



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**Available online at: <http://www.iajps.com>

Review Article

**GASTROENTERITIS, COMPLICATIONS AND THERAPEUTIC
OPTIONS, REVIEW****Ahmed Hussain Al Asmari, Nawaf M. Alyahya, Ghanem Ali Alshahrani, Ali J Alshehri,
Mohammed Salem Alqahtani, Abdullah S. Almalki****Abstract:**

Background: Gastroenteritis is defined as the inflammation of the mucous membrane layers of the stomach system and also is identified by looseness of the bowels or vomiting.

Objective: The main purpose of this article was to review the gastroenteritis from different clinical perspectives including etiology, complications and then treatment options

Methods: We search major databases; PubMed (MEDLINE) and Embase for the identification most important and recent reviews and clinical trials on the following treatments of gastroenteritis and also the complications and etiology of it, we searched the mentioned databases through July 2017 using combined terms which lead to easier search

Conclusion: Gastroenteritis is a very common disease. It creates considerable death in creating nations as well as substantial economic burden to industrialized nations. Infections are in charge of around 70% of episodes of intense gastroenteritis in children and also rotavirus is one of the most effective studied of these viruses. Oral rehydration treatment is as reliable as intravenous treatment in treating mild to moderate dehydration in severe gastroenteritis as well as is strongly recommended as the initial line therapy.

Corresponding author:**Ahmed Hussain Al Asmari,**

QR code



Please cite this article in press Ahmed Hussain Al Asmari et al., *Gastroenteritis, Complications and Therapeutic Options, Review.*, Indo Am. J. P. Sci, 2018; 05(12).

INTRODUCTION:

Gastroenteritis is defined as the inflammation of the mucous membrane layers of the stomach system and also is identified by looseness of the bowels or vomiting. Children in developing countries are particular at risk of both morbidity and also mortality. Worldwide, gastroenteritis impacts 3 to 5 billion youngsters annually, as well as represent 1.5 to 2.5 million fatalities each year or 12% of all deaths among children less than 5 years old (1,2).

Acute gastroenteritis (AGE) continues to be a common reason for facility sees and hospitalizations in the United States. An estimated 179 million instances old take place annually, causing millions of facility visits, almost 500 000 hospital stays, as well as 5000 deaths (3,4). Undercooked, or wrongly stored prepared or processed meats (hen, beef, pork) as well as fish and shellfish are common resources of bacterial virus. Consumption of food including toxins produced by microbial pollutants triggers rapid beginning of vomiting or diarrhoea (or both). Water may be contaminated with bacteria, viruses, or protozoa including (2,3).

There more than 20 various types of infections that have been identified as etiological agents (5). Worldwide, rotavirus is still one of the most common infection causing this illness as well as accounts for some 30% to 72% of all the hospitalizations and 4% to 24% of severe gastroenteritis at the neighborhood level (6). Rotavirus infection is seasonal in warm climates, coming to a head in late winter months, although it takes place throughout the year in the tropics. The peak age for infection arrays from 6 months to 2 years. Other typical viruses causing gastroenteritis consist of calicivirus, astrovirus and adenovirus. It is important to examine hydration in gastroenteritis as hydration status identifies the immediate monitoring of this problem. The infant or youngster with profuse watery diarrhoea and also constant vomiting is most in jeopardy. Clinicians often overstate the degree of dehydration. Clinical signs are normally not present until a kid has lost a minimum of 5% of his/her body weight. Recorded current weight lost is a good indication of the degree of dehydration, but this details are hardly ever offered. The very best clinical signs of more than 5% dehydration are long term capillary refill, irregular skin turgor, and absent rips (7). The recommendations for managing and examining dehydration is a very important primary intervention

as recommended by World Health Organization classification as well as are supported by the literary works (7,8,9).

The main purpose of this article was to review the gastroenteritis from different clinical perspectives including etiology, complications and then treatment options, and since gastroenteritis is more common among children younger than 3 years old we mostly discussed this condition concerning children this review

METHODOLOGY:

We search major databases; PubMed (MEDLINE) and Embase for the identification most important and recent reviews and clinical trials on the following treatments of gastroenteritis and also the complications and etiology of it, we searched the mentioned databases through July 2017 using combined terms which lead to easier search. Furthermore, references list of each article included in this review were searched manually for more relevant studies.

