The Red Book Through the Ages

abstract

The first edition of the Red Book was published in 1938. Since then, there have been numerous advances in the fields of infectious diseases and public health that have decreased morbidity and mortality of infants, children, and adolescents. Over the years, emerging pathogens and disease complexes have been described, sophisticated diagnostic techniques developed, advances in antimicrobial therapy have occurred, and immunizations have been implemented to prevent previously deadly diseases. Of the 18 diseases or organisms in the 1938 edition, 13 are now vaccine-preventable. Since inception of the Red Book, the aims of the editors have been to keep pace with these innovations and to continue to inform the medical community. These goals have made the Red Book a fundamental resource for pediatricians and other health care professionals in terms of guiding diagnosis, therapy, and prevention of infectious diseases. The list of 18 diseases or organisms originally described in the 1938 Red Book has expanded to include over 160 diseases or organisms in the 2012 edition. The pace of biomedical discovery, as well as the amount of information available and the number of methods for its delivery, will continue to accelerate in the future. Integration of information into future editions of the Red Book will ensure that practitioners continue to rely on the Red Book in its various electronic formats for clinical guidance and support. Pediatrics 2013;132:898–906

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ABBREVIATIONS

AAP—American Academy of Pediatrics
ACIP—Advisory Committee on Immunization Practices
COID—Committee on Infectious Diseases
FDA—US Food and Drug Administration
GRADE—Grading of Recommendations Assessment, Development, and Evaluation

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In the course of providing a comprehensive guide to management and prevention of infectious diseases in children, the process and scope of the American Academy of Pediatrics’ (AAP) Red Book has evolved continuously and dramatically.\textsuperscript{1–17} The first Red Book was published by the AAP in 1938 as an 8-page document (Fig 1). The 2012 Red Book, Report of the Committee on Infections Diseases is the 29th edition and is an internationally recognized authoritative reference source, which has become a comprehensive, preeminent guide to diagnosis, treatment, management, and prevention of pediatric infectious diseases.

The 2012 edition is 1058 pages in length (Fig 2), is published in 5 languages (including English) (Table 1) and also is available in electronic format with references to \textasciitilde 2600 related images.

Growth and evolution of the Red Book during the 75 years since the first publication in 1938 reflects changes and tremendous advances in the fields of infectious diseases, public health, antimicrobial therapy, diagnostic assays and technologies, and immunizations.\textsuperscript{13} The Red Book continues to evolve to keep pace with changing clinical practice and innovations in pediatric care. An application for mobile devices including smartphones and tablets was introduced, so practitioners can access the wealth of information in the Red Book at any time.\textsuperscript{5}

Preparation of the Red Book by the Committee on Infectious Diseases (COID) is a laborious, 3-year process, involving not only committee members but also multiple liaisons, collaborators, consultants, and reviewers appointed by the AAP Board of Directors. Stanley A. Plotkin, the COID Chair from 1987 to 1990, in the preface to the 1988 edition, noted as follows: “Despite all this, The Red Book manages to come out as one of the best textbooks on infectious diseases available, and certainly the handiest. Moreover, the creation of this book, difficult and frustrating though it often is, remains a joy and pride for the Committee members, all of whom believe they are contributing to something useful and important.”

