Acute Medical Problems in the Postoperative Patient

Edited by

George A. Porter, M.D.

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PREFACE

Acute Medical Problems in the Postoperative Patient began as do many good things, following a sumptuous meal. The dinner involved a faculty that was convened to discuss issues in the medical–surgical treatment of patients with end-stage renal disease. All agreed that a book that addresses the practical needs of house officers and practitioners, managing a wide variety of medical problems in postoperative patients, would be desirable.

This book is the result of that discussion. My co-authors and I have focused on commonly encountered postoperative problems to establish a framework for clinical decision-making.

Frequency and treatability are the criteria for inclusion of the postoperative medical problems in this book. Tables consolidate diagnostic possibilities or treatment options. Traditional organ-system classification is mainly followed, although presentations that are more systemic in nature are dealt with in separate sections. When applicable we build on pathophysiology to develop treatment rationale.

We welcome comments and suggestions from our readers.

George A. Porter, M.D.

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1

PREOPERATIVE CONSIDERATIONS

Stephen R. Jones Robert C. Kimbrough
George A. Porter Michael Walczyk

PREVENTING INFECTIONS

Stephen R. Jones and Robert C. Kimbrough

Preoperative Considerations

Factors Predisposing to Infection

A variety of local and systemic factors may be present before surgery, and may compromise the ability of the host to deal with contamination:

Extracellular fluid depletion
Protein-calorie malnutrition
Alcoholism
Use of immunosuppressive drugs
Remote infection
Prolonged hospitalization

Nutrition

The incidence of postoperative infection appears to be related in a general way to the underlying physical well-being of the patient. Malnutrition is one potentially reversible component of a high-risk status. It then stands to reason that whenever possible, malnutrition should be corrected by feedings high in calories and biologic value. The details of hyperalimentation are beyond the scope of this writing, and an appropriate reference should be consulted (see below).

Table 1-1. Recommendations Regarding Prophylactic Antibiotics for Various Surgical Procedures with a High Incidence of Infection

Surgical Procedure	Agent	Dose/Route/Duration
Head and Neck (if oral cavity)	Penicillin-G	1 million units/IM/on call to OR
Colorectal	Neomycin and erythromycin	1 g each/PO/at 1 PM, 3 PM, and 11 PM on the day before surgery. A mechanical bowel preparation should be given too
	Cefazolin	1 g/IM/on call to OR and q8h × 2 postoperatively
Appendectomy	Cefazolin	1 g/IM/on call to OR and q8h × 2 postoperatively
Biliary tract (if obstructed and in elderly)	Cefazolin	1 g /IM/on call to OR and q8h × 2 postoperatively
Gastric (if obstructed)	Cefazolin	1 g/IM/on call to OR and q8h × 2 postoperatively
C-section	Cefazolin	1 g/IM/on call to OR and q8h × 2 postoperatively
Hysterectomy (vaginal)	Cefazolin	1 g/IM/on call to OR and q8h × 2 postoperatively

Prophylactic Antimicrobials

Several principles apply to logical consideration of the appropriateness of administering prophylactic antimicrobials to prevent infection in a given surgical situation:

High Risk. If the incidence of infection for a surgical procedure is high enough, a randomized, double-blind controlled trial will almost certainly have been done and will be available in the literature. If that study has demonstrated benefit, then antimicrobial prophylaxis is justified.

Disastrous Consequences. Even if the risk of an infection is slight and a controlled trial is not statistically feasible, prophylactic antimicrobials may be appropriate if the consequence of the infection would be disastrous (e.g., hip replacement).

Timing. If justified by either of the above situations, antimicrobials are effective only if appreciable blood and tissue levels are achieved at the time of surgical intervention, with its inevitable tissue damage and microbial inoculation.

Table 1-2. Recommendations Regarding Prophylactic Antibiotics for Various Surgical Procedures with a Low Incidence of Infection

Prosthetic heart valve or pacemaker placement	Cefazolin	1 g/IM/on call to OR and q8h × 2 days
Total joint replacement	Cefazolin	1 g/IM/on call to OR and q8h × 2 days

Table 1-3. Fifteen Most Frequently Isolated Pathogens on Surgical Services

Pathogen	Percentage of Infections
*Escherichii coli**	16.1
Pseudomonas aeruginosa	12.4
Staphylococcus aureus	10.8
Enterococci	10.8
Klebsiella spp*	7.8
Enterobacter spp*	7.3
Staphylococcus epidermidis	6.1
Proteus spp*	5.6
Candida spp	4.6
Serratia spp*	2.6
Other fungi	1.4
Bacteroides spp	1.8
Group B streptococcus	0.7
Abnobacter spp*	1.4
Other anaerobes	0.9
All others	10.2

* All are Enterobacteriaceae.