DISCUSSION:**Etiology of gastroenteritis:**

Infections are the most crucial etiology and are responsible for around 70% of the episodes of intense gastroenteritis (10). There are over 20 various kinds of viruses that have actually been recognized as etiological representatives (11). Worldwide, rotavirus is still the most typical virus causing this disease and represent some 30% to 72% of all the hospitalizations and 4% to 24% of acute gastroenteritis at the neighborhood level (12,13). Virtually all children have been infected with rotavirus by the age of 3 years (13). Rotavirus infection is seasonal in temperate climates, peaking in late winter season, although it happens throughout the year in the tropics. The peak age for infection ranges from 6 months to 2 years. Other common viruses triggering gastroenteritis consist of calicivirus, adenovirus and astrovirus (14,15). Bacterial infection accounts for 10% to 20% of all the intense gastroenteritis (16,17). (TABLE. 1) (18) lists some causes of severe gastroenteritis in kids. Worldwide, the majority of cases are due to viral infection, Rotavirus pressures differ by season and geographically within countries (18).

TABLE. 1: Causes of acute gastroenteritis in children ⁽¹⁸⁾	
Viruses (~70%)	
•	Rotaviruses
•	Noroviruses (Norwalk-like viruses)
•	Enteric adenoviruses
•	Caliciviruses
•	Astroviruses
•	Enteroviruses
Protozoa (<10%)	
•	Cryptosporidium
•	<i>Giardia lamblia</i>
•	<i>Entamoeba histolytica</i>
Bacteria (10-20%)	
•	<i>Campylobacter jejuni</i>
•	Non-typhoid <i>Salmonella</i> spp
•	Enteropathogenic <i>Escherichia coli</i>
•	<i>Shigella</i> spp
•	<i>Yersinia enterocolitica</i>
•	Shiga toxin producing <i>E coli</i>
•	<i>Salmonella typhi</i> and <i>S paratyphi</i>
•	<i>Vibrio cholerae</i>
Helminths	
•	<i>Strongyloides stercoralis</i>

Complications of Gastroenteritis:

Hypnatremia was found to be a rare, however severe, as well as evidently particular problem of AGE. This outcome is independent of pre-existing persistent or acute concomitant conditions or signs. Hypnatremia is a measure of hypertonic dehydration as well as puts kids at unique danger for neurological sequelae, either because of hypertonicity itself or due to analytical edema, which might be caused by as well quick decrease of sodium focus in serum after initiation of intravenous rehydration. Our results are substantiated by some instance reports concerning very high salt levels done in context with AGE (19,20), and also the Swedish research (21) searching for hypnatremia as a result of AGE in about 10% of situations. We have revealed that hypnatremia seems to be a particular problem in rotavirus condition in contrast to various other infectious diarrheal pathogens. Hypnatremia often indicates extreme disease, serious dehydration, and also was called "infant toxicosis" or "hyperpyretic toxicosis" in the old pediatric literary works (22). Various other study (23) recommends that rotavirus

is without a doubt the most constant source of infant toxicosis. Because treatment of hypnatremia is an emergency and also often difficult, every initiative needs to be made to avoid it. As over 75% of instances with hypnatremia was because of Motor Home infection, avoidance of Motor Home infection is the key. This is best achieved by inoculation of all infants against Motor Home. Kids with ongoing AGE must get early dental rehydration therapy with low sodium concentrations (60 mmol/l) (23). In spite of anecdotal evidence (24,25), validates previous findings that Recreational Vehicle infection typically does not follow a much more severe course in terms of demand for intensive care treatment in youngsters with underlying conditions. Nevertheless, Recreational Vehicle infection was located to result in longer a hospital stay in constantly ill kids. The research study (23) have located neurological complications in 2% of the RV+ AGE people. That is much less usual than in a Swedish research with 4% (26).

