

## Letters to the Editor

### Can Breast Cancer Be Prevented?

*To the Editor:* I read with special interest and pleasure the editorial by Dr. Robert Stuart, "Can Breast Cancer Be Prevented?" in the September 1998 issue of the *Annals of Saudi Medicine*. With interest because I have been a member of the Chemoprevention Program here at the National Cancer Institute for over 10 years, and with pleasure because you were kind enough to reference a publication of mine.

In the past, it has been mildly frustrating to see the oncology field continue to focus on clinical cancer when the early detection of precancer, and its treatment, offers so much more promise. It was therefore gratifying to read [this] article concerning the future health care potential of cancer chemoprevention.

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### Anastomosis Workshops: The Saudi Experience

*To the Editor:* Manipulative surgical skills are traditionally taught in the operating room. With growing interest in this aspect of psychomotor skills, several workshops have been designed as part of postgraduate surgical training. The anastomosis workshop which was pioneered by the Royal College of Surgeons of England (RCSE) represents a landmark in this field. Teaching anastomosis techniques and basic skills is time-consuming, and is considered to be an unaffordable activity in several service hospitals. Therefore, providing surgical trainees with the opportunity of having hands-on experience while learning anastomotic techniques in a relaxed environment during an anastomosis workshop would enable them to perform and excel in mastering those techniques. We present our experience of four anastomosis workshops at the King Fahad National Guard Hospital in Saudi Arabia.

Four anastomosis workshops were jointly conducted by the Royal College of Surgeons of England (RCSE) and the King Fahad National Guard Hospital (KFNGH) between 1988 and 1994. Communication between KFNGH and the RCSE took place well ahead of each workshop for organizational reasons. Equipment necessary for the workshops, including sutures, staplers, jigs, pelvic simulators and freeze-dried material were provided courtesy of Ethicon (Saudi Arabia Ltd) (Table 1).

The faculty of the first workshop were from the RCSE. They conducted the workshops and trained potential local faculty at KFNGH. The last workshop was conducted by the local faculty, with one consultant and the Technical Manager from the RCSE. Each workshop was attended by 24 surgical residents from Saudi Arabia, and lasted 3½ days. Each day was divided into two sessions, and each session started with two lectures to cover the theoretical background of the subject. This was followed by a demonstration of the anastomotic technique before the students actually started to practice. Each workshop had the following sessions: intestinal, esophagogastric, colorectal suturing, colorectal stapling, ureteric and vascular anastomosis.

In the last workshop, we utilized specimens prepared in sodium hypochlorite solution. The fresh hypochlorite specimen has proven to be superior to the freeze-dried material. The various layers of fresh specimen were much better defined than in the freeze-dried specimen. Preparation of fresh anatomical materials is described in the literature.<sup>2,3</sup>

After each workshop, a questionnaire was given to the surgical residents and the results of the last workshop were as shown in Table 2.

Of the various postgraduate teaching modalities, workshops are considered a well-accepted activity. There is considerable time spent on acquiring hands-on experience. The enthusiasm for the success of the anastomosis workshop is well illustrated by the response of the residents to the questionnaire. Though the workshop has been conducted free in Saudi Arabia, surgical residents are willing to pay for it.

The opportunity for surgical trainees to practice outside the operating room has proven as successful in Saudi Arabia as in England. The hospital staff assigned to the workshops were qualified faculty members, and this can actually be accomplished in other places. The contribution

TABLE 1. *Course contents and organization.*

|  |
|--|
| Contents   |
| Small bowel anastomosis  |
| Large bowel anastomosis  |
| Gastroesophageal anastomosis   |
| Vascular anastomosis (including graft anastomosis and aortic aneurysm) |
| Ureterovascular anastomosis  |
| Ideal number of candidates   |
| Maximum of 24  |
| Minimum of 16  |
| Duration of the workshop   |
| 3.5 days   |
| Special equipment required for the workshop                            |
| Anastomotic jibs   |
| Pelvic simulators  |
| Knotting practice boards   |
| Circular staplers  |
| Linear staplers  |

TABLE 2. Response to the questionnaire (24 respondents).

