YEAR BOOK®

YEAR BOOK OF PEDIATRICS® 1991

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1991

The Year Book of PEDIATRICS®

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Mosby Year Book

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A Year Book Medical Publishers imprint of Mosby-Year Book, Inc.

Mosby-Year Book, Inc.
11830 Westline Industrial Drive
St. Louis, MO 63146

Printed in the United States of America

Editorial Office:
Mosby-Year Book, Inc.
200 North LaSalle St.
Chicago, IL 60601

International Standard Serial Number: 0084-3954
International Standard Book Number: 0-8151-6586-2

Journals Represented

Mosby–Year Book subscribes to and surveys nearly 850 U.S. and foreign medical and allied health journals. From these journals, the Editors select the articles to be abstracted. Journals represented in this YEAR BOOK are listed below.

Acta Chirurgica Scandinavica
Acta Neurologica Scandinavica
Acta Orthopaedica Scandinavica
Acta Psychiatrica Scandinavica
Allergy
American Heart Journal
American Journal of Cardiology
American Journal of Clinical Nutrition
American Journal of Clinical Pathology
American Journal of Diseases of Children
American Journal of Emergency Medicine
American Journal of Epidemiology
American Journal of Medicine
American Journal of Obstetrics and Gynecology
American Journal of Pediatric Hematology/Oncology
American Journal of Psychiatry
American Journal of Public Health
American Journal of Sports Medicine
American Review of Respiratory Disease
Anesthesia and Analgesia
Anesthesiology
Annals of Allergy
Annals of Emergency Medicine
Annals of Internal Medicine
Annals of Surgery
Archives of Dermatology
Archives of Disease in Childhood
Archives of General Psychiatry
Archives of Otolaryngology–Head and Neck Surgery
Blood
British Heart Journal
British Journal of Obstetrics and Gynaecology
British Journal of Radiology
British Medical Journal
Canadian Journal of Public Health
Canadian Medical Association Journal
Cancer
Child Development
Child's Nervous System
Circulation
Clinical and Experimental Allergy
Clinical Pediatrics
Critical Care Medicine
Developmental Medicine and Child Neurology
Ear, Nose, and Throat Journal

Endodontics and Dental Traumatology
Family Practice
International Journal of Cardiology
International Journal of Pediatric Otorhinolaryngology
Italian Journal of Neurological Sciences
Journal of Adolescent Health Care
Journal of Allergy and Clinical Immunology
Journal of Bone and Joint Surgery (American Volume)
Journal of Bone and Joint Surgery (British Volume)
Journal of Child Neurology
Journal of Child Psychology and Psychiatry
Journal of Clinical Endocrinology and Metabolism
Journal of Clinical Oncology
Journal of Craniofacial Surgery
Journal of Dermatologic Surgery and Oncology
Journal of Developmental and Behavioral Pediatrics
Journal of Emergency Medicine
Journal of Laryngology and Otology
Journal of Neurosurgery
Journal of Pediatric Gastroenterology and Nutrition
Journal of Pediatric Ophthalmology and Strabismus
Journal of Pediatric Orthopedics
Journal of Pediatric Surgery
Journal of Pediatrics
Journal of Perinatology
Journal of Pharmacology and Clinical Therapeutics
Journal of Rheumatology
Journal of Thoracic and Cardiovascular Surgery
Journal of Trauma
Journal of Urology
Journal of the American Academy of Child and Adolescent Psychiatry
Journal of the American College of Cardiology
Journal of the American Medical Association
Journal of the American Podiatric Medical Association
Lancet
Laryngoscope
Medical Journal of Australia
Neuropediatrics
New England Journal of Medicine
Obstetrics and Gynecology
Otolaryngology–Head and Neck Surgery
Pediatric Dentistry
Pediatric Emergency Care
Pediatric Infectious Disease Journal
Pediatric Pulmonology
Pediatric Radiology
Pediatric Research
Pediatrics
Plastic and Reconstructive Surgery
Quintessence International Dental Digest
Reviews of Infectious Diseases

Science
Skeletal Radiology
Southern Medical Journal
Transfusion

Standard Abbreviations

The following terms are abbreviated in this edition: acquired immunodeficiency syndrome (AIDS), the central nervous system (CNS), cerebrospinal fluid (CSF), computed tomography (CT), electrocardiography (ECG), and humanimmunodeficiency virus (HIV).

