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Prophylaxis of Cesarean Sections

To the Editor:

In a recent letter by Dougherty and Williams[1] published without editorial comment, the authors imply a link between cefotetan prophylaxis and a transient increase in postoperative wound infections following urgent cesarean sections. While they include the caveat that factors other than microbial resistance to cefotetan may have contributed to these infections, the reader is left with the unmistakable impression that this outbreak resulted from a failure of cefotetan as a prophylactic agent. No mention is made of other factors that may have contributed, however, including timing of prophylaxis, use of postoperative drains, commonality of operating room personnel, method and timing of skin preparation, etc. No microbiological data are presented to support the notion that cefotetan-resistant organisms lead to this outbreak.

In this era of cost consciousness, I believe it is unfortunate that such hypotheses are published without additional scientific support. In fact, there is no evidence that any second or third generation cephalosporin is superior to first generation cephalosporins in prophylaxis for cesarean section. A recent issue of the *Medical Letter on Drugs and Therapeutics*[2] advocates the use of a single dose of cefazolin for prophylaxis in high-risk cesarean sections. The three prospective studies[3-5] cited by Dougherty and Williams also fail to indicate any superiority of one agent over another, whether that agent be cefoxitin, cefotetan or cefazolin.

In any institution, small transient increases in infection rates are inevitable. In our experience, the mere recognition of the epidemic usually heralds its disappearance.

Elliot Frank, MD, FACP
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Steve H. Dougherty, MD and Vickie S. Williams, DO, were asked to respond to this letter.

We appreciate Dr. Franks point that factors other than failure of antibiotic prophylaxis may have been responsible for the outbreak of postoperative infections experienced among our caesarean section patients and agree that the problem might well have been resolved by the substitution of prophylactic agents other than cefoxitin or cefotetan, i.e., cefazolin. However, cefazolin prophylaxis has been used intensively for many years in a variety of surgical settings, and in two recent comparative trials in cardiac surgery, it proved to be inferior to either cefamondole[1,2] or cefuroxime[2] in preventing wound infections. Such findings have led to speculation that prolonged use of cefazolin may have finally decreased its clinical usefulness.[3] We can only wonder whether or not the intensive use of cefotetan prophylaxis among our C-section patients over a three-year period may have likewise led to decreased drug effectiveness.

Some of our patients who developed infection received their first dose of cefotetan prophylaxis as much as two hours preoperatively; some received their first dose intraoperatively. Because the plasma half-life of cefotetan is 3 to 4.6 hours after intravenous injection, a two-hour delay between administration of an intital 2 g dose and the commencement of C-section should still have allowed for adequate tissue levels. Intraoperative administration of the first dose of antibiotic prophylaxis at the time of clamping of the umbilical cord is a common practice that appears to be effective.[4,5] Postoperative drains are uncommonly used as an adjunct to caesarean section and were not used in our patients. To our knowledge, no changes in operating room personnel were made in connection with the outbreak of infections.