Treatment options:

Rehydration treatment as first step (Oral & IV):

The World Health Organization (WHO) all highly sustain using dental rehydration therapy as the first-line treatment for the therapy of severe gastroenteritis, except in cases of severe dehydration (27,28). The performance of oral rehydration therapy in treating severe gastroenteritis, with mild to regulated dehydration, has actually been shown by numerous randomized regulated trials. In a Cochrane meta-analysis of 17 tests from 1982 to 2005, in which 9 trials were from the established nations, 7 trials from developing nations and also 1 test including developed as well as much less developed countries (29). Included in this analysis were more than 1800 participants. The information revealed that there were no crucial professional distinctions between dental hydration treatment and also intravenous treatment for rehydration second to severe gastroenteritis in children; which children treated with oral rehydration therapy spent much less time in medical facilities. Patients receiving intravenous therapy had a 2.5% danger of phlebitis that did not take place in the dental rehydration team. Importantly, this result is unlikely to change with more trials since there is currently adequate power to sustain the observed outcomes as well as further research study comparing oral rehydration treatment and also intravenous treatment is not warranted and also might be underhanded. The performance of oral rehydration treatment is not isolated to just scientific tests it can additionally be reflected in the reduced death rate. In 1970's the diarrheal ailment associated fatalities were 4.6 million/year globally (30).

The oral rehydration remedy is considered one of the most crucial medical advancements of the 20th century. There is much proof to sustain the use of dental rehydration with various released standards and many professional companies suggesting its use, oral rehydration option is still explained as an underused basic therapy (31). Intravenous treatment is still usually chosen rather than oral rehydration treatment. Information from Europe, Australia as well as Canada reveal that 80% to 94% of hospitalized children do not have any indicators of dehydration and yet they still obtain intravenous therapy (32,33,34). Information from Hong Kong, that assessed more than 7000 episodes of admission

because of gastroenteritis in children under 5 years of age, likewise showed that just 1.3% to 8.4% had indications of dehydration and yet as much as 48% of the patients obtained intravenous treatment (35). The price of intravenous therapy was also higher in the rotavirus team. Inning accordance with a current survey, 45% of physicians still liked intravenous fluid therapy instead of oral rehydration treatment in dealing with moderate dehydration in acute gastroenteritis (36).

The reasons for the underuse of oral rehydration therapy are not completely recognized. In 2002 Ozuah as well as colleagues published a nationwide arbitrary study of emergency situation physicians chosen from the mailing list of the AAP that resolved this problem (37). An overall of 176 doctors responded (73% action price). Their feedbacks can be divided right into four categories: the medical professional elements; client variables; parental problem; and setting or social aspects. Relating to the physician variables; in contrast to the team of doctors not familiar with the AAP guidelines, the familiar team was more likely to make use of dental rehydration treatment in scenarios of moderate dehydration (81% versus 66%) and modest dehydration (25% versus 10%). Parental concern regarding dehydration (overlooking the real hydration standing of the patients) would certainly make 31% of the emergency division medical professionals choose intravenous therapy over oral rehydration therapy. A crowded or emergency situation department with long waiting times would certainly trigger 22% of the physicians to pick intravenous treatment. Concerning the intensity of dehydration, 49.4% of emergency division medical professionals would offer intravenous treatment also in moderate dehydration. In terms of signs, only 8% of the emergency situation division physicians would certainly consider intravenous treatment when diarrhea was a significant sign. On the other hand, clients choosing not to drink was one of the most likely factor for selecting intravenous treatment (as much as 96%) (**Table 2**). Vomiting was the second most important reason given for intravenous treatment, with approximately 85% of the physicians being most likely to utilize intravenous treatment when throwing up was the predominant signs and symptom. In one more research study, approximately 36% of the checked medical professionals thought that vomiting was a contraindication for oral rehydration therapy (38).

Table 2: Assessment and management of dehydration

Dehydration (% weight loss)	Clinical signs	Pinch test*	Management
No dehydration	None	Normal (skin fold retracts immediately)	Most can be managed at home; encourage normal diet and fluids (continue breast milk); consider admission if high risk of dehydration (very young, diagnosis in doubt, large losses)
Some dehydration: includes previous categories of mild (5%) and moderate (6-9%) dehydration	Two or more of restlessness or irritability, sunken eyes, thirst (eagerness to drink)	Slow (skin fold visible <2 sec)	Some can be managed at home with oral rehydration therapy; some need to be observed and, if therapy is not tolerated or large ongoing losses occur, may need nasogastric or intravenous fluids over 4-6 h; normal diet when tolerated
Severe dehydration ($\geq 10\%$) with or without shock	Two or more of abnormally sleepy or lethargic, sunken eyes, drinking poorly or not at all†	Very slow (skin fold visible >2 sec)	Check acid base status, urea, electrolytes before intravenous fluids; if shock present, first resuscitate with intravenous bolus; rehydrate intravenously (enteral fluids have been used) over 4-6 h with regular clinical and biochemical review