Publisher's Preface

Publication of the 1991 YEAR BOOK OF PEDIATRICS marks the end of an outstanding era of YEAR BOOK editorship by Frank A. Oski, M.D. During Dr. Oski's 13 years of editorship, the volume's readers have been treated to perceptive commentary of the highest caliber. Moreover, we at Mosby-Year Book, Inc., have been treated to an enjoyable and rewarding association. We extend our deepest appreciation to Dr. Oski for the service he has provided and for his unending support and enthusiasm for the YEAR BOOK. He will be missed by all of us here, and we wish him the very best in all his future endeavours.

James A. Stockman, III, M.D., who has been editing the YEAR BOOK OF PEDIATRICS with Dr. Oski since 1979, will be assuming sole editorship of the YEAR BOOK commencing with the 1992 edition.

Introduction

This edition of the YEAR BOOK marks the thirteenth year that these editors have had the opportunity to review the world's literature and to comment on the important issues in Pediatrics. One might think that 13 years is a long period and that the possibility of boredom might arise on the part of the writers. Not so! The face of Pediatrics is ever changing. No 2 years' literature, much less any month's, are the same. Pediatrics is alive and prospering, and the literature reflects how dynamic our field is. Take, for example, the following topics included in this year's YEAR BOOK:

- Infant sleep and bedtime cereal.
- A 40-year follow-up of overweight children.
- Cocaine intoxication presenting as seizures.
- The impact of a total ban on smoking in the Johns Hopkins Children's Center (two guesses who selected this article).
- What's in a teaspoon? Underdosing with acetominophen.
- Identification of the cystic fibrosis gene.
- Lyme disease in childhood.
- Human herpesvirus 6, the cause of exanthem subitum.
- Liver transplantation for children.
- The tall athlete and Marfan syndrome.
- The effect of recombinant colony-stimulating factor on congenital neutropenia.
- Parvovirus B19 in patients with cancer.
- Testicular oximetry to assess the viability in testicular torsion.

The baker's dozen above represents only 13 of the 280 articles abstracted in this YEAR BOOK. Note that when these editors first took on the challenge of the preparation of the YEAR BOOK in 1979, 9 of the 13 topics listed had not yet been described. How quickly liver transplantation, Lyme disease, cocaine, and the others have become the equivalent of household names in Pediatrics.

Our commentaries, we hope, provide additional insight into the topics abstracted. Perhaps you will not agree with all of the commentaries. Frankly, it's much easier to learn from controversy than from bland fact— no one likes watching touch football.

If there are comments you wish to share with us, please do not hesitate to do so. We all benefit from the thoughts and experiences of others.

James A. Stockman, III, M.D.

A Personal Note

It has been a privilege for me to have co-edited the YEAR BOOK for a dozen or so years with Frank Oski. Dr. Oski has been a mentor of mine since the start of my residency training in the 1960s. He guided me through fellowship training. He was my chairman during my initial academic appointment as an Instructor of Pediatrics and was responsible for this editor's faculty development up through the professional ranks at SUNY, Syracuse.

In 1979 when Frank took on the editorship of the YEAR BOOK, he asked if I would be an associate editor. The following year he asked if I would co-edit the YEAR BOOK. It's been a phenomenal union ever since, despite Frank's move to become Professor and Chairman at Hopkins in the mid-1980s and a similar move for me to Northwestern. Even though separated by 800 miles, we have collaborated on what must be one of the best endeavors in Pediatrics, preparing the YEAR BOOK. Change seems to come to everything, however. Frank has decided that this year will be his last year as co-editor of the YEAR BOOK. I suppose we all recognized that, at some time, this decision would come.