\textbf{EARLY HISTORY OF THE COID}

After the establishment of the AAP in 1930 in the library of Harber Hospital in Detroit, committees were formed to study and make recommendations on a broad range of issues involving health care and disease prevention for children. In 1933, the AAP established a Special Committee on Prophylactic Procedures Against Communicable Diseases, chaired by Edward B. Shaw of San Francisco and including J. E. Gordon of Detroit and John A. Toomey of Cleveland. This committee produced a 6-page...
The report entitled, “Routine measures for the prophylaxis of communicable diseases,” which was published in 1935. The report provided practical recommendations concerning diphtheria, scarlet fever, typhoid fever, whooping cough, measles, smallpox, poliomyelitis, epidemic (meningococcal) meningitis, mumps, chickenpox, rabies, and tetanus. This 6-page report was the forerunner of the first Red Book; 11 of the 12 aforementioned diseases are now vaccine-preventable. This group disbanded, but because of the importance of addressing the many infectious diseases of childhood, the AAP Executive Board in 1936 created the Committee on Immunization Procedures as a permanent standing committee. Toomey was chosen as chairman in part because of his involvement in the 1935 report and also because of his research on poliomyelitis. The 5 other members of the committee were Shaw, Horton Casparis (Nashville), E. J. Hueneekens (Minneapolis), Charles McKhann (Boston), and Bela Schick (New York).

The first effort of this committee was published as a mimeographed report in 1937. Subsequently the committee prepared a more comprehensive report on the value of various methods of active and passive immunity available at the time. The report was published by the AAP in January 1938 and distributed to all AAP members (Fig 1). The guide, which was in essence a handbook for the practicing pediatrician, was titled, Report of the Committee on Immunization Procedures of the American Academy of Pediatrics and was the first “Red Book.” This title was the first of 7 formal names for the Red Book (Table 2). The 1938 pamphlet was revised and published almost every year for the next 10 years (1938–1947), a reflection of the rapid pace of advances in medicine at the time. According to James Hughes, “a great demand from physicians, medical students, health departments, and pharmaceutical houses” ensued. Printed with a bright red cover, the report became known as “the Red Book.”

The AAP’s executive board then created a publication fund in 1962, dedicated to financing the publishing and distribution of the Red Book. The actual assembly and publication of the Red Book is the responsibility of the COID, a committee of 13 AAP members with expertise in infectious diseases, vaccinology, and public health appointed by the Board of Directors of the AAP. Once approved by the AAP Board of Directors, the Red Book is published as official AAP policy.

EDITORS AND ASSOCIATE EDITORS OF THE RED BOOK

John Toomey, who also served as AAP president from 1947 to 1948, edited the first 8 editions of the Red Book from 1938 to 1947. Nine subsequent editors of the 22 editions of the Red Book, from 1948 to 2015, have followed Toomey’s tenure (Table 3). In the 1970s, according to Samuel Katz, COID chair from 1966 to 1976, liaison representatives from the Centers for Disease Control and Prevention (CDC), the Canadian Pediatric Society, and the US Food and Drug Administration (FDA) were added to the COID, and also contributed to Red Book content.
In preparing the 1982 edition, then-editor Jerome O. Klein was the first to appoint associate editors, each of whom was responsible for specific sections and chapters. The first associate editors were Vincent Fulginiti, James Cherry, and Philip Brunell, the latter of whom was COID chair from 1983 to 1987. All subsequent Red Book editions have had associate editors (Table 4).

By the mid-1980s, preparation of the Red Book had become increasingly difficult due to the overwhelming amount of available information, undermining efforts of the AAP to provide timely publication at regular intervals of every 2 to 3 years. To address this challenge, the decision was made in 1986 to appoint a permanent editor. After a search, Georges Peter, who had edited the 1986 edition, was appointed. He provided oversight for 5 editions, and then served as editor emeritus through the 2000 edition, which was dedicated to him. His successor, Larry Pickering, served as editor through the 2012 edition, after having served as associate editor, with Dr Peter, for 2 editions. The most recently appointed editor of the 2015 edition, David Kimberlin, was an associate editor of the 2009 and the 2012 editions.

The 2012 edition had 5 associate editors, 2 of whom consulted exclusively on electronic delivery of information in the Red Book, serving as Online Associate Editor and Visual Red Book Associate Editor. More information on the Red Book in the digital age is provided later in this article.

