

Tony Dixon

Breast Cancer: The Debates Continue

FOR EVERY COMPLEX problem, H.L. Mencken once wrote, there is a solution that is simple, direct and wrong, and the history of medical approaches to breast cancer underlines the truth in his statement. It is a field that seems to be characterized by thinking that is both wishful and simplistic.

As long ago as 1888, A. Jackson¹ noted the lack of evidence that simple mastectomy was inferior to more radical operations, which in those days included operations to remove all the axillary nodes, clear the whole axilla, remove the supraclavicular nodes, or remove the arm at the shoulder joint, as well as total mastectomy. He thought these more radical operations unscientific and needlessly cruel, and warned against ignoring clinical experience which had shown that surgery, however radical, did not prevent recurrence of the tumour. The introduction of Halstead's operation 10 years later, in 1898, made no further impact on the survival of breast cancer patients,² although it remained the surgical standard for almost the next one hundred years, despite the fact that local mastectomy with irradiation was found to be preferable to radical mastectomy back in 1928.³

The 'simple' solution of surgery—cut everything out, and you will get rid of the tumour as well as the problem—has been found wanting, and Skrabanek⁴ finds the evidence that breast cancer cannot be cured with present methods to be overwhelming. He comments that "it is surely complacent to continue our current practice of subjecting . . . women with primary disease to a futile mutilating procedure", and quotes Lowe's⁵ assertion that survival is much more closely related to the intrinsic malignancy of the tumour than to early diagnosis and treatment.

An alternative solution—the early detection of breast cancer—seems to

have replaced surgery as the 'holy grail' to be pursued in the 1980s, although the logic of early detection may be suspect in the absence of an intervention of demonstrated benefit. There are two screening procedures currently available, breast self-examination (BSE) and mammography. While magnetic resonance imaging provides good pictures, it is, at present, prohibitively expensive. Thermography, despite initial enthusiasm, is unreliable, and ultrasound is insensitive.⁴

BSE has been heavily promoted by health professionals and cancer societies, to such an extent that casting any doubt on its effectiveness seems sacrilegious.⁶ In a recent comprehensive review of the literature, however, Frank and Mai⁷ argue that women who find asymptomatic benign breast lesions by BSE are exposed to unnecessary anxiety, unnecessary medical investigations and invasive procedures, and potential risks of false reassurance. They found that false-positives so greatly outnumber patient-detected cancers below ages 30 to 35 that the potential of benefit to women in this age group is remote, and they conclude that BSE in younger women, by encouraging invasive and costly medical investigation of many asymptomatic benign breast lumps needing no treatment, may do more harm than good. They comment:

There is no convincing evidence, as yet, of net health benefits, in terms of reduced mortality or morbidity, accruing to women of any age who practise BSE . . . Whether unequivocal evidence of BSE effectiveness can actually be produced in the current social climate of widespread BSE promotion is very doubtful. In the meantime, there are substantial risks, as well as many personal costs, for the overwhelming majority of young women who present with breast masses found by BSE,

only to have unpleasant subsequent investigations reveal no pathology of significance.

What about mammography? In this issue of *Canadian Family Physician* Dr. Cornelia Baines, who is deputy director of the National Breast Screening Study, reviews the current evidence on screening mammography and its implications for practice. She concludes that the evidence to date shows women aged 50 and over to be the only ones who benefit from mammography in terms of reduced mortality. Recommendations about the screening of women aged 40 to 49 must await the results of the National Breast Screening Study due in the next few years. Dr. Baines makes the important point that it makes no sense to use mammography for screening unless the facilities and staff for such screening are "excellent". This means that mammography screening cannot just be added on to the normal clinical load of already existing radiology departments, but demands the development of a specialized free-standing service. The financial implications of such a development are considerable, and the literature contains estimates of cost as high as \$195,000 per cancer detected.⁸

Dr. Baines' review of the subject is timely. This spring the American Cancer Society is launching its annual fund-raising campaign under the banner of mammographic breast screening. With the slogan "Have a mammogram. Give yourself the chance of a lifetime," the Society is recommending "baseline" mammography for women aged 35–39, routine mammograms every one to two years in the 40–49 year group, and annual mammograms for those aged 50 and over. "A mammogram", the Society's advertising announces ". . . helps your doctor 'see' breast cancer before there's a lump, when the cure rates are

AMOXIL*

(amoxicillin trihydrate)

ANTIBIOTIC

ACTION AMOXIL exerts a bactericidal action against sensitive organisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell wall mucopeptide.

INDICATIONS AND CLINICAL USES AMOXIL may be indicated in the treatment of infections due to susceptible strains of the following organisms: gram-negative: Haemophilus influenzae, Escherichia coli, Proteus mirabilis and Neisseria gonorrhoeae; gram-positive: Streptococci, Diplococcus pneumoniae and non-beta-lactamase-producing staphylococci.

In emergency cases, before the causative organism is identified, therapy may be initiated with AMOXIL, based on clinical judgment while awaiting the results of bacteriologic studies to isolate the infecting organism, and to determine its sensitivity.