As someone makes the transition from one activity to others, you normally might wish them the best of all fortune and luck and, although we do so for Frank, we know he has never needed this. So what we will say, Frank, is thank you for the best 13 years the YEAR BOOK has ever had. I will miss the privilege of working with you.

The readers of the YEAR BOOK may think they will miss the words of Frank Oski. I don't think they will, for Frank has agreed to be called on to be a guest commentator many times in the future.

The Introduction of the 1979 YEAR BOOK began with the words, "Fools rush in where angels fear to tread." The words referred to the difficult, if not impossible, task that Frank Oski and I had assumed filling the shoes of Sydney Gellis when he retired as Editor of the YEAR BOOK. The publishers of the YEAR BOOK have asked if I would continue editing the YEAR BOOK and this "fool" gladly does so. Frank, wish me some of the luck that you don't need.

James A. Stockman, III, M.D.

Table of Contents

The material covered in this volume represents literature reviewed through May 1990.

1 The Newborn

Jaundice With Hypertrophic Pyloric Stenosis: A Possible Early Manifestation of Gilbert Syndrome

Labrune P, Myara A, Huguet P, Trivin F, Odievre M (Hôp Antoine Beclere, Clamart, France; Hôp Saint Joseph, Paris)

J Pediatr 115:93–95, 1989 1–1

Some infants with hypertrophic pyloric stenosis become jaundiced. Because the jaundice clears rapidly after pyloromyotomy, tests of enzyme activity are not performed later in life. Two infants with pyloric stenosis and prolonged jaundice had decreased hepatic activity of bilirubin uridine diphosphate-glucuronyltransferase (UDPG-T) several months after surgery, suggesting the possibility of Gilbert's syndrome.

Male infant, breast-fed after a normal birth, became jaundice on day 3 of life. His serum bilirubin concentration reached 238 μmol/L on day 5. Pyloric stenosis was diagnosed when the infant began vomiting at 6 weeks. Jaundice cleared completely within a few days of pyloromyotomy. At 4 months an assay of hepatic UDPG-T found the serum bilirubin concentration to be 5 μmol/L, which increased to 20 μmol/L after a 12-hour fast. Results of a complete blood cell count were normal.

Both infants underwent needle biopsy of the liver at the time of UDPG-T activity assay. In the first infant enzyme activity was compared with that of normal children and adults and with that of children and adults with Gilbert's syndrome. Activity in the second infant was compared with that measured in the liver of an adult Wistar rat. The UDPG-T activity was 12.6 nmol/min/g in the first infant, a mean of 41 in controls, and a mean of 4 in patients with Gilbert's syndrome; UDPG-T activity was 7 in the second infant and 77 in the Wistar liver tissues.

The infants' low activity levels suggest a possibly genetic and permanent deficiency in bilirubin glucuronidation; the fathers of both infants had episodes of jaundice. It may even be that all patients with jaundice associated with pyloric stenosis have an early manifestation of Gilbert's syndrome. Projectile vomiting with unconjugated hyperbilirubinemia should alert the physician to a possible diagnosis of hypertrophic pyloric stenosis and Gilbert's disease.

▶ Felsher and associates were the first to suggest that the jaundice seen in infants with pyloric stenosis was a manifestation of Gilbert's disease (1). It all makes good sense when you recall that mild starvation produces a rise in bilirubin levels in patients with Gilbert's disease, and patients with severe pyloric stenosis are mildly to severely starved. What we often forget is that approxi-

mately 5% of the population are believed to have Gilbert's disease, and that this disease can manifest itself in the newborn period as idiopathic hyperbilirubinemia. When was the last time you made a diagnosis of Gilbert's disease in a jaundiced neonate?—F.A. Oski, M.D.