| Question  | Excellent (%)        | Good (%)               | Fair (%)              |
|---|----------------------|------------------------|-----------------------|
| How would you evaluate the anastomosis workshop?                        | 18 (75)              | 6 (25)                 | 0                     |
| What is your opinion about the faculty and instructors of the workshop? | 19 (79)              | 5 (21)                 | 0                     |
| Give your assessment of the following practical sessions                |                      |                        |                       |
| Small intestinal anastomosis  | 15 (63)              | 7 (29)                 | 2 (8)                 |
| Ureteric anastomosis  | 18 (75)              | 6 (25)                 | 0                     |
| Large bowel anastomosis   | 19 (79)              | 5 (21)                 | 0                     |
| Stapling anastomosis  | 15 (63)              | 7 (29)                 | 2 (8)                 |
| Vascular anastomosis  | 21 (88)              | 1 (4)                  | 1 (4)                 |
| Aortic aneurysm anastomosis   | 20 (83)              | 3 (13)                 | 1 (4)                 |
| Esophagogastric anastomosis   | 18 (75)              | 5 (17)                 | 2 (8)                 |
| Do you think that this workshop should be repeated?                     | Yes 24 (100)         | No (0)                 |                       |
| How often do you think the workshop should be conducted?                | Once per year 7 (29) | Twice per year 15 (63) | More than twice 2 (8) |

will not only reduce costs but will also enhance the teaching commitment of the staff. The benefits of the workshop are quite evident for the new trainee, and we feel that discussion generated between faculty members during the workshop also enhances the exchange of technical ideas.

Freeze-dried materials are often used in overseas anastomosis workshops, however, in our experience, fresh hypochlorite-treated material has proven to be superior as far as tissue handling and delineation of layers are concerned.

We believe that organizing and conducting the workshops is within the capacity of good-sized hospitals outside the United Kingdom.<sup>4,5</sup> In 1995, similar workshops were run at the Colombo General Hospital, Sri Lanka, and also in the United Arab Emirates. We also feel that other hospitals in various parts of Saudi Arabia with postgraduate training programs should consider the introduction of an anastomosis workshop.

We also think that the RCSE should have well-written protocols available to any center interested in conducting such workshops. These protocols could be assembled in a manual to serve as a guide and to facilitate organizational matters. Since the RCSE has pioneered these workshops, the College is required to have some degree of supervision in the conducting of such workshops.

One of the most difficult tasks during the workshop is dealing with the personal bias of how to perform the anastomosis. This sometimes creates a conflict between what the demonstrator describes as an ideal method of anastomosis and what other faculty members would demonstrate during practical sessions. To overcome this obstacle, the RCSE should consider describing in the protocols a well-proven and widely acceptable way to perform a given anastomosis, e.g., single layer bowel

anastomosis versus two-layer. These well-structured protocols will help teach everyone a single, proven, safe way to perform a given anastomosis. This will not only help to run a smooth workshop, but also help surgical trainees in their future practical life to adopt safe and accepted techniques. With our local experience, such protocols and the training of the trainer (the faculty) can be achieved locally.

The anastomosis workshop is now an important part of the curriculum for surgical residents in the UK, and we believe it should be the same in any training program in Saudi Arabia.

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#### ***Pediculus Humanus Capitis* Infestation in a Shiraz Rural Area, Iran**

*To the Editor:* Despite improvements in health standards, head lice infestation remains a problem worldwide. The prevalence in school age children ranges from 6.8% in Sierra Leone<sup>1</sup> to 81.5% in Argentina.<sup>2</sup>

While Mexican Americans and whites are reported to have higher infestation rates, it is generally accepted that head lice can be seen at all socioeconomic levels.<sup>2</sup> Children of school age are the population at greatest risk, with the most affected age range being 7-11 years.<sup>2,3</sup>

According to a study conducted more than 30 years ago in the rural areas of Shiraz, Iran, 30.9% of the total population were found to be infected with head lice, with the most affected range being 7-11 years, with a prevalence of 51.7%.<sup>4</sup> Since there has not been any new surveillance in this area, this study was conducted.