CONTRAINDICATIONS A history of an allergic reaction to the penicillins or cephalosporins.

WARNINGS Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis occurs more frequently following parenteral therapy, it has happened in patients on oral penicillins. These reactions are more apt to occur in individuals with a history of sensitivity to multiple allergens. It has also been reported that individuals with a history of penicillin hypersensitivity have had severe reactions when treated with cephalosporins. Before initiating therapy with AMOXIL or any other penicillin careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, AMOXIL therapy should be discontinued and appropriate therapy instituted.

Serious anaphylactoid reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should also be used as indicated.

PRECAUTIONS Periodic assessment of renal, hepatic, and hematopoietic function should be made during prolonged AMOXIL therapy.

AMOXIL is excreted mostly by the kidney. The dosage administered to patients with renal impairment should be reduced proportionately to the degree of renal function.

The possibility of superinfections with mycotic or bacterial organisms should be kept in mind during therapy. If superinfections occur (usually involving Aerobacter, Pseudomonas or Candida), the drug should be discontinued and appropriate therapy instituted.

Evidence is lacking concerning safety of AMOXIL in the treatment of infections during pregnancy. Benefits of the drug should then be weighed against its possible hazards to the mother and child.

Morbilliform rashes following the use of ampicillin and amoxicillin in patients with infectious mononucleosis are well documented. AMOXIL may therefore be contraindicated in cases where infectious mononucleosis is suspected or confirmed.

ADVERSE REACTIONS As with other penicillins, presumably the most common untoward reactions will be related to sensitivity phenomena, similar to those observed with ampicillin. They are more likely to occur in individuals who have previously demonstrated hypersensitivity to penicillins and in those with a history of allergy, asthma, hay fever or urticaria. The following adverse reactions have been reported as associated with the use of AMOXIL: **Gastrointestinal** — nausea, vomiting and diarrhea. **Hypersensitivity reactions** — erythematous maculopapular rashes and urticaria. **Note:** Urticaria, other skin rashes and serum sickness-like reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids. Whenever such reactions occur, AMOXIL should be discontinued unless, in the opinion of the physician, the condition is life-threatening and amenable only to AMOXIL. **Liver** — moderate rises in serum glutamic oxaloacetic transaminase (SGOT), alkaline phosphatase and lactic dehydrogenase have been noted, but the significance of these findings is unknown. **Hemic and lymphatic systems** — anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia, neutropenia and agranulocytosis have been reported during therapy with the penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena.

TREATMENT OF OVERDOSAGE The treatment of overdose would likely be needed only in patients with severely impaired renal function, since patients with normal kidneys excrete penicillins at a fast rate. Dialysis is, therefore, the main form of treatment.

In cases of severe allergic reactions, general supportive measures - (if the patient is in shock) or symptomatic therapy similar to that applied to all cases of hypersensitivity are recommended.

DOSAGE AND ADMINISTRATION Infections of the ear, nose and throat due to streptococci, pneumococci, and non-beta-lactamase-producing staphylococci. Infections of the upper respiratory tract due to H. influenzae; infections of the genitourinary tract due to E. coli, P. mirabilis and S. faecalis; infections of the skin and soft tissues due to streptococci, non-beta-lactamase producing staphylococci, and E. coli: **Usual Dose:** Adults: 250 mg every 8 hours. Children: 25 mg/kg/day in divided doses every 8 hours. This dosage should not exceed the recommended adult dosage.

In severe infections, or infections where sensitivity determinations indicate higher blood levels may be advisable: Adults: 500 mg every 8 hours. Children: 50 mg/kg/day in divided doses every 8 hours.

Infections of the lower respiratory tract due to streptococci, pneumococci, non-beta-lactamase-producing staphylococci and H. influenzae: **Usual Dose:** Adults: 500 mg every 8 hours. Children: 50 mg/kg/day in divided doses every 8 hours. This dosage should not exceed the recommended adult dosage. Urethritis due to non-beta-lactamase-producing N. gonorrhoeae: 3 g as a single oral dose. Before prescribing AMOXIL a dark field examination should be done in patients in whom syphilis is also suspected, and monthly serologic tests should be carried out for at least 4 months.

In the treatment of chronic urinary tract infections, frequent bacteriologic and clinical evaluations are essential. Smaller doses than those recommended above should not be used. In stubborn infections, therapy may be required for several weeks, sometimes at doses higher than those recommended above. Concurrent bacteriologic sensitivity monitoring is recommended. It may be necessary to continue clinical and/or bacteriologic follow-up for several months after cessation of therapy.

Treatment must be continued for 48 to 72 hours beyond the time the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. At least 10 days' treatment is recommended for infections caused by Group A beta-hemolytic streptococci to prevent acute rheumatic fever or glomerulonephritis.

DOSAGE AND ADMINISTRATION OF PEDIATRIC DROPS For all indications except infections of the lower respiratory tract: Total daily dosage: 25 mg/kg/day in divided doses every eight hours. eg: Under 6 kg (13 lb) - 0.5 ml every 8 hours. 6 - 8 kg (13-18 lb) - 1 ml every 8 hours.