Reference

1. Felsher BF, et al: *J Lab Clin Med* 83:90, 1974.

Neonatal Hyperbilirubinemia at High Altitude

Leibson C, Brown M, Thibodeau S, Stevenson D, Vreman H, Cohen R, Clemons G, Callen W. Grindlay Moore L (Univ of Colorado; Univ of Colorado Health Sciences Ctr, Denver; Children's Hosp, Denver; Stanford Univ; Santa Clara Valley Med Ctr, San Jose, Calif; et al)

Am J Dis Child 143:983–987, 1989 1–2

Infants born in Colorado have an increased frequency of neonatal hyperbilirubinemia at altitudes of more than 3,100 m when compared with

Comparison of Bilirubin and Hematologic Characteristics at 1,600 m and 3,100 m*

	Altitude		
	1,600 m	3,100 m	P†
Total bilirubin, μmol/L			
Birth	32±2 (37)	38±2 (23)	.01
72 hours	149±9 (49)	178±12 (31)	.06
Breast-fed	156±10 (41)	178±17 (21)	.25
Formula-fed	115±20 (8)	180±14 (10)	.02
Conjugated bilirubin, μmol/L			
Birth	6±0 (36)	5±1 (21)	.52
72 hours	8±0 (40)	6±1 (11)	.003
Hematocrit			
Birth	0.51±0.01 (28)	0.54±0.01 (27)	.08
72 hours	0.54±0.01 (31)	0.62±0.01 (30)	.000
Breast-fed	0.55±0.01 (26)	0.62±0.01 (21)	.000
Formula-fed	0.51±0.03 (5)	0.60±0.02 (10)	.02
Erythropoietin, ln mU/mL			
Birth	3.6±0.1 (30)	4.0±0.02 (17)	.05
Carboxyhemoglobin, corrected %			
Saturation, STPD, %	0.64±0.06 (8)	1.17±0.14 (17)	.02
Breast-fed	0.59±0.08 (6)	1.17±0.22 (10)	.07
Formula-fed	0.78±0.00 (2)	1.16±0.14 (7)	.31

*Values are given as mean plus or minus standard error of the mean. Numbers in parentheses are sample sizes. *ln* indicates natural log transformation; *STPD*, a volume of gas at standard temperature and pressure that contains no water vapor.

†All *P* values were derived with a 2-tailed *t*-test except for those for hematocrit for formula-fed infants, which were derived by the Mann-Whitney *U* Test.

(Courtesy of Leibson C, Brown M, Thibodeau S, et al: *Am J Dis Child* 143:983–987, 1989.)

findings in neonates at lower altitudes. The incidence of neonatal hyperbilirubinemia was compared in 49 infants born at an elevation of 1,600 m and 31 infants born at 3,100 m. Only white, singleton, full-term, healthy infants were studied. Hyperbilirubinemia was defined as a serum bilirubin level of 205 μmol/L or higher at 72 hours after birth. All samples were analyzed in the same laboratory for both total and conjugated bilirubin. Transcutaneous bilirubin measurements were obtained on days 1, 2, 3, 5, 7, and 14. The study groups were similar with respect to most risk factors for neonatal hyperbilirubinemia.

Twelve of the 31 infants (39%) born at 3,100 m and 8 of the 49 infants (16%) born at 1,600 m had neonatal hyperbilirubinemia as determined by serum bilirubin levels on day 3. Infants born at 3,100 m had higher carboxyhemoglobin, hematocrit, and erythropoietin values at day 3 when compared with infants born at 1,600 m (table). The effect of altitude was most apparent when formula-fed infants born at different elevations were compared. Mean bilirubin values measured transcutaneously on day 7 for formula-fed infants born at 3,100 m remained significantly above cord blood levels, whereas values on day 7 for formula-fed infants born at 1,600 m had returned to cord blood levels.