The study took place in February 1998 in Norouzan, one of the rural areas of Shiraz. This area with a population of about 2900 has about 524 primary school age children (7-11 years), consisting of 248 girls and 276 boys. The majority of the villagers have a high socioeconomic status. Home tap water supply and bathing facilities are available at all houses in the village, and the villagers maintain relatively good personal hygiene.

A program conducted by the Ministry of Education requires all the boys to shave their heads during school months, but not the girls. Local health nurses are involved in the control of the head lice infestation, but usually no treatment is offered, due to shortage of drugs. All the schoolchildren were examined for head lice infestation. All areas of the head were examined and the subject was considered to be infested if lice and/or nits were seen, regardless of their color and their distance from the scalp. Fisher's exact test and chi-square test were used to analyze the difference between boys and girls, and between current prevalence and that of the previously reported study.

Lice and nits were found in 41 of the 248 girls (16.5%). The prevalence of lice infestation was highest among children of seven years of age (22%), and the lowest rate was among children of 11 years of age, with a rate of 8.69%. Among the girls, there were 35 pairs of sisters of which in 30 pairs (85%), none was infested, in four pairs 11.4% were infested, and in one pair, only one of the sisters was infested (2.8%). The expected rates were 69.7%, 2.7% and 27.6%, respectively, if random distribution had occurred.

Surprisingly, none of the 276 boys was infested. The difference between boys and girls was significant, using Fischer's exact test ( $P < 0.00001$ ). The overall rate of infestation in this area would be 7.8%. The previous data from our area had shown an overall rate of 30.9% (819 of 2649), with a rate of 13.4% (153 of 1140) in boys, and 44.1% (666 of 1509) in girls.<sup>4</sup> The decline in prevalence, comparing this data with the previously published data from our area, was also significant for boys, girls and for children of the same age, using Fischer's exact test and chi-square test ( $P < 0.0000001$ ,  $P < 0.000001$ , and  $P < 0.000001$ , respectively.)

Eradication of head lice has proved to be a difficult problem. Although 1% permethrin or 0.5% malathion are recommended as the drugs of choice, increasing resistance and treatment failures,<sup>5</sup> and the fact that when measures are relaxed, the prevalence rate increases rapidly,<sup>2</sup> have reduced the effectiveness of this strategy. The use of repellents, the treatment of entire households, the laundering of clothing and bedding in hot water, the regular inspection of primary schoolchildren for head lice and treatment, isolation of infested individuals, and the supply of good tap water, are helpful in minimizing recurrence.

While there has not been any significant difference among the sexes in some studies,<sup>2,3</sup> others have shown a female predominance. In this study, the girls were infested significantly more than the boys. The two groups had the same socioeconomic status. Besides the gender, the only other attributable health measure difference between these two groups was the length of the hair. It has generally been accepted that hair length and style have little effect on infestation rates.<sup>2,3</sup> In a study by Mumcuoglu et al., it was noticed that medium length hair in boys and short hair in girls, which correspond to approximately the same length of hair, were the types most likely to be infected.<sup>3</sup> Curly and frizzy hair had a significantly lower incidence of infestation than straight and wavy hair in that study.<sup>3</sup> None of these studies had a target population with shaved heads, which was present in this study. So it can be concluded that although short hair is not a preventive measure for head lice infestation, shaving the head may reduce the prevalence significantly. The significant decline in the prevalence of head lice infestation in our area can be attributed to this program, although improvements in other health measures should not be ignored.

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## Congenital Anomalies on Endoscopic Retrograde Cholangiopancreatography (ERCP)

*To the Editor:* We describe the incidence of congenital anomalies in 240 ERCP patients, performed at the Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan, between February 1990 and May 1995. Indications for ERCP included obstructive jaundice, recurrent cholangitis, unexplained right hypochondrial pain, mass and cholestasis. There were 146 male (60.8%) and 94 female (39.2%) patients aged between 14 and 90 years. The total number of pancreatobiliary anomalies detected was 9/249 (3.75%). The incidence of various entities was as follows: low biliary confluence 2/240 (0.82%); cystic duct entering