Steve H. Dougherty, MD
Vickie S. Williams, DO
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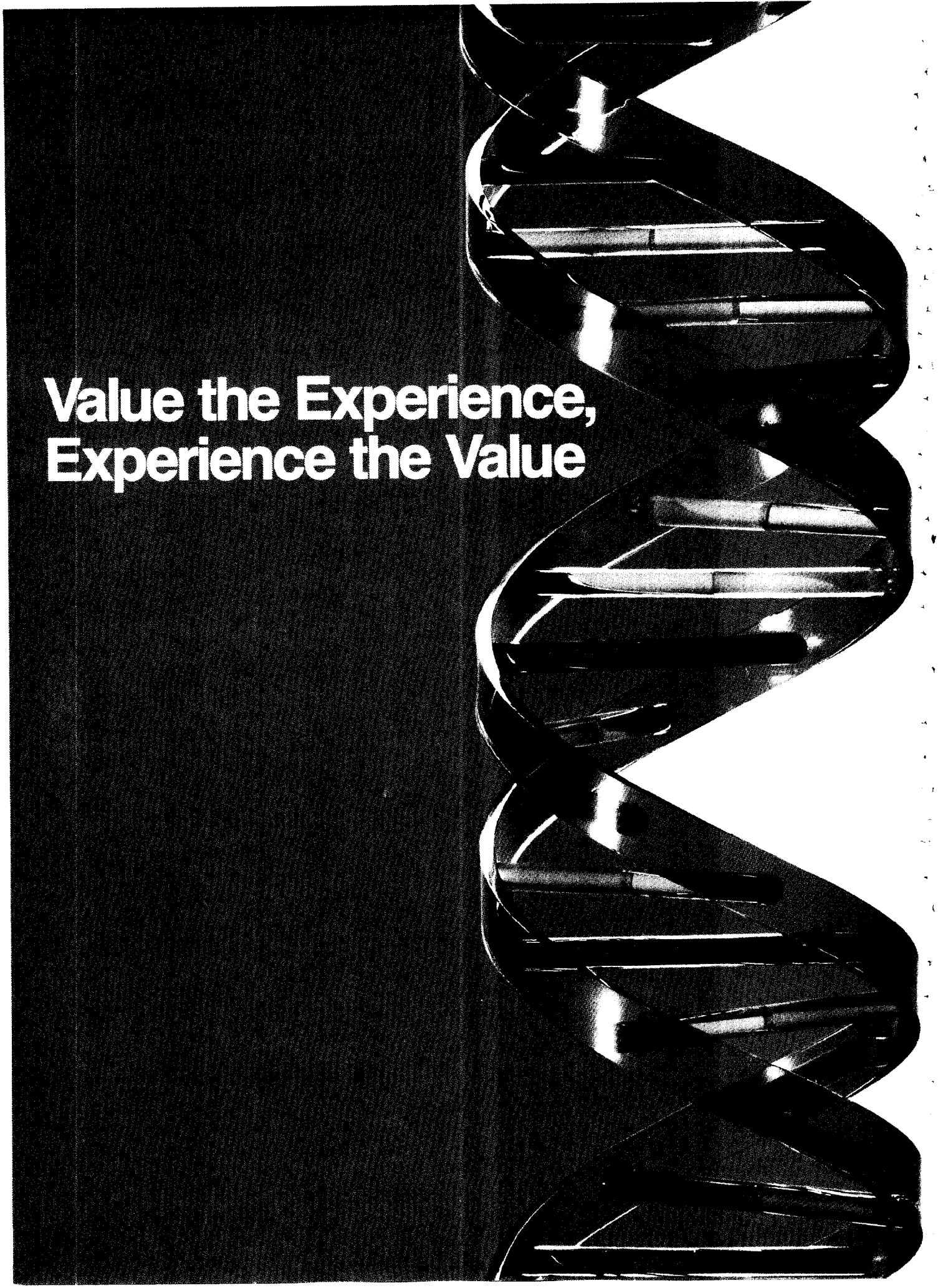

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INDICATIONS AND USAGE

RECOMBIVAX HB is indicated for vaccination against infection caused by all known subtypes of hepatitis B virus. RECOMBIVAX HB Dialysis Formulation is indicated for vaccination of adult predialysis and dialysis patients against infection caused by all known subtypes of hepatitis B virus.

Vaccination with RECOMBIVAX HB is recommended in persons of all ages who are or will be at increased risk of infection with heoatitis B virus. In areas with high prevalence of infection, most of the population are at risk of acquiring hepatitis B infection at a young age. Therefore, vaccination should be targeted to prevent such transmission. In areas of low prevalence, vaccination should be limited to those who are in groups identified as being at increased risk of infection.

CONTRAINDICATIONS

Hypersensitivity to yeast or any component of the vaccine.

WARNINGS

Patients who develop symptoms suggestive of hypersensitivity after an injection should not receive further injections of the vaccine (see CONTRAINDICATIONS).