**THE RED BOOK IN CONTEXT OF DEVELOPMENTS IN INFECTIOUS DISEASE TREATMENT**

The Red Book was published every 1 to 5 years between 1938 and 1986. Since 1988, the Red Book has been updated every 3 years and includes AAP statements dealing with vaccines and infectious diseases that are published in Pediatrics between Red Book editions and, more recently, at http://aappublications.org/. The first non-English language edition was published in Spanish in 1970 (Table 1). At the time of the publication of the first Red Book in 1938, children frequently were hospitalized for pneumonia, bacterial meningitis, diphtheria, typhoid fever, tuberculosis, endocarditis, syphilis, or rheumatic fever (for none of which was specific, effective antimicrobial treatment available, other than the new sulfa agents).
Alexander Fleming's discovery of penicillin occurred in 1929, the first dose was not given in the United States until 1942. As a result, most hospitalized children with bacterial infections in 1938 suffered sequelae or died.

Knowledge about the natural history of many infectious diseases existed at the time of the Red Book's first publication and provided the basis for development of both prevention and cure for these diseases. The 1938 Red Book included 18 diseases (Table 5), each of which was addressed under 1 of the following 3 headings: A. Tests; B. Active Immunity; and C. Passive Immunity. The only 3 tests available at the time were the Dick test for susceptibility to scarlet fever, the Schick test for immunity to diphtheria, and the tuberculin skin test. Advances in the fields of molecular and biomedical technology have led to development of many diagnostic methods that are now used or will be used in the future in diagnosis and management of infectious diseases. All Red Book editions have added information about newer assays and technologies.

**ANTIMICROBIAL DEVELOPMENT**

In 1937, elixir sulfanilamide, containing the poisonous solvent diethylene glycol, killed 105 people, many of whom were children, across 15 states. This tragedy highlighted the need to establish drug safety before marketing and to enact the pending food and drug law. In 1938, the Federal Food, Drug, and Cosmetic Act was passed by Congress, requiring new drugs to be demonstrated as safe before marketing, which started a new system of drug regulation (http://www.fda.gov/AboutFDA/WhatWeDo/History/ForSHistory/CDER/CenterforDrugEvaluationandResearchBrochureandChronology/ucm114463.htm).

In 1938, recommendations for antimicrobial therapy were minimal and consisted of only 1 antimicrobial agent (sulfanilamide), which was mentioned in the first Red Book to treat 3 conditions: erysipelas, epidemic (meningo-coccal) meningitis, and pneumococcal pneumonia (for the latter, combined with type-specific antiserum). The first use of an antibiotic in America occurred in 1935 when a sulfonamide compound was given to a 10-year-old girl at Babies Hospital of the Columbia Medical Center in New York to treat, ultimately unsuccessfully, invasive Hemophilus influenzae b meningitis. By contrast to the 8-page 1938 version, Section 4 of the 2012 Red Book, entitled "Antimicrobial agents and related therapy," is 71 pages in length and includes subsections dealing with antimicrobial stewardship; principles of appropriate use; and drug doses for antibacterial, antifungal, and antiviral agents; as well as drugs for parasitic infections and recommendations for treatment of sexually transmitted infections. In addition, guidance for use of tetracyclines and fluoroquinolones in children has been updated and standardized in the 2012 edition. The chronology of drug regulation and FDA approval in the United States can be reviewed, by drug, at http://www.