right hepatic duct, 1/240 (0.41%); long cystic duct with spiral termination, 1/240 (0.41%); type I choledochal cyst 1/240 (0.41%); Caroli's disease 1/240 (0.41%); short pancreatic duct 2/240 (0.82%); and duplication of pancreatic duct. Perivaterian diverticulum (PVD) was present in 8/240 (3.33%) of ERCP. All the PVD were small and located in the descending duodenum. There was no cannulation failure due to PVD. ERCP demonstrated type I choledochal cyst, Caroli's disease, long cystic duct with spiral termination, and short pancreatic duct in 4/240 (1.66%) of these subjects with PVD. Recurrent cholangitis was suspected in the first two of these patients, and unexplained abdominal pain in the other two. The remaining four (1.66%) ERCP with PVD did not demonstrate an anomaly. Thus, four of the total 9/240 congenital anomalies co-existed with PVD.

Biliary anomalies are reported in 5%-10% of ERCP. The most common of these include low biliary confluence, cystic duct entering right hepatic duct, and termination of common bile duct in the third part of the duodenum. Cholelithiasis and malignancy complicate 63% and 8%-18% of biliary anomalies, respectively.<sup>1-3</sup> Longer and wider cystic duct facilitates migration of biliary crystals and stones. Hence this anatomical aberration is an important differentiating feature between symptomatic and asymptomatic gallstone disease and biliary pancreatitis. Short pancreatic duct is another common pancreatic anomaly which stimulates ductal shortening from trauma, malignancy and pancreatitis. Duplication of pancreatic duct may represent *pancreas divisum*, which requires santorinogram with needle catheter for proper evaluation. PVD is seen in 10%-15% of ERCP, and about 70% of symptomatic PVD is associated with pancreatobiliary anomalies.<sup>4</sup>

We therefore conclude that ERCP is an essential investigation which serves to rule out congenital anomaly as a cause of unexplained jaundice and right hypochondrial pain, especially in the presence of PVD. Association of pancreatobiliary anomalies with polycystic kidney, portal hypertension and cholangiocarcinoma, further strengthens the diagnostic role of ERCP in such patients.

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### **Paralytic Ileus: A Possible Complication of Cefuroxime**

*To the Editor:* Cephalosporins are beta-lactam antibiotics which were first introduced in the 1960s. They are derived from cephalosporin C, which is a natural antimicrobial substance produced by the fungus *Cephalosporium acremonium*. The antimicrobial spectrum differs for first-, second- and third-generation cephalosporins, but in general activity increases with generation level. Cefuroxime (Zinacef, Glaxo Wellcome), a second-generation cephalosporin, is a commonly used drug in the pediatric population, mainly because of its wide range of anti-bacterial action and safety.

#### **Case 1**

The patient was a five-month-old boy, the product of a full-term pregnancy and normal vaginal delivery, with a birth weight of 3.2 kg. He required an incubator for three days because of tachypnea. From the age of 40 days, he had recurrent episodes of wheezing, mainly precipitated by upper respiratory tract infections, and resolved with nebulized salbutamol for 3-5 days. At the age of five months, he was admitted with right middle lobe pneumonia and exacerbation of his asthma. His arterial blood gas (ABG) analysis on oxygen showed: pH 7.32, PCO<sub>2</sub> 6.02 Kpa, PO<sub>2</sub> 12.99 Kpa, and HCO<sub>3</sub> 23.1 mmol/L. He was started on intravenous (IV) aminophylline, hydrocortisone 100 mg/kg, nebulized salbutamol, as well as IV cefuroxime and cloxacillin 100 mg/kg each. Bronchodilators were stopped on the fifth day, but on the eighth day of starting antibiotics, he suddenly developed gross abdominal distention, which resulted in increasing tachypnea. This was shortly followed by the passage of watery stools. Investigations showed serum potassium 4.0 mmol/L, sodium 137 mmol/L, and bicarbonate 12 mmol/L. A repeat ABG analysis on room air showed metabolic acidosis: pH 7.26, PCO<sub>2</sub> 2.51 Kpa, PO<sub>2</sub> 15.72 Kpa, HCO<sub>3</sub> 8.2 mmol/L, and saturation 97.3%. Blood and stool cultures yielded no growth. The patient was kept nil by

TABLE 1. Adverse effects associated with cephalosporins.