For infections of the lower respiratory tract: Total daily dosage: 50 mg/kg/day in divided doses every eight hours. eg: Under 6 kg (13 lb) - 1 ml every 8 hours. 6 - 8 kg (13-18 lb) - 2 ml every 8 hours.

After reconstitution, the required amount of suspension should be placed directly on the child's tongue for swallowing.

DIRECTIONS FOR MIXING ORAL SUSPENSION Prepare suspension at time of dispensing as follows: 75 ml size - add 65 ml of water; 100 ml size - add 87 ml of water; 150 ml size - add 130 ml of water. Shake vigorously. Each 5 ml (teaspoonful) contains amoxicillin trihydrate equivalent to 125 mg or 250 mg amoxicillin.

DIRECTIONS FOR MIXING PEDIATRIC DROPS Prepare suspension at time of dispensing as follows: Add 13 ml of water and shake vigorously. Each 1 ml of suspension will contain 50 mg of amoxicillin (as the trihydrate).

Keep bottle tightly closed. The reconstituted suspension is stable for 7 days at room temperature 70°F (20°C) and 14 days refrigerated at 40°F (4.5°C).

SUPPLY: CAPSULES: No. 695 - AMOXIL-250 Each capsule contains amoxicillin trihydrate equivalent to 250 mg amoxicillin, in bottles of 100 and 500. **No. 696 - AMOXIL-500** Each capsule contains amoxicillin trihydrate equivalent to 500 mg amoxicillin, in bottles of 100 and 250.

ORAL SUSPENSIONS: No. 697 - AMOXIL-125 Each 5 ml of reconstituted suspension contains amoxicillin trihydrate equivalent to 125 mg amoxicillin, in bottles of 75, 100 and 150 ml. **No. 698 - AMOXIL-250** Each 5 ml of reconstituted suspension contains amoxicillin trihydrate equivalent to 250 mg amoxicillin, in bottles of 75, 100 and 150 ml. **No. 694 - AMOXIL Pediatric Drops** Each 1 ml of reconstituted suspension contains amoxicillin trihydrate equivalent to 50 mg amoxicillin, in bottles of 15 ml. **CHEWABLE TABLETS: No. 690 - AMOXIL CHEWABLE TABLETS:** Each tablet contains amoxicillin trihydrate equivalent to 125 mg amoxicillin, in bottles of 100 and 10 blister strips of 10. **No. 691 - AMOXIL CHEWABLE TABLETS** Each tablet contains amoxicillin trihydrate equivalent to 250 mg amoxicillin, in bottles of 100 and 10 blister strips of 10.

Ayerst AYERST LABORATORIES
Division of Ayerst, McKenna & Harrison, Inc.
Montreal, Canada

Made in Canada by arrangement with BEECHAM INC.

*Reg'd TM

Product Monograph available on request.

835

PAAB

near 100% . . . It's essential you have a mammogram." In a slide-tape show designed to reinforce the message that "Breast cancer has virtually nowhere to hide," the comment is made that "Mammography should be as routine as a Pap test. It's the best way to detect breast cancer at a very early, highly curable stage."

At best, such recommendations reflect well-intentioned enthusiasm that glosses over both practical and economic realities. At worst, they are a confusing mixture of half-truths, unsupported by the scientific literature to date, which can only add to the anxiety and uncertainty that always seem to cloud the rational discussion of what knowledge we do—and more especially do not—have, about breast cancer. Once again, physicians trying to provide balanced and realistic advice to their patients will find themselves battling against the flip one-line slogans beloved of some health-care institutions.

There is, at present, no simple solution to the complex challenge of breast cancer, nor is there likely to be in the foreseeable future. Any answers that do come will require the sort of difficult research undertaken by Dr. Baines and her colleagues in the National Breast Screening Study. Simplistic solutions will not work, no matter how often, or how fervently, they are proposed. ●

References

1. Jackson A. On carcinoma of the breast and its treatment. *Med Press* 1888; i:552-3.
2. Baum M, Edwards MH. Management of early carcinoma of the breast. *Lancet* 1972; 2:85.
3. Lee BJ. Conservatism in the treatment of primary operable cancer of the breast. In: Report of the international conference on cancer, London, 1928. British Empire Cancer Campaign. London: J. Wright, 1928.
4. Skrabenek P. False premises and false promises of breast cancer screening. *Lancet* 1985; 2:316-20.
5. Lowe CR. Breast cancer. In: Screening in medical care. Reviewing the evidence. Nuffield Provincial Hospitals Trust. London: Oxford University Press, 1968:33.
6. Moore FD. Breast self-examination. *N Engl J Med* 1978; 299:305.
7. Frank JW, Mai V. Breast self-examination in young women: more harm than good? *Lancet* 1985 2:654-7.
8. Haagensen CD, Bodrum C, Haagensen DE. Breast carcinoma: risk and detection. Philadelphia: W.B. Saunders, 1981.