### TABLE 5 Chapters and Immunization Recommendations in the 1938 Red Book 2012

<table>
<thead>
<tr>
<th>Chapter Title</th>
<th>Antimicrobial Active Immunity</th>
<th>Passive Immunity</th>
<th>Active Immunization</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. The common cold</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>II. Diphtheria</td>
<td>None</td>
<td>Toxin antitoxin; diphtheria toxoid; alum precipitated; toxoid</td>
<td>Yes</td>
</tr>
<tr>
<td>III. Epidemic encephalitis</td>
<td>None</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>IV. Erysipelas</td>
<td>Sulfanilamide</td>
<td>Yes for recurrent disease</td>
<td>Yes</td>
</tr>
<tr>
<td>V. Epidemic meningitis</td>
<td>Sulfanilamide</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>VI. Epidemic parotitis</td>
<td>None</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>VII. Pertussis</td>
<td>None</td>
<td>Krueger's endo-antigen; Sauer's vaccine; Old fashioned vaccine</td>
<td>Yes</td>
</tr>
<tr>
<td>VIII. Pneumonia</td>
<td>Sulfanilamide</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>IX. Poliomyelitis</td>
<td>None</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>X. Babies</td>
<td>None</td>
<td>Semple's or Cumming's vaccine post exposure</td>
<td>Yes</td>
</tr>
<tr>
<td>XI. Measles</td>
<td>None</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>XII. Scarlet fever</td>
<td>None</td>
<td>Streptococcus toxin</td>
<td>Yes</td>
</tr>
<tr>
<td>XIII. Staphylococcal infections</td>
<td>None</td>
<td>Staphylococcus toxic (experimental)</td>
<td>None</td>
</tr>
<tr>
<td>XIV. Tetanus</td>
<td>None</td>
<td>Tetanus toxoid</td>
<td>Yes</td>
</tr>
<tr>
<td>XV. Tuberculosis</td>
<td>None</td>
<td>BCG</td>
<td>Yes</td>
</tr>
<tr>
<td>XVI. Typhoid fever</td>
<td>None</td>
<td>Typhoid fever vaccine</td>
<td>Experimental</td>
</tr>
<tr>
<td>XVII. Varicella</td>
<td>None</td>
<td>Vesicle contents</td>
<td>Yes</td>
</tr>
<tr>
<td>XVIII. Varicella</td>
<td>None</td>
<td>Calf vaccine smallpox virus</td>
<td>None</td>
</tr>
</tbody>
</table>

* For certain bacteria.
DEVELOPMENT OF IMMUNIZATION

Of the 18 diseases or disease-causing organisms included in the 1938 edition of the Red Book, vaccines were available for prevention of 7 infections. Except for variola (smallpox) recommendations for active or passive protection, the 6 other vaccines were believed to be ineffective, had not been appropriately tested, and were not licensed by the FDA. Eleven of the 18 diseases or organisms discussed in the 1938 Red Book now are prevented by immunization, variola has been eradicated, and wild-type poliomyelitis has not occurred in the Western Hemisphere since 1991. Since promulgation of the first yearly, national immunization schedule in 1995, which was published in the 1997 Red Book (Fig 3), the number of recommended vaccines has increased from 9 to 16 in the childhood and adolescent immunization schedules (http://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html). A separate and expanded adolescent schedule was first added to the Red Book in 2009. Zoster vaccine is now included in the adult immunization schedule (http://www.cdc.gov/vaccines/schedules/hcp/adult.html). In addition to prevention of infectious diseases, vaccines for hepatitis B and for human papillomavirus prevent several types of cancer. A timeline of vaccine development is shown in Fig 4. Currently available vaccines have demonstrated remarkable success in preventing human infectious diseases and have heralded the arrival of a new era and expanded horizon for vaccines.14,15

LIAISONS AND COLLABORATORS

From its earliest days, evolution of the Red Book has gone hand-in-hand with the ever-changing development of the COID. Since its inception, the size of the COID, including liaison members, has more than doubled. The committee increasingly has included liaisons from other AAP sections, from professional organizations with related interests, such as the Pediatric Infectious Diseases Society, and from governmental agencies (Table 6). Whereas the 1977 Red Book listed only 3 CDC collaborators, the 2012 edition listed a total of 348 collaborators, of whom 180 were from the CDC, 55 were from the FDA, and 4 from the National Institutes of Health. Beginning with the 1986 edition, each chapter has had at least 1 CDC and at least 1 FDA reviewer. The COID has drawn not only on resources in the public sector but also upon resources from academia and from physicians in private practice. Former COID Chair Philip Brunell noted in the introduction to the 1986 edition that the committee has “tried to seek out the most knowledgeable individuals for each subject; others have volunteered information, which has been gratefully received.” For each edition of the Red Book, the editors also have appointed consultants on an as-needed basis.
including experts on parasitology, mycoses, infection control, and antimicrobial agents, as well as former COID members. This process of seeking broad participation in preparation of each edition illustrates the work and challenges of committee members, and particularly the editors, in seeking concise, comprehensive, and practical recommendations for management of pediatric infectious diseases. Furthermore, this process has established the Red Book as a highly authoritative source of information on the most current treatments and preventive measures.

