 10 WBC/hpf, negative nitrite/nitrate
- CBC WBC 5,000 to 15,000/mm², ABC < 1,500/mm²
- CSF: Negative if obtained
- Stool ≤ 5 WBC/hpf, hemocultic negative

**Antibiotic Therapy**
- PO: Cefixime (double 1st dose)
- IM/IV: Ceftriaxone
- Meningitic doses are used initially
- Add Vancomycin if CSF WBC >10/mm³, abnormal protein/glucose, OR gram-positive organism on gram stain

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**Initial Work-up**
- CBC with diff
- Blood culture
- UA/UC
- R/V if indicated
- Stool WBCs/CX/hemocult (if diarrhea)
- CSF if 5x or WBC>20K

**D/C Criteria**
- Feeding well
- No soc/ftl concern
- Reliable follow-up in 12-24 hours
- Outpatient plan accepted by PCP and family

**Follow-up**
- 24h

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**3-6 Month Old Infant**
Fever ≥ 39°C or 102.2°F

**Antibiotics Admission**
- **N** IM/IV Ceftriaxone
- **Y** LP normal

**Antibiotics Admission**
- **N** N
- **Y** IM/IV Ceftriaxone

**PO** Cefixime (double 1st dose)

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**Meets D/C Criteria**

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**Meets All Low Risk Clinical & Lab Criteria**

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**Initial Work-up**

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3 to 6 Month Old Infant
Fever ≥ 39°C or 102.2°F

- Laboratory work up/ laboratory low risk inclusion criteria are the same as the 0 to 90 day old infants
  - CBC with diff
  - Blood culture
  - UA/ UCx
  - RVP if indicated
  - CXR if respiratory symptoms or WBC > 20K
  - Stool leukocytes/culture/ hemoccult if diarrhea
- Low risk clinical criteria are same as 61-90 day old infant
  - No PMHx
  - No systemic antibiotics within 72 hours
  - Well appearing
  - No serious focal source

Initial Work-up

Meets ALL Low Risk Clinical & Lab Criteria

- CBC with diff
- Blood culture
- UA/ UCx
- RVP if indicated
- Stool WBC/UCx/hemoccult (if diarrhea)
- CXR if 3a or WBC>20K

Clinical Criteria
- No PMHx
- No systemic abx w/ 72°
- Well appearing
- No serious focal source

Laboratory Criteria
- UA ≤ 10 WBC/3μl, negative enzyme/ nitrites
- CBC: WBC 5,000 to 15,000/μl, ABC < 1,500 mm³
- CXR: Negative if obtained
- Stool ≤ 5 WBC/μl, hemoccult negative

Antibiotic Therapy
- PO Cefixime (double 1st dose)
- IM/IV Ceftriaxone
- Meningic doses are used initially
- Add Vancomycin if CSF WBC ≥ 10/mm³, abnormal protein/glucose, OR gram positive organism on gram stain

Antibiotics Admission

Meets D/C Criteria

- N
- WBC < 5,000 or > 15,000 OR
  - ABC > 1,500
  - Regardless of UA result
- LP normal
- IM/IV Ceftriaxone

Tolerating PO

PO Cefixime (double 1st dose)

Follow-up 24°
3 to 6 Month Old Infant

- WBC abnormal < 5000 or > 15000/ mm³ or ABC abnormal > 1500/ mm³
- Regardless of UA results

LP (strongly recommended!!!!!)
Ceftriaxone IM/IV
24 hour follow up
Must meet low risk discharge criteria

Journal of Pediatrics
1994 124: 505-512

- Conclusion:
  - Ceftriaxone eradicated bacteremia, prevented significantly more definite focal bacterial complications, and was associated with less persistent fever
3 to 6 Month Old Infant
Probable UTI with normal WBC/ABC

- If tolerating fluids
  - PO Cefixime po (double first dose)
- If vomiting - parenteral treatment indicated
  - Perform LP
  - IV/IM Ceftriaxone
- 24 hour follow up
  - Must meet low risk discharge criteria
  - If urine culture is positive
    - Complete 14 days course of Cefixime
    - Renal work up
Urinary Tract Infections Prevalence

- 0 to 3 months 7.2%
  - Girls 7.5%
  - Circumcised boys 2.4%
  - Uncircumcised boys 20.1%
- 3 to 6 months 6.6%
  - Girls 5.7%
  - Boys 3.3%
- 6 to 12 months of age 5.4%
  - Girls 8.3%
  - Boys 1.7%
- 12 to 24 months of age 4.5%
  - Girls 2.1%
  - Circumcised boys < 1%

Urinary Tract Infections Prevalence

- Accounts for 1/3 of all bacterial disease in febrile infants < 3 months of age
Urinalyses

- Urine screening tests markedly improve the ability to detect UTI
- Negative dipstick does not exclude UTI
  - 20% of febrile infants with pyelonephritis had absent pyuria
  - 50% of infants with UTI had negative nitrites