Antiemetic medications:

Vomiting is normally specified as a terrible expulsion of the belly components with the mouth as well as being a very undesirable signs and symptom. It can additionally be related to nausea or vomiting and retching. The system of throwing up has actually been well identified, first by Borison as well as Wang in 1953⁽³⁹⁾. The vomiting center controls and integrates the act of throwing up. It is located in the side reticular development of the medulla oblongata, which is close to various other facilities that manage respiration, vasomotor, as well as various other autonomic features. These centers as well could also play an added function in throwing up. Emetic stimuli can be sent directly to the vomiting center or through the chemoreceptor trigger zone. The chemoreceptor trigger area, located in the area postrema of the fourth ventricle and also outside the blood-brain obstacle, is exposed to both cerebrospinal liquid and blood⁽⁴⁰⁾. This would allow the chemoreceptor trigger zone to pick up the chemical signals from both cerebrospinal liquid and also blood

stream (such as bacterial contaminants or create metabolic problems that occur with uremia) and function as a sensory arm or leg to the vomiting facility; however, it cannot individually mediate the act of vomiting without the communication of throwing up facility. On the other hand, the throwing up center does not only obtain information from the chemoreceptor trigger area, it can additionally receive details and also excitement from the cerebral cortex and limbic system, the vestibular system, and also the vagal and also splanchnic afferents^(39,41,42). Mental anxiety such as worry can act on analytical cortex as well as limbic system to generate vomiting by means of the vomiting. Throwing up due to nausea establishes consequent to stimulation of the vestibular system, with impulses that take a trip from the labyrinth of the inner ear to the vomiting center. The numbers of randomized controlled trials for different antiemetics, dosages as well as routes of administration, and also special considerations are summarized in (Table 3).

Table 3: Summary of antiemetic drugs

Drug	No. of RCT	Route/dose	Consideration
Ondansetron	7 RCTs	PO: 2 mg for BW 8–15 kg 4 mg for BW 15–30 kg 8 mg for BW >30 kg IV: 0.1–0.15 mg/kg BW	Minimal adverse effects, with good evidence for reduced admission and intravenous therapy
Dimenhydrinate	1 RCT	PO/PR/IM/IV: 1.25 mg/kg BW	Sedative effect
Promethazine	1 RCT	PO/PR/IM/IV: 0.25–1 mg/kg BW	FDA black box warning
Metoclopramide	2 RCTs	PO/IM/IV: 0.1 mg/kg BW	High frequency of extra-pyramidal reaction
Droperidol	No RCT	IM/IV: 0.05–0.06 mg/kg BW	FDA black box warning
Domperidone	2 RCTs	PO: 0.3–0.6 mg/kg BW PR: <2 yr: 10 mg, 2–6yr: 30 mg, >6 yr: 60 mg	No IV as increase cardiac arrhythmias
Prochlorperazine	No RCT	PO: 0.1–0.2 mg/kg BW PR: 0.1–0.2 mg/kg BW IM: 0.15 mg/kg BW	Not recommended if <2y/IV dosing not recommended in pediatric patients
Trimethobenzamide	2 RCTs	PO: 4–5 mg/kg BW PR: 4–5 mg/kg BW	PR form was removed from the manufacture/IM/IV routes not recommended in pediatric patients

Abbreviations: BW, body weight; PO, per os; PR, per rectum; IM, intramuscular; IV, int

CONCLUSION:

Gastroenteritis is a very common disease. It creates considerable death in creating nations as well as substantial economic burden to industrialized nations. Infections are in charge of around 70% of episodes of intense gastroenteritis in children and also rotavirus is one of the most effective studied of these viruses. Oral rehydration treatment is as reliable as intravenous treatment in treating mild to moderate dehydration in severe gastroenteritis as well as is strongly recommended as the initial line therapy. However, the oral rehydration remedy is called an underused straightforward remedy. Vomiting is one of the primary reasons to discuss the underuse of dental rehydration treatment. Antiemetics are not routinely advised in dealing with acute gastroenteritis, though they are still commonly suggested.