Birth at high altitudes is associated with a more than twofold increase in the proportion of infants with neonatal hyperbilirubinemia. Whether elevated bilirubin values observed at high altitude are benign or toxic remains to be determined.

▶ There is no evidence that a jaundiced neonate living at altitude is at any greater risk for neurologic sequelae than an infant living by the sea. There is precious little evidence that hyperbilirubinemia in term infants without hemolytic disease is of any consequence regardless of geographic location. It is worth quoting from the presentation of Newman and Maisels at the Spring meetings of the Pediatric Research Societies (1). After an extensive review of the literature on the subject these investigators conclude, "There is no evidence that hyperbilirubinemia is hazardous to term babies without hemolysis. At levels below 25 mg/dL (where sample sizes have been adequate), there is good evidence that hyperbilirubinemia does *not* cause significant cognitive, neurologic, or hearing impairment."—F.A. Oski, M.D.

Reference

1. Newman TB, Maisels MJ: *Pediatr Res* 27:250A (part 2), 1990.

Diarrhoea in Jaundiced Neonates Treated With Phototherapy: Role of Intestinal Secretion

De Curtis M, Guandalini S, Fasano A, Saitta F, Ciccimarra F (Univ of Naples, Italy)

Arch Dis Child 64:1161–1164, 1989 1–3

Jaundiced newborns undergoing phototherapy often have watery and greenish stools. Although the pathogenesis of this diarrhea has not yet

TABLE 1.—Details of Infants Studied

	Birth weight (g)	*Gestational age (weeks)*	*Age at beginning of study (hours)*
Jaundiced infants receiving phototherapy (n=10)	3402 (95)	38·9 (0·2)	88 (3)
Jaundiced infants not receiving phototherapy (n=10)	3368 (146)	39·6 (0·3)	86 (3)
Infants not jaundiced (n=10)	3547 (67)	39·2 (0·4)	83 (3)

Values are expressed as mean (SEM).
(Courtesy of De Curtis M, Guandalini S, Fasano A, et al: *Arch Dis Child* 64:1161–1164, 1989.)

been elucidated, earlier studies have suggested that it is a secretory type. The role of intestinal secretion in diarrhea of jaundiced neonates was further investigated.

Fecal osmolality and electrolyte concentrations were measured in 30 newborn infants with uncomplicated hyperbilirubinemia and diarrhea when exposed to blue light and in 30 healthy newborns without jaundice or diarrhea. The infants were matched for birth weight, gestational age, postnatal age at the beginning of the study, and feeding regimens. In a

TABLE 2.—Stool Osmolality and Electrolyte Concentrations

	Jaundiced infants receiving phototherapy (n=30)	*Healthy infants (n=30)*	*p Value*
Stool osmolality (mOsm/l)	269 (10)	284 (13)	>0·1
Sodium (mmol/l)	63 (4)	38 (6)	<0·001
Potassium (mmol/l)	52 (3)	31 (5)	<0·001
Anion gap (mmol/l)	37 (4)	144 (17)	<0·001

Values are expressed as mean (SEM).
(Courtesy of De Curtis M, Guandalini S, Fasano A, et al: *Arch Dis Child* 64:1161–1164, 1989.)

second experimental series, rectal water and electrolyte absorption was measured with the use of a rectal dialysis bag in 10 jaundiced infants with diarrhea undergoing photography, 10 jaundiced infants not receiving phototherapy, and 10 healthy control infants. All were matched for birth weight, gestational age, and age at the start of the study (Table 1). Whether electrolyte transport changes also were associated with phototherapy was determined in a third of 8 jaundiced breast-fed newborn infants both during and after phototherapy.

The data obtained in the osmolality and electrolyte concentration studies were consistent with a secretory pattern for the diarrhea (Table 2). The second series of experiments showed a clear inhibition of water and electrolyte absorption in jaundiced infants receiving phototherapy when compared with each of the control groups. The difference was statistically highly significant (Table 3). In the third study series, the diarrhea in jaundiced infants completely disappeared after phototherapy was stopped and jaundice regressed (Table 4).