Cost. If all other matters are equal, use the least expensive antimicrobial prophylaxis regimen.

The surgical procedures listed in Table 1-1 are associated with a relatively high incidence of infection. They have been studied, and patients have been found to benefit from the prophylactic antimicrobials suggested. Often, multiple antimicrobial regimens have been studied and in such cases the ones listed are regarded as equally efficacious and the most cost-effective.

For the surgical procedures listed in Table 1-2, the incidence of infection is low; however, prophylaxis is recommended because the consequence of infection is so serious that the use of preventive antimicrobials is probably cost-effective. The selection of antimicrobials for prophylaxis in the surgical patient is guided by the distribution of pathogens as summarized in Table 1-3.

RISK OF CONTRAST STUDIES

George A. Porter

During the preoperative evaluation, diagnostic procedures are necessary to identify organ dysfunction within body cavities. Although modern technology continuously strives to achieve such imaging without the aid of either invasive procedures or contrast agents, we still depend substantially on contrast-enhanced imaging in the preoperative evaluation of patients, especially those with acute problems. Because of this, the risk of contrast-induced nephropathy must be considered when weighing the benefit-risk of any radiographic procedure.

Historically, a wide variety of potential clinical risk factors have been proposed as predisposing a patient to the development of contrast-induced nephropathy. Included in this list are multiple myeloma, dehydration, hypertension, diabetes mellitus, proteinuria, liver disease, large doses of contrast agent,

an age of 60 years or older, peripheral vascular disease, and pre-existing renal disease. From the accumulated published data, the following summarizes current thinking regarding the profile of patients predisposed to contrast-induced nephropathy: In 9 of 10 patients in whom contrast-induced nephropathy develops, pre-existing renal insufficiency is present. This is the only independent variable to emerge as statistically confirmed. The apparent predominance of diabetic patients in reported series of cases of contrast-induced nephropathy relates to two coincidences. First, there is a high incidence of renal impairement in diabetes. Second, because of the vascular disease that complicates diabetes, these patients are more frequently studied using contrast agents. Thus, as a group, they are at increased risk because of the greater likelihood of exposure to contrast media, but the incidence of contrast-induced nephropathy is dictated by a single independent variable: the relative degree of renal insufficiency.

Over 90 percent of patients with confirmed contrast-induced nephropathy have renal insufficiency. Therefore, it is of paramount importance that all patients undergoing contrast-agent studies have an evaluation of their renal function. For most patients, the glomerular filtration rate (GFR) can be estimated from creatinine clearance. However, in many instances there is neither time nor the facilities to record an accurate 24-hour urine volume, a key component in the clearance formula (i.e., $C = UV/P$, where C = clearance, U = urine concentration of creatinine, V = timed urine volume, and P = plasma concentration of creatinine). A shortcut that has been validated in clinical practice is the Gault-Cockcroft formula (see equation on page 27) for calculating creatinine clearance (C_{Cr}) using body weight, age, and serum creatinine × 72, this figure was derived from regression analysis. We have compared the measured C_{Cr} with the calculated C_{Cr} in patients with both normal renal function and stable renal insufficiency. The calculated C_{Cr} was found to reflect the measured C_{Cr} in most cases, two notable exceptions being patients weighing less than 120 pounds and pregnant women.

If a patient with renal insufficiency must undergo contrast studies, there are precautions that will minimize but not eliminate the risk of contrast-induced injury. In particular, patients with a pre-angiographic serum creatinine above 1.8 mg/dl, should get a specific prophylactic hydration infusion consisting of 0.5 L of 20 percent mannitol to which 100 mg of furosemide has been added for each mg/dl of serum creatinine. The infusion rate is set at 20 ml/hour. The infusion is begun 1 hour before the procedure and continued for 6 hours after the procedure. Urine is replaced on a milliliter for milliliter basis using 0.45 percent saline in 5 percent dextrose with 30 mEq of KCl/L added.