REFERENCES:

1. by-Payne J, Elliott E. Gastroenteritis in children. *Clin Evid.* 2004;12:443–454.
2. King CK, Glass R, Bresee JS, Duggan C. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. *MMWR Recomm Rep.* 2003;52(RR-16):1–16.
3. Wilhelmi I, Roman E, Sanchez-Fauquier A. Viruses causing gastroenteritis. *Clin Microbiol Infect.* 2003;9(4):247–262.
4. Rivest P, Proulx M, Lonergan G, Lebel MH, Bedard L. Hospitalisations for gastroenteritis: the role of rotavirus. *Vaccine.* 2004;22(15–16):2013–2017.
5. Parashar UD, Gibson CJ, Bresse JS, Glass RI. Rotavirus and severe childhood diarrhea. *Emerg Infect Dis.* 2006;12(2):304–6.

6. Leung AK, Kellner JD, Davies HD. Rotavirus gastroenteritis. *Adv Ther.* 2005;22(5):476–487.
7. Steiner MJ, DeWalt DA, Byerley JS. Is this child dehydrated? The rational clinical examination. *JAMA*2004;291:2746-54.
8. World Health Organization. The treatment of diarrhoea—a manual for physicians and other senior health workers. 4th rev. Geneva: WHO, 2005.
9. Acute Gastroenteritis Guideline Team. Cincinnati Children's Hospital Medical Center. Evidence-based care guidelines. Gastroenteritis. 2005. www.cincinnatichildrens.org/svc/alpha/h/health-policy/ev-based/gastro.htm.
10. Webb A, Starr M. Acute gastroenteritis in children. *Aust Fam Physician.* 2005;34(4):227–231.
11. Wilhelmi I, Roman E, Sanchez-Fauquier A. Viruses causing gastroenteritis. *Clin Microbiol Infect.* 2003;9(4):247–262.
12. Rivest P, Proulx M, Lonergan G, Lebel MH, Bedard L. Hospitalisations for gastroenteritis: the role of rotavirus. *Vaccine.* 2004;22(15–16):2013–2017.
13. Ehlken B, Laubereau B, Karmaus W, Petersen G, Rohwedder A, Forster J. Prospective population-based study on rotavirus disease in Germany. *Acta Paediatr.* 2002;91(7):769–775.
14. Andreasi MS, Cardoso DD, Fernandes SM, et al. Adenovirus, calicivirus and astrovirus detection in fecal samples of hospitalized children with acute gastroenteritis from Campo Grande, MS, Brazil. *Mem Inst Oswaldo Cruz.* 2008;103(7):741–744.
15. Caracciolo S, Minini C, Colombrita D, Foresti I, Avolio M, Tosti G, et al. Detection of sporadic cases of Norovirus infection in hospitalized children in Italy. *New Microbiol.* 2007;30(1):49–52.
16. Fodha I, Chouikha A, Dewar J, Trabelsi A, Boujaafar N, Steele AD. Prevalence of adenovirus antigens in children presenting with acute diarrhoea. *Med Trop (Mars)* 2007;67(3):256–258.
17. Jakab F, Peterfai J, Meleg E, Banyai K, Mitchell DK, Szucs G. Comparison of clinical characteristics between astrovirus and rotavirus infections diagnosed in 1997 to 2002 in Hungary. *Acta Paediatr.* 2005;94(6):667–671.
18. Elliott EJ. Acute gastroenteritis in children. *BMJ: British Medical Journal.* 2007;334(7583):35-40. doi:10.1136/bmj.39036.406169.80.
19. Jacobson J, Bohn D (1993) Severe hypernatremic dehydration and hyperkalemia in an infant with gastroenteritis secondary to rotavirus. *Ann Emerg Med* 22(10):1630–1632
20. . Price TG, Kallenborn JC (2000) Infant hypernatremia: a case report. *J Emerg Med* 19(2):153–157
21. Johansen K, Hedlund KO, Zwegyberg-Wirgart B, Bennet R (2008) Complications attributable to rotavirus-induced diarrhoea in a Swedish paediatric population: report from an 11-year surveillance. *Scand J Inf Dis* 40(11–12):958–964
22. Schulte S (1985) *Lehrbuch der Kinderheilkunde.* Fischer Verlag, Stuttgart, p 133
23. Kaiser P, Borte M, Zimmer KP, Huppertz H. Complications in hospitalized children with acute gastroenteritis caused by rotavirus: a retrospective analysis. *Eur J Pediatr.* 2012 Feb;171(2):337-45. doi: 10.1007/s00431-011-1536-0. Epub 2011 Aug 11.
24. Stelzmueller I, Wiesmayr S, Eller M et al (2007) Enterocolitis due to simultaneous infection with rotavirus and Clostridium difficile in adult and pediatric solid organ transplantation. *J Gastrointest Surg* 11:911–917
25. Stelzmueller I, Wiesmayr S, Swenson BR et al (2007) Rotavirus enteritis in solid organ transplant recipients: an underestimated problem? *Transpl Infect Dis* 9:281–285
26. Iyadurai S, Troester M, Harmala J, Bodensteiner J (2007) Benign afebrile seizures in acute gastroenteritis: is rotavirus the culprit? *J Child Neurol* 22:887–890
27. Walker-Smith JA, Sandhu BK, Isolauri E, et al. Guidelines prepared by the ESPGAN Working Group on Acute Diarrhoea. Recommendations for feeding in childhood gastroenteritis. European Society of Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr.* 1997;24(5):619–620.
28. Practice parameter: the management of acute gastroenteritis in young children American Academy of Pediatrics, Provisional Committee on Quality Improvement, Subcommittee on Acute Gastroenteritis. *Pediatrics.* 1996;97(3):424–435.
29. World Health Organization The treatment of diarrhoea. A manual for physicians and other senior health care workers. World Health Organization. 4th rev edn. 2005. Available from: http://whqlibdoc.who.int/publications/2005_9241593180.pdf.
30. Hartling L, Bellemare S, Wiebe N, Russell K,