The colon apparently has a role in the pathogenesis of secretory diarrhea, and both hyperbilirubinemia and phototherapy are necessary for the development of abnormal water and electrolyte absorption patterns.

▶ My ex-departmental colleague from the State University of New York Health Science Center at Syracuse, Dr. David Hakanson, prepared the commentary. Dr Hakanson, an Associate Professor of Pediatrics, writes:

▶ Since phototherapy was first used for the treatment of neonatal jaundice (1), the presence of watery green stools has been observed in about 10% of infants receiving such treatment (2). This diarrhea is characterized by increased fecal water loss (3) and decreased gut transit time (4). In some affected infants intestinal lactase deficiency has been found (5), but recent studies have not confirmed this (6, 7).

A photoproduct of bilirubin is presumed to be involved in the pathogenesis of this diarrhea because *both* light and hyperbilirubinemia are required for its development (4). Loose stools are less frequent in infants exposed to light to prevent hyperbilirubinemia than in very jaundiced infants receiving phototherapy

TABLE 3.— Rectal Net Absorption of Water and Electrolytes

	Jaundiced infants receiving phototherapy (n=10)	*p Value*	*Jaundiced neonates not receiving phototherapy (n=10)*	*p Value*	*Neonates not jaundiced (n=10)*
Water (μl/min/cm^2)	2·1 (0·04)*	<0·01	3·6 (0·006)	>0·05	3·3 (0·09)
Sodium (μmol/min/cm^2)	286 (8)*	<0·01	357 (8)	>0·05	331 (10)
Chloride (μmol/min/cm^2)	291 (11)*	<0·01	500 (11)	<0·01	358 (13)
Potassium (μmol/min/cm^2)	3 (3)*	<0·01	69 (2)	>0·05	58 (6)

Values are expressed as mean (SEM).
(Courtesy of De Curtis M, Guandalini S, Fasano A, et al: *Arch Dis Child* 64:1161–1164, 1989.)

(4), supporting the hypothesis that a photoproduct of bilirubin is responsible for the diarrhea.

Studies in Gunn rats by Guandalini et al. (8) indicate that photoproducts of bilirubin inhibit, in a dose-dependent fashion, the absorption of water and electrolytes; net secretion of water was not observed.

The mechanism by which photoproducts of bilirubin act as secretagogues has not been explained. They do not increase the tissue concentration of cyclic adenosine monophosphate or of cyclic guanosine monophosphate, known in-

TABLE 4.—Net Absorption of Water and Electrolytes During and After Phototherapy

	Water ($\mu l/min/cm^2$)	*Sodium* ($\mu mol/min/cm^2$)	*Chloride* ($\mu mol/min/cm^2$)	*Potassium* ($\mu mol/min/cm^2$)
During phototherapy	2·6 (0·1)	248 (8)	266 (8)	6 (1)
After phototherapy	3·6 (0·2)	308 (9)	329 (11)	13 (3)
p Value	<0·001	<0·01	<0·01	=0·016

Values are expressed as mean (SEM).
(Courtesy of De Curtis M, Guandalini S, Fasano A, et al: *Arch Dis Child* 64:1161–1164, 1989.)

tracellular mediators of secretion. The possibility exists that photoproducts of bilirubin exert their secretory effect by modifying the intracellular activity of calcium (8). A decrease in the serum calcium is a known consequence of phototherapy but only in response to white, not blue, phototherapy lamps, which were used in the current study (9). It is unlikely that phototherapy-induced hypocalcemia plays a role in the mechanism involved in the diarrhea associated with phototherapy.—D. Hakanson, M.D.

References

1. Cremer RJ, et al: *Lancet* 1:1094, 1958.
2. John E: *Austr Paediatr J* 11:53, 1975.