|                        |  |
|------------------------|--|
| Hypertensive reactions | Maculopapular rash; urticaria, pruritis; angioedema, anaphylaxis   |
| Gastrointestinal       | Diarrhea; nausea, vomiting; transient mild increase in liver enzymes (1-7%)  |
| Hematologic            | Eosinophilia (4%); thrombocytosis; clinically insignificant positive Coomb's test (3%) (hemolytic anemia is rare); reversible neutropenia (rare); clotting abnormalities related to platelet aggregation |
| Miscellaneous          | Superinfections; chemical thrombophlebitis (1-5%)  |

mouth (NPO) and all IV antibiotics were stopped. He showed marked improvement within 48 hours of stopping medications and was discharged home two days later.

### Case 2

This patient was an 18-month-old boy, the product of 26 weeks' gestation and normal vaginal delivery, with a birth weight of 820 g. He developed hyaline membrane disease and required assisted ventilation, which was complicated by grade II intraventricular hemorrhage. He later developed epilepsy and bronchopulmonary dysplasia. He experienced repeated episodes of bronchospasm and was on prophylactic sodium cromoglycate. He was admitted with an acute exacerbation of asthma, and was started on nebulized salbutamol, ipratropium bromide and IV hydrocortisone. Five days later, he suddenly deteriorated with increasing respiratory distress, and his chest x-ray revealed consolidation of the right middle and lower lobes. He was started on IV cefuroxime 100 mg/kg/day, and after the sixth day of starting cefuroxime, he developed gross abdominal distention with no vomiting. Bowel sounds were exaggerated and abdominal x-ray showed multiple fluid levels. His serum electrolytes were normal, with potassium 4.9 mmol/L, and bicarbonate 28 mmol/L. Shortly afterwards, the patient passed watery stools with no mucus. Blood and stool cultures were negative. Cefuroxime was changed to cefotaxime and cloxacillin. A nasogastric tube was introduced, and he was kept NPO. He improved within 48 hours with resolution of the abdominal distention and diarrhea.

### Case 3

The patient was a 10-month-old twin boy, the product of 32 weeks' gestation, who developed hyaline membrane disease and required ventilation therapy for 20 days, which was complicated by grade IV intraventricular hemorrhage. He later developed bronchopulmonary dysplasia, retinopathy of prematurity, and developmental delay. He was admitted because of left-sided bronchopneumonia and started on IV cefuroxime. On the ninth day, the patient developed severe abdominal distention and constipation,

and abdominal x-ray showed multiple fluid levels. Two days later, it was followed by watery stools. His serum electrolytes were normal, with potassium 3.9 mmol/L and bicarbonate 26 mmol/L. Oxygen saturation by pulse oximetry was 97% on room air. Cefuroxime was discontinued and the patient was treated conservatively. He showed marked improvement 48 hours later, with resolution of the abdominal distention and the diarrhea. Stool microscopy showed no white or red blood cells, and stool culture was negative.

### Discussion

Cephalosporins are classified into first-, second-, and third-generation agents, based on their antibacterial spectrum, potency, stability to beta-lactamases, serum half-life, route of excretion, and penetration of the central nervous system.<sup>1</sup> Cefuroxime, a second-generation cephalosporin, is a useful drug for the treatment of severe infections of the lower respiratory tract, urinary tract, skin, bones and joints.<sup>2</sup> It is four to eight times more potent than the first-generation cephalosporins against *Hemophilus influenzae* and some enteric gram-negative bacilli, a characteristic which makes it a useful drug for treating infections in young children between three months and five years who are susceptible to infections from *H. influenzae*. These characteristics, along with the fact that it is less expensive than the third-generation cephalosporins, make cefuroxime the drug of choice for the treatment of pneumonia in children less than five years of age in our hospital. Cefuroxime sodium (Zinacef, Glaxo Wellcome) is the most commonly used drug in our inpatient pediatric population, with a dose of 100-300 mg/kg/day in 3-4 divided doses. Cephalosporins, in general, have a favorable profile of toxicity compared to other antimicrobial agents. Adverse effects occur least with ceftriaxone. The most common adverse effects are allergic, ranging from rash and urticaria to hypersensitivity reactions, including anaphylaxis. Diarrhea may either be related to increased biliary excretion of cephalosporins, or to *Clostridium difficile* colitis.<sup>3</sup> Other adverse effects are listed in Table 1.