The diagnosis of contrast-induced nephropathy is one of association: it follows closely on the heels of an angiographic study. Characteristically, contrast-induced nephropathy presents as a non-oliguric acute renal failure. Within 12 to 24 hours following the angiographic procedure, the serum creatinine or blood urea nitrogen or both begin to rise often peaking on the third to fifth day post-procedure. Examination of the urinary sediment is rarely diagnostic. If oliguria is present, some authors have advocated measurement of the fractional sodium excretion; however, in our experience, non-oliguria is such a frequent presentation that a fractional sodium excretion measurement is difficult if not impos-

sible to interpret. While a persistent nephrogram 24 hours after the study confirms the diagnosis, its inconsistency and expense lead us to recommend serial serum creatinine measurements in all adult patients whose pre-study serum creatinine is 1.8 mg/dl or greater.

DRUG ADJUSTMENTS IN RENAL DISEASE

Michael Walczyk

Since most drugs require routes of elimination, it is not surprising that an increased frequency of adverse drug reactions occur in patients with renal insufficiency. Therefore, in order to provide safe and effective drug therapy for patients with reduced kidney function, appropriate adjustments in drug dosage regimens should be made to avoid toxic drug levels. In addition, many drugs that can be safely used in patients with normal renal function may impose excessive metabolic loads on patients with renal failure (Table 1-4). Proper drug administration to these patients requires a basic understanding of the pharmacologic principles that determine drug accumulation as well as a knowledge of how these factors may be altered in the setting of renal failure. This section will deal with the practical aspects of drug administration to patients with renal failure.

Pharmacologic Principles

The amount of administered drug that reaches the circulation and subsequently the sites of drug action depends on the processes of drug absorption and bioavailability, distribution within the body, biotransformation to either active or inactive metabolites, and drug elimination.

The absorption of orally administered drugs depends on the characteristics of the absorption surface and the physiochemical properties of the drug. Bioavailability refers to the rate of drug arrival at sites of action; it is measured clinically as the peak drug level following a dose of the drug. The above process

Table 1-4. Drugs with Significant Metabolic Loads

Metabolic Load	Drug
Sodium	Ampicillin (3.0 mEq/g), oxacillin (2.5 mEq/g), carbenicillin (4.7 mEq/g), cephalothin (2.4 mEq/g), Kayexalate (1.5 mEq/g), antacids, oral hyperalimentation fluids
Potassium	Potassium penicillin (3 mEq/million units), salt substitutes, K-sparing diuretics, neuromuscular blocking agents, blood transfusions, or hyperalimentation, protein
Magnesium	Laxatives, antacids
Urea	Glucocorticosteroids, tetracyclines, hyperalimentation, protein
Acid	Acetazolamide, NH_4Cl, aspirin, methenamine mandelate, ethanol, paraldehyde
Alkali	Antacids, carbenicillin, plasma protein concentrates, oral hyperalimentation
Water	Nonsteroidal antiinflammatory drugs, hypoglycemics, carbamazepine

Table 1-5. Clinically Significant Active Drug Metabolites

Parent Drug	Metabolite Activity	Used in Renal Failure
Acetohexamide	Lowers blood glucose	No
Allopurinol	Inhibits xanthine oxidase; accumulates in renal failure, causing side effects	Reduced dose
Cephalothin	Metabolites has 50% of antibacterial potency	Yes
Chlordiazepoxide	Antianxiety	Yes
Chlorpropamide	Insulin release	Yes
Diazepam	Antianxiety	Yes
Meperidine	Seizures and psychotic changes	With caution
Methsuximide	Anticonvulsant	With caution
Primidone	Anticonvulsant	With caution
Procainamide	Antiarrhythmic; possible cardiac toxicity	With caution
Propoxyphene	Analgesic	With caution
Propranolol	Beta blocker	With caution
Rifampin	Antibiotic	With caution
Sulfadiazine	May produce nausea, vomiting, and rash	With caution

may be altered in renal failure by nausea, vomiting, decreased gastrointestinal motility, and gut edema, any of which will decrease bioavailability and absorption.

Once absorbed, drugs distribute themselves in a characteristic fashion. The apparent volume of distribution, Vd (L/kg), a mathematical concept rather than a true anatomical compartment, can be derived by giving a known intravenous dose (D) of drug and measuring the steady-state plasma level (Cp):

$$Vd = D/Cp$$

Since drug distribution, and hence Vd, depends on factors such as drug lipid solubility and the binding of drug to protein, the Vd for drugs may change in the setting of renal failure. Thus, for example, uremia may lead to edema and decreased drug–protein binding, which will increase Vd. In general, drugs that are highly protein bound are restricted to the extracellular fluid (ECF) or vascular space, and have a low Vd. In contrast, drugs with a high lipid solubility or high binding affinity for tissue receptor sites (e.g., digitalis) have a large Vd which often exceeds the total body water volume, and thus are relatively unavailable for renal elimination.