- Klassen TP, Craig W. Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children. *Cochrane Database Syst Rev*. 2006;3:CD004390.
31. Kosek M, Bern C, Guerrant RL. The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. *Bull World Health Organ*. 2003;81(3):197–204.
 32. Avery ME, Snyder JD. Oral therapy for acute diarrhea. The underused simple solution. *N Engl J Med*. 1990;323(13):891–894.
 33. Sandhu BK, Isolauri E, Walker-Smith JA, et al. A multicenter study on behalf of the European Society of Paediatric Gastroenterology and Nutrition Working Group on Acute Diarrhoea. Early feeding in childhood gastroenteritis. *J Pediatr Gastroenterol Nutr*. 1997;24(5):522–527.
 34. Elliott EJ, Backhouse JA, Leach JW. Pre-admission management of acute gastroenteritis. *J Paediatr Child Health*. 1996;32(1):18–21.
 35. Ford-Jones EL, Wang E, Petric M, Corey P, Moineddin R, Fearon M. Hospitalization for community-acquired, rotavirus-associated diarrhea: a prospective, longitudinal, population-based study during the seasonal outbreak. The Greater Toronto Area/Peel Region PRESI Study Group. *Pediatric Rotavirus Epidemiology Study for Immunization. Arch Pediatr Adolesc Med*. 2000;154(6):578–585.
 36. Chow CM, Choi K, Nelson EA, et al. Use of intravenous fluids in Hong Kong children hospitalised for diarrhoea and relationship to severity and aetiology. *Vaccine*. 2009;27(Suppl 5):F55–F60.
 37. Ozuah PO, Avner JR, Stein RE. Oral rehydration, emergency physicians, and practice parameters: a national survey. *Pediatrics*. 2002;109(2):259–261.
 38. Reis EC, Goepp JG, Katz S, Santosham M. Barriers to use of oral rehydration therapy. *Pediatrics*. 1994;93(5):708–711.
 39. Borison HL, Wang SC. Physiology and pharmacology of vomiting. *Pharmacol Rev*. 1953;5(2):193–230.
 40. Freedman SB, Fuchs S. Antiemetic therapy in pediatric emergency departments. *Pediatr Emerg Care*. 2004;20(9):625–633.
 41. Wang SC, borison HL. The vomiting center; a critical experimental analysis. *Arch Neurol Psychiatry*. 1950;63(6):928–941.
 42. Kovac AL. Prevention and treatment of postoperative nausea and vomiting. *Drugs*. 2000;59(2):213–243.