ADDRESSING CHALLENGES AND LIMITATIONS

The AAP strives to provide evidence-based recommendations. All recommendations made by the COID and included in the Red Book are based on evidence, but not all undergo a formalized process of data evaluation.11

In 2010, the Advisory Committee on Immunization Practices (ACIP) of the CDC approved adoption of an evidence-based method for making vaccine recommendations.1,18 The system adopted was Grading of Recommendations Assessment, Development, and Evaluation (GRADE). The GRADE process was introduced by the ACIP in October 2011, is now fully implemented, and will be used on all future ACIP vaccine recommendations.1 GRADE also is used by the Strategic Advisory Group of Experts, an independent advisory committee with a mandate to advise the World Health Organization on immunization policy and related infectious disease practice.8 GRADE has been implemented by more than 60 professional societies and organizations. GRADE also ensures transparency and scientific credibility.
of recommendations. For vaccine recommendations, the AAP accepts the GRADE evidence assessments of ACIP. Two COID members serve as liaison members to ACIP, and current COID members are well represented in ACIP work groups, reflecting the active role of the AAP in making national vaccine recommendations for infants, children, and adolescents.

Other COID recommendations in the Red Book are based on thorough literature reviews as part of the process of preparing, revising, and vetting each Red Book chapter, but do not entail a standard process such as GRADE. A recent study evaluated the quality of development and reporting of AAP guidelines and also determined the level of evidence underlying the recommendations by using the Appraisal of Guidelines for Research and Evaluation II. The AAP guidelines scored low on the Appraisal of Guidelines for Research and Evaluation II scale. This report did not enumerate differences among specific committee recommendations. All information in the Red Book is supported by thorough literature review, input from experts, and discussion by COID members. The AAP is working to develop and implement a standard, transparent process for guideline development, similar to that which is used for vaccine development.

A complete listing of references in the Red Book, while often reviewed in COID discussions, is not feasible. This issue is addressed partially by citation of AAP policy statements that are prepared by the COID and published in Pediatrics. The Red Book also cites each ACIP vaccine recommendation, as well as other CDC infectious diseases recommendations published in Morbidity and Mortality Weekly Report and evidence-based guidelines from other societies including the Infectious Diseases Society of America and the American Heart Association. Examples include statements on specific vaccines in the childhood and adolescent immunization table, as well as yearly influenza vaccine updates. Citation and cross-referencing will become easier, and with online versions of Red Book editions, more feasible.

Some recommendations and guidelines in the Red Book are based on expert opinion and in circumstances with limited or inconclusive evidence. Though the reviews by outside experts and discussions at COID meetings often result in consensus, in some instances no single recommendation can be made, as several options for management are deemed acceptable. To incorporate these differences of opinion, the committee adopted the following guidelines, set forth in the introduction of the 1994 Red Book:

“In making its recommendations, the Committee acknowledges those differences in viewpoints by judicious use of the phrases ‘most experts recommend...’ and ‘some experts recommend...’ Both phrases indicate valid recommendations, but the first signifies more support among experts, and the second, less support. Hence, ‘some experts recommend...’ indicates a minority view that is based on data and/or experience and is sufficiently valid to warrant consideration.”

For future recommendations, the COID plans to adopt standards for development of all clinical recommendations in Policy Statements, Clinical Reports, and Technical Reports. GRADE will continue to be used for vaccine recommendations.