Following absorption and distribution, drugs may undergo metabolic biotransformation in the liver to water-soluble active or inactive metabolites, many of which require renal routes of elimination (Table 1-5). Biotransformation may proceed by either microsomal oxidation or hepatic reduction, hydrolysis, conjugation, or acetylation reactions. Renal failure may lead to alterations in the hepatic metabolism of some drugs. In general, microsomal oxidation proceeds normally in patients with renal failure, whereas reduction, hydrolysis, conjugation, and acetylation reactions may be slowed.

Most drugs are eliminated from the body by first-order kinetics, so that the amount of drug eliminated per unit time is directly proportional to the amount

Table 1-6. Antimicrobial Agents

Drug Toxicity; Notes	Elimination and Metabolism	Half-life (h) (Normal/ESRD)	Plasma Protein Binding (%)	Volume of Distribution (L/kg)	Adjustment for Renal Failure				
					Method	GFR (ml/min) >50	GFR (ml/min) 10–50	GFR (ml/min) <10	Supplement for Dialysis
Aminoglycosides									
All agents ototoxic and nephrotoxic; need usual loading dose in renal failure. Subsequent adjustment by a combination of D and I methods. Need ½ and ¾ loading dose after hemodialysis. Blood levels best guide to therapy.									
Amikacin	R	2–3/30	<5	.22–.29	D I	60–90 Every 12–18	30–70 Every 12	20–30 Every 24	Yes (He, P)
Gentamicin Concurrent penicillins may result in subtherapeutic blood levels; absorption of 50% of intraperitoneal dose in 6-h CAPD exchange; poor clearance from blood to peritoneum in CAPD.	R	2/24–48	<5	.23–.26	D I	60–90 Every 8–12	30–70 Every 12	20–30 Every 24	Yes (He, P)
Kanamycin	R	2–3/27–30	<5	.19–.23	D I	60–90 Every 8–12	30–70 Every 12	20–30 Every 24	Yes (He, P)
Netilimicin	R	2.7/40	<5	.22–.26	D I	60–90 Every 8–12	30–70 Every 12	20–30 Every 24	Yes (He, P)
Streptomycin Minimal nephrotoxicity.	R	2.5/100	35	.26	I	24	24–72	72–96	Yes (He)

(*Continued*)

Table 1-6. Antimicrobial Agents (*Continued*)

Drug Toxicity; Notes	Elimination and Metabolism	Half-life (h) (Normal/ESRD)	Plasma Protein Binding (%)	Volume of Distribution (L/kg)	Adjustment for Renal Failure				
					Method	GFR (ml/min) >50	GFR (ml/min) 10–50	GFR (ml/min) <10	Supplement for Dialysis
Tobramycin Concurrent penicillins may result in subtherapeutic blood levels; see gentamicin notes.	R	2.5/56	<5	.22–.25	D I	60–90 Every 8–12	30–70 Every 12	20–30 Every 24	Yes (He, P)
Antifungal Drugs									
Amphotericin B Nephrotoxic; renal tubular acidosis; hypokalemia; nephrogenic diabetes insipidus.	NR	24/24	90	4	I	24	24	24–36[a]	No (He, P)
Flucytosine Hepatic dysfunction; marrow suppression more common in uremia.	R	3–6/75–200	<10	.6	I	6	12–24	24–48[b]	Yes (He, P)
Ketoconazole	H	1.5–3.3/1.8	99	1.9	D	None	None	None	No (He)
Miconazole Drug-induced hyponatremia.	H	20–24/20–24	90	21	D	None	None	None	No (He, P)
Antituberculous Drugs									
Ethambutol Peripheral neuritis may mimic uremia.	R	4/7–15	30	1.6	I	24	24–36	48	Yes (He, P)
Isoniazid Genetic variation in hepatic acetylation.	H (R)	slow acetylators 2–4/10 rapid acetylators .5–1.5/2	<10	.6	D	100	100	66–75	Yes (He, P)
Rifampin May cause acute renal failure.	H	2–5/2–5	60–90	.9	I	None	None	None	No (He)