Because of the long incubation period for hepatitis B, it is possible for unrecognized infection to be present at the time the vaccine is given. The vaccine *may not* prevent hepatitis B *in* such patients.

PRECAUTIONS

General

As with any percutaneous vaccine, epinephrine should be available for immediate use should an anaphylactoid reaction occur

Any serious active infection is reason for delaying use of the vaccine except when. in the ooinion of the physician, withholding the vaccine entails a greater risk.

Caution and appropriate care should be exercised in administering the vaccine to individuals with severely compromised cardiopulmonary status or to others in whom a febrile or svstemic reaction could pose a significant risk.

Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with the vaccine. It is also not known whether the vaccine *can* cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. The vaccine should be given to a pregnant woman only if clearly needed.

Nursing Mothers

It is not known whether the vaccine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when the vaccine is administered to a nursing woman.

Pediatric Use

RECOMBIVAX HB has been shown to be usually well tolerated and highly immunogenic in infants and children of all ages. Newborns also respond well; maternally transferred antibodies do not interfere with the active immune response to the vaccine. See DOSAGE AND ADMINISTRATION for recommended pediatric dosage and for recommended dosage for infants born to HBsAg-positive mothers.

The safety and effectiveness of RECOMBIVAX HB Dialysis Formulation in children have not been established.

ADVERSE REACTIONS

RECOMBIVAX HB and RECOMBIVAX HB Dialysis Formulation are generally well tolerated. No serious adverse reactions attributable to the vaccine have been reported during the course of clinical trials. No adverse experiences were reported during clinical trials which could be related to changes in the titers of antibodies to yeast. As with any vaccine, there is the possibility that broad use of the vaccine could reveal adverse reactions not observed in clinical trials.

In a group of studies, 3.258 doses of RECOMBIVAX HB were administered to 1,252

RECOMBIVAX HB"
(Hepatitis B Vaccine [Recombinant], MSD)

healthy adults who were monitored for 5 days after each dose. Injection-site and systemic complaints were reported following 17% and 15% of the injections, respectively.

The following adverse reactions were reported:

Incidence Equal to or Greater Than 1% of Injections

LOCAL REACTION (INJECTION SITE)

Injection-site reactions consisting principally of soreness and including pain, tenderness, pruritus, erythema, ecchymosis, swelling, warmth, and nodule formation.

BODY AS A WHOLE

The most frequent systemic complaints include fatigue/weakness; headache; fever (≥100°F); malaise.

DIGESTIVE *SYSTEM*

Nausea; diarrhea.

RESPIRATORY SYSTEM

Pharyngitis; upper respiratory infection.

Incidence Less Than 1% of Injections

BODY AS A WHOLE

Sweating; achiness; sensation of warmth; lightheadedness chills: flushing.

DIGESTIVE SYSTEM

Vomiting; abdominal pains/cramps; dyspepsia; diminished appetite.

RESPIRATORY SYSTEM

Rhinitis; influenza; cough.

NERVOUS SYSTEM

Vertigo/dizziness; paresthesia.

INTEGUMENTARY SYSTEM

Pruritus; rash (non-specified); angioedema; urticaria.

MUSCULOSKELETAL SYSTEM

Arthralgia including monoarticular; myalgia; back pain; neck pain; shoulder pain; neck stiffness.

HEMIC/LYMPHATIC SYSTEM

Lymphadenopathy.

PSYCHIATRIC/BEHAVIORAL

Insomnia/disturbed sleep.

SPECIAL SENSES

Earache.

UROGENITAL SYSTEM

Dysuria.

CARDIOVASCULAR SYSTEM

Hypotension.

The following additional adverse reactions have been reported with use of the marketed vaccine. In many instances, the relationship to the vaccine was unclear

Hypersensitivity: Anaphylaxis and symptoms of immediate hypersensitivity reactions including rash, pruritus, urticaria. edema, angioedema, dyspnea, chest discomfort, bronchial soasm. palpitation, or symptoms consistent with a hypotensive episode have been reported within the first few hours after vaccination. An apparent hvoersensitivity syndrome (serum-sickness-like) of delayed onset has been reported days to weeks after vaccination, including arthralgia/arthritis (usually transient), fever, and dermatologic reactions such as urticaria, erythema multiforme, ecchymoses. and erythema nodosum (see WARNINGS and PRECAUTIONS).