**VISUAL RED BOOK AND RED BOOK ONLINE**

Not only has the content of the 2012 Red Book been updated, but in the digital age, delivery of information also has undergone significant advancements by using technology that provides point-of-care access to current medical information. The Red Book Online Visual Library contains more than 2600 images, embedded as pop-up visual guides in the online and mobile versions of the 2012 edition. Unlike the print edition, the Red Book Online can be updated as new AAP Policy Statements and Clinical Reports, as well as other publications, become available between Red Book publication cycles. The electronic version of the Red Book includes both online access and mobile downloads via smartphone and/or tablet (Android and Apple) to provide more effective delivery of current medical information to health care professionals in a mobile health care environment.

**FUTURE OF THE RED BOOK IN THE ELECTRONIC AGE**

The pace of biomedical discovery and advancement is accelerating and will continue to do so in the future. Huge data sets on large populations will be available for analysis. Biomedical research will produce innovations that will require integration into clinical practice. Enhancements in technology will make information from electronic health records, with the potential for embedded algorithms for clinical care, and data from scientific investigations available everywhere within the health care matrix, promoting efficient use of resources in prevention and treatment of disease.

As progress continues, development and implementation of clinical guidelines will need to be increasingly science-based and transparent. The amount of information available will be extensive, confusing, and potentially overwhelming. Future editions of the Red Book will need to process and categorize huge amounts of information in an accessible and digestible format and embrace advances in technology and distribution platforms, all while continuing to demonstrate scientific rigor and evidential basis for recommendations for care of
children and adolescents, including accepted evidence-based, transparent approaches used to make recommendations. In these ways, the AAP can ensure that practitioners will continue to rely on the Red Book in its many formats for clinical guidance and support.

ACKNOWLEDGMENTS
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REFERENCES


An error occurred in the article by Eric Biondi et al, titled “Epidemiology of Bacteremia in Febrile Infants in the United States” published in the December 2013 issue of Pediatrics (2013;132[6]:990–996; originally published online November 11, 2013; doi:10.1542/peds.2013-1758). On page 990, in Authors, this reads: “Vivan Lee; Children’s Hospital of Los Angeles.” This should have read: “Vivian Lee; Children’s Hospital Los Angeles.”

doi:10.1542/peds.2013-4017


An error occurred in this article by Pickering et al, titled “The Red Book Through the Ages” published in the November 2013 issue of Pediatrics (2013;132[5]:898–906; originally published online October 14, 2013; doi:10.1542/peds.2013-2538). On page 899, under Early History of the COID, the first line reads: “After the establishment of the AAP in 1930 in the library of Harber Hospital…” This should have read: “After the establishment of the AAP in 1930 in the library of Harper Hospital…”

doi:10.1542/peds.2013-4105


doi:10.1542/peds.2014-0173


Two errors occurred in the article by Simpson et al, titled “A New Leukocyte Hyperadhesion Syndrome of Delayed Cord Separation, Skin Infection, and Nephrosis” published in the January 2014 issue of Pediatrics (2014;133[1]:e257–e262; doi:10.1542/2013-0884). On page e261, under Treatment With Glucocorticoids on line 31, this reads: “Whereas the exact mechanism causing the hyperadhesiveness of the integrins is not known, the symptoms bear resemblance to mice expressing constitutively active LFA-1 in which excessive adhesion prevents leukocytes from entering injured tissues and, when tested in vitro, causes increased adhesion and stalled migration.15,16” This should have not been inserted. Additionally, on the same page (e261) in the next section, Leukocyte Hyperadhesiveness, on line 12, this reads: “Whereas the exact mechanism causing the hyperadhesiveness of the integrins is not known, the symptoms bear resemblance to mice expressing constitutively active LFA-1 in which excessive adhesion prevents leukocytes from entering injured tissues and, when tested in vitro, causes increased adhesion and...
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The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/early/2013/10/09/peds.2013-2538