Antiviral Agents									
Acyclovir	R	2.1–3.8/20	15–30	.6–.8	I	8	24	48	Yes (He)
Amantadine	R	12/500	?	4–5	I	12–24	48–72	168	No (He, P)
CNS toxicity in patients with renal failure.									
Vidarabine	R (H)	1.5/5	20–30	?	D	100	100	75	Yes (He)
Active hypoxanthine metabolite is 50% excreted by the kidney.									
Cephalosporins									
May be nephrotoxic in combination with aminoglycoside antibiotics, diuretics and volume depletion. Rare allergic interstitial nephritis. Absorbed well from peritoneal fluid in CAPD; however, transfer from blood to peritoneum is poor.									
Cefaclor	R (H)	.75/2.8	25	.24–.36	D	100	50–100	33	Yes (He)
Cefadroxil	R	1.4/20–25	20	.31	I	8	12–24	24–48	Yes (He)
Cefamandole	R	1/11	75	.16–.25	I	6	6–8	8	Yes (He)
Cefazolin	R	1.4–2.2/18–36	80	.13	I	8	12	24–48	Yes (He)
Cefoperazone	NR	1.6–2.4/2.1	90	.14–.20	I	None	None	None	Yes (He)
Ceforanide	R	2.2–3/25	80	.16–.19	I	12	24–48	48–72	Yes (He)
Cefotaxime	R (H)	1/2.6	38	.15	I	6–8	8–12	12–24	Yes (He)
Active desacetyl metabolite with 1½ of 10 h in ESRD.									
Cefoxitin	R	.7/13–22	75	.13	I	8	8–12	24–48	Yes (He) No (P)
Cefroxadine	R	.8–1/40	10	.2–.3	D	65–100	15–65	10–15	?
Cefuroxime	R	1.6–2.2/17	33	.13–1.8	I	8–12	24–48	48–72	Yes (He, P)
Cefsulodin	R	1.7–2/13	15	.22–.31	D	50–100	15–50	10–15	Yes (He)
Ceftizoxime	R	1.4/30	30–50	.35–.40	D	45–100	10–45	5–10	?

(*Continued*)

Table 1-6. Antimicrobial Agents (*Continued*)

Drug Toxicity; Notes	Elimination and Metabolism	Half-life (h) (Normal/ESRD)	Plasma Protein Binding (%)	Volume of Distribution (L/kg)	Adjustment for Renal Failure				
						GFR (ml/min)			
					Method	>50	10–50	<10	Supplement for Dialysis
Cephalothin	R (H)	.5–9/3–18	65	.26	I	6	6	8–12	Yes (He, P)
Cephalexin	R	.9/20–40	15	.18–.25	I	6	6–8	12	Yes (He)
Cephapirin	R (H)	.6–.8/2.4–2.7	45	.2	I	6	6–8	12	Yes (He)
Cephradine	R	1.3/8–15	10	.25–.33	D	100	50	25	Yes (He, P)
Moxalaciam	R	2.3–18–23	35–50	.25–.40	I	8	12	12–24	Yes (He)
Chloramphenicol Ineffective for urinary infections when GFR <40 ml/min.	H (R)	2–4/3–7[c]	60	.5–2	D	None	None	None	Yes (He) No (P)
Chloroquine Refers to treatment of malaria.	R (H)	48/?	55	Very large	D	100	100[d]	50[e]	No (He)
Clindamycin	H	2–4/3/5	60–95	.6–1.2	D	None	None	None	No (He, P)
Erythromycin	H	1.2–2.6/4–6	70–75	.5	D	None	None	None	No (He, P)
Lincomycin	H (R)	4–5/10–20	70–80	.31–.6	I	6	12	24	No (He, P)
Methenamine Mandelate Contributes to uremic gastrointestinal symptoms; ineffective in renal failure.	R	3–6/?	?	?	D	100	Avoid	Avoid	?
Metronidazole Vestibular toxicity; gastrointestinal symptoms may mimic uremia.	H (R)	6–14/8–15[f]	20	.6–.8	I	8	8–12	12–24	Yes (He) No (P)
Nalidixic Acid Metabolites accumulate; metabolic acidosis with overdose.	H (R)	6–7/21	88–91	.25–.45	D	100	Avoid	Avoid	?
Nitrofurantoin Peripheral sensory neuropathy due to metabolite accumulation; ineffective when GFR <30 ml/min.	NR (R)	1–1.7/?	60	.3–.7	D	100	Avoid	Avoid	Yes (He)