In this report, we share our observation of possibly another adverse reaction, which is paralytic ileus. It is manifested by abdominal distention, multiple fluid levels on plain radiographs, followed by or associated with diarrhea, and resolved by conservative measures with cessation of oral feeds and deflation of the stomach by nasogastric tube insertion. It occurred in three patients who were three years old or younger, two of them with pre-existing lung pathology of bronchopulmonary dysplasia. All presented with lower respiratory tract infection, mainly lobular pneumonia with exacerbation of bronchospasm, and required prolonged IV cefuroxime therapy. Abdominal distention was observed at least six days after starting

treatment. Paralytic ileus could not be attributed to any electrolyte disturbance, since all of the patients had normal serum electrolytes. Also, it could not be fully explained by associated hypoxia, since ABG analysis performed in Case 1 did not show any hypoxemia or hypercarbia. Furthermore, all of the patients were showing signs of improvement of their chest problem when they suddenly developed signs of paralytic ileus, and they all improved immediately after stopping cefuroxime or changing to another antibiotic.

In conclusion, although diarrhea is a recognized complication of cephalosporins in general, there has been no report of this being preceded by paralytic ileus, a matter which needs further observation, especially in the susceptible group of patients described above.

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**Sickle Cell Disease in the Kingdom of Saudi Arabia: East and West**

*To the Editor:* In his editorial, Dr. Pearson<sup>1</sup> mentions that "it is well known that the sickle cell disease seen in many patients from the Arabian Gulf area has distinct clinical and electrophoretic differences from that observed in the United States and Africa." This may hold true only in some of the Arabian Gulf areas, but not in the Kingdom of Saudi Arabia.

It has been widely reported here by Al-Awamy,<sup>2</sup> El-Hazmi,<sup>3</sup> Sergent,<sup>4</sup> and Opawoye,<sup>5,6</sup> that there are two distinct types of sickle cell anemia in the Kingdom. In the Eastern Province, the Saudi-Indian haplotype has been identified, and in the southern regions, the Benin haplotype has been found among Africans and Black Americans. The studies showed that, in general, the sickle cell disease in the Eastern Province runs a milder clinical course. The mildness in symptoms is attributed to the protective effect of the high level of HbF, and also partly because of the co-existence of  $\alpha$ -thalassemia, while in the

other provinces, especially the Western/Southwestern provinces, a severe form of sickle cell anemia was encountered with features similar to those reported in communities in Africa and the US. The majority of the patients from these regions of Saudi Arabia suffered from severe and frequent episodes of crises, required blood transfusions frequently, and some suffered from hand and foot syndromes.

I agree with Dr. Pearson that in an area such as the Western/Southwestern provinces of the Kingdom where the Benin haplotype of sickle cell disease is found, the need for neonatal screening of the disease cannot be over-emphasized.

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**Reply**

*To the Editor:* Dr. Opawoye's letter underscores and supports several points I made in my editorial comments on the papers of Nasserullah et al.<sup>1</sup> and Hawasawi et al.,<sup>2</sup> concerning the heterogenous clinical and hematological manifestations of the sickle cell disease encountered in the Kingdom of Saudi Arabia.<sup>1,2</sup> In general, in the Eastern Province and the other Gulf countries, the disease is usually mild. The main reason for this is that it is associated with the so-called "Indian-Saudi" DNA haplotype. Although  $\alpha$ -thalassemia is also prevalent in these regions, the moderating effect of  $\alpha$ -thalassemia on homozygous hemoglobin S is controversial (at least in the United States). On the other hand, in Western and Southern Saudi Arabia, where the disease is more severe, "African" DNA haplotypes predominate, and the clinical disease resembles that seen in Africa and the Western world.

In central parts of Saudi Arabia, both mild and severe disease may occur, owing to relocation of individuals from Western or Eastern regions. The differences must be taken

into consideration when assessing the public health value of large neonatal screening programs.

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