Urine culture

- Urine culture remains the gold standard
- Urine cultures should be obtained by urethral catheterization or suprapubic tap
800 infants not initially tested
- Found few late diagnoses of UTIs
- No cases of UTIs with bacteremia
Diagnosis and Management of Bacteremic UTI in Infant

- 1379 UTIs in infants < 1 year of age
  - 52% blood cultures obtained
    - Bacteremia incidence of 4.1% overall
    - Bacteremia incidence of 8% in which BCx obtained
  - No significant difference in clinical presentation between the 2 groups
  - Risk of bacteremia with UTI
    - Inversely related to age (bacteremia is more if < 6 months)
    - Higher serum band count
    - Higher incidence noted with high grade VUR or obstruction

Oral Versus Initial Intravenous Therapy for Urinary Tract Infections in Young Febrile Children

- Study. Trial of oral Cefixime for infants aged 1 to 24 months with UTI, 13 patients had bacteremia; 5 in the oral Cefixime only arm and 8 in the IV Cefotaxime (3 days) plus oral Cefixime (11 days) arm.

- All 13 patients had clearance of bacteremia within 24 hours with no renal scarring.
6-24 Month Old Infant/Toddler
Increased Clinical Risk of Bacteremia

- Incomplete primary series of pneumococcal/HIB vaccines
- Temp > 40.5°C
- Fever > 5 days
- Immunocompromised
- Chronic illness
- Soft tissue/ bone/ joint infection
6-24 Month Old Infant/Toddler
Increased Clinical Risk of Bacteremia

- Follow the 3 to 6 month old infant algorithm

Post Conjugate Vaccine Era

- With a rate of pneumococcal bacteremia < 0.5%
  - WBC plus selective blood cultures are no longer cost-effective
### “Other” Organisms of Occult Bacteremia

- N. meningitidis
- Group A streptococcus
- Salmonella species
- E. coli
- Staphylococcus aureus

*Laboratory parameters (such as WBC > 15,000/ microL) may be less reliable predictors of bacteremia with these pathogens*

### Urinary Tract Infection Prevalence

- Accounts for ~ 7% of febrile illnesses between the ages of 2 months to 2 years
Urinalysis/ Catheterized or Suprapubic Ucx

- All girls < 2 years of age
- All circumcised boys < 6 months of age
- All uncircumcised boys < 12 months of age

Journal of Pediatrics
1993 123:17-23

- No difference found in rate of UTI in those children without a source for infection (5.9%) and those with other likely sources, i.e. OM or immunization reaction, (5.1%).
6-24 Month Old Infant
Temperature > 39 C or 102.2 F

- **Bacteremia Risk Factors**
  - Incomplete primary series of pneumococcal/HBV vaccines
  - Temp > 40.5
  - Fever > 5 days
  - Immunocompromised
  - Chronic illness
  - Soft tissue/ bone/ joint infection

- **Initial Work-up**
  - UA/UCx
  - All girls
  - Uncircumcised boys < 12 months

- **Observation**
  - Cefixime (double 1st dose)

- **Complete 14 day course of Cefixime & Renal Work-up**

- **UA < 10 WBCs/hpf**
  - Esterase/Nitrite negative

- **Tolerating PO**

- **IM/IV Ceftriaxone**
  - Consider UP < 12 months

- **Stool leukocytes/culture if bloody diarrhea**

- **CXR if respiratory symptoms**

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6 to 24 Months Old Infant/Toddler
Fever ≥ 39°C or 102.2°F

- **UA/ UCx**
  - All girls
  - Uncircumcised boys < 12 months

- **RVP PCR if indicated**

- **Stool leukocytes/culture if bloody diarrhea**

- **CXR if respiratory symptoms**
6 to 24 Month Old Infant/Toddler

- **Abnormal UA**
  - Cefixime if able to tolerate po
    - Remember to double first dose
  - Ceftriaxone (consider LP at younger age range)
  - Need follow up with PCP
  - If urine culture positive
    - Complete 14 days course of cefixime
    - Renal work up

2016 On-going Concerns

- **Serotype replacement for IPD**

- **New invasive serotypes have emerged since the older 7 valent conjugated pneumococcal vaccine was introduced**

- **“Newer” conjugated pneumococcal vaccine now includes 13 serotypes**

- **HOWEVER…**
  - Honeymoon period never lasts forever!
Dr Prober’s Golden Rules

- The younger the child the greater the uncertainty
- A toxic appearance demands immediate action
- A nontoxic appearance fuels controversy
- Careful follow-up must be assured
- Recommendations continue to evolve
- Respond to test results or do not order test
- Document what you are and are not doing
- No rules are golden

Fever and the Pediatrician
DS Smith 1970

“… since the advent of modern clinical thermometry by Wunderlich in 1871, the ritual of temperature taking has been surpassed only by Alexander Graham Bell’s invention in 1874 as the major curse of pediatrics.”
My One Last Addition for 2016

… unfortunately the thermometer and telephone have since been dwarfed as the major bane of pediatrics by J. C. R. Licklider in 1957 with his first conception of the internet.