Nervous System: Peripheral neuropathy including Bell's Palsv: muscle weakness: Guillain-Barré syndrome.

Special Senses: Optic neuritis.

Potential ADVERSE EFFECTS

In addition, a variety of adverse effects not observed in clinical trials with RECOMBIVAX HB or RECOMBIVAX HB Dialysis Formulation have been reported with HEPTAVAX-B® (Hepatitis B Vaccine, MSD)(plasma-derived hepatitis B vaccine). Those listed below are to serve as alerting information to physicians:

Nervous *System*: Neurological disorders such as myelitis including transverse myelitis; acute radiculoneuropathy; herpes zoster.

Hematologic: Thrombocytopenia.

Special Senses: Tinnitus; visual disturbances.

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DOSAGE AND ADMINISTRATION

Do not inject intravenous/y or intradermally.

RECOMBIVAX HB DIALYSIS FORMULATION (40 mcg/mL) IS INTENDED ONLY FOR ADULT PREDIALYSIS/DIALYSIS PATIENTS.

RECOMBIVAX HB (10 mcg/mL) IS NOT INTENDED FOR USE IN PREDIALYSIS/DIALYSIS PATIENTS.

RECOMBIVAX HB and RECOMBIVAX HB Dialysis Formulation are for intramuscular injection. The deltoid muscle is the preferred site for intramuscular injection in adults, Data suggest that injections given in the buttocks are frequently given into fatty tissue Instead of into muscle. Such injections have resulted in a lower seroconversion rate than was expected. The *anterolateral* thigh is the recommended site for intramuscular injection in infants and young children.

For persons at risk of hemorrhage following intramuscular injection, RECOMBIVAX HB may be administered subcutaneously. However, when other aluminum-adsorbed vaccines have been administered subcutaneously, an increased incidence of local reactions including subcutaneous nodules has been observed. Therefore. subcutaneous administration should be used only in persons (e.g., hemophiliacs) who are at risk of hemorrhage following intramuscular injections.

The vaccine should be used as supplied; no dilution or reconstitution is necessary. The full recommended dose of the vaccine should be used.

The RECOMBIVAX HB vaccination regimen consists of 3 doses of vaccine. The volume of vaccine to be given on each occasion is as follows:

Age group	Initial	1 month	6 months [1]
Birth' through 10 years of age	0.25 mL (2 5 mcg)	0.25 mL (2.5 mcg)	0.25 mL (2 5 mcg)
Il-19 years Of age	0.5 mL (5 mcg)	0.5 mL (5 mcg)	0.5 mL (5 mcg)
≥20 years	1 ml (10 mcg)	1 ml (10 mcg)	1 ml (10 mcg)

'Infants born of HBsAg-negative mothers.

The recommended RECOMBIVAX HB Dialysis Formulation vaccination regimen for predialysis/dialysis patients is as follows:

Group	Formulation	Initial	1 month	6 months
Predialysis and Dialysis Patients	Dialysis 40 mcg/mL	1 mL	1 mL	1 mL

Whenever revaccination or administration of a booster dose is appropriate, RECOMBIVAX HB may be used.

The recommended regimen for infants born of HBsAg-positive mothers is as follows:

	Birth	Within 7 days	1 month	6 months
RECOMBIVAX HB		0.5 mL (5 mcg)	0.5 mL (5 mcg)	0.5 mL (5 mcg)
HEPATITIS B IMMUNE GLOBULIN	0.5 mL	—	—	—

Storage

Store vials at 2°–8°C (36°–46°F). Storage above or below the recommended temperature may reduce potency.

Do not freeze since freezing destroys potency

For more detailed information,, consult your MSD Representative or see Prescribing Information.

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