Family Practice Grand Rounds

Carcinoma of the Bladder

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Dayton, Ohio

DR. CHARLES SMITH, JR. (Director, Miami Valley Hospital Family Practice Residency Program, and Assistant Professor, Department of Family Practice): Our case presentation today focuses on a 58-year-old man who recently had a bladder tumor removed. In addition to discussing his disease, we will be looking at the reactions of this couple to the whole episode. The case will be presented by Dr. David Perilman, a thirdyear resident in the family practice program. Dr. Henry Dimlich will discuss the patient from the urologist's viewpoint. Dr. William Merkel, who is Director of Behavioral Science at the Wright State Department of Family Practice and who teaches at our Family Health Center, will interview the patient and his wife. Then our presenters will discuss the case and respond to questions.

DR. DAVID PERILMAN (Third-year family practice resident): Our patient, Mr. P., is a 58year-old white man who presented to the emergency room at 8:00 PM on the day of admission with a chief complaint of bloody urine that had occurred for the first time several hours earlier. The patient was asymptomatic with no pain, burning, fever, chills, or back or flank discomfort. He had voided four times and described dark red, bloody urine that occurred at the beginning of the stream and did not clear. He passed a few small clots but no definite stones. Mr. P. discussed the problem with his wife and decided to come to the emergency room for evaluation. His family history is negative for renal disease, cancer, kidney stones, and diabetes. Medications included aspi-

rin, one tablet daily. The patient had no history of surgery. He was hospitalized one year ago for a myocardial infarction but has been symptom-free since discharge. He has had no pain, dyspnea, orthopnea, or cardiac symptoms. Mr. P. is employed by a local municipality. He had been a light smoker until he stopped one year ago. He does not drink alcohol. This is the second marriage for both him and his wife. They have no children by previous marriages. The review of systems was negative. Physical examination revealed a well-tanned, healthy, alert, white man in no acute distress. Blood pressure was 154/90 mmHg, pulse 92/min with no orthostatic change, respirations 18/min and temperature 98° F. The only pertinent, positive physical finding was grossly bloody urine. Laboratory results were hemoglobin 13.8 gm/100 mL, hematocrit 38.5 percent, white cell count 6,8000/mm³ with normal differential, platelets 354,000/mm³, and activated partial prothromboplastin time 25 sec. On urinalysis, albumin was 3+, and there were 200 red blood cells per high power field with no casts. Electrolytes, total protein, albumin, liver enzymes, calcium, phosphorus, glucose, and cholesterol were normal. Urine culture was negative, tuberculin (PPD) skin test was negative, electrocardiogram was normal, abdominal film showed no radio-opaque stones, and chest x-ray examination was negative; intravenous pyelogram (IVP) on the morning following admission revealed two left-sided bladder diverticulae and moderate bladder trabeculation. A computed tomographic scan of the abdomen and pelvis revealed only the left-sided diverticulae.

Mr. P. underwent cystoscopy, which revealed a tumor within one of the bladder diverticulae. Biopsy revealed grade II to III papillary transitional cell carcinoma. The patient underwent a diverticulectomy, and the pathology was described as a urothelial grade III carcinoma with the mar-

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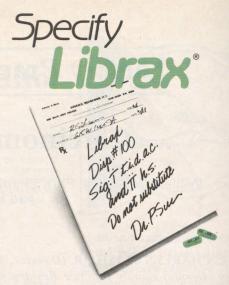
0094-3509/82/090415-06\$01.50 © 1982 Appleton-Century-Crofts gins free of tumor. Although the tumor did seem to extend into the muscle, the muscle was quite thin in the diverticulum. The postoperative course was uneventful, and the patient left the hospital after nine days. He received a course of irradiation of the bladder and aortic lymph node areas as an outpatient.

DR. HENRY DIMLICH (*Urologist*): The patient is a 58-year-old white man with a history of cardiac disease and gross painless hematuria of short duration. There was a history of heavy cigarette smoking in the past. He was regularly taking aspirin, but this is probably insignificant.

I have been asked to comment on the evaluation of a patient who has hematuria. First of all, hematuria must be adequately evaluated. I deplore the use of antibiotics for a week or so while waiting for the hematuria to "go away." The cost of an initial outpatient evaluation of hematuria amounts to about \$650. I start off with the more routine tests: a urinalysis, a urine culture, an IVP, and usually a cystoscopy. This is a brief workup, but more can be done later if necessary. In this patient, the IVP showed no involvement of the upper urinary tracts. We did not see any satellite or primary lesions in the renal pelvis or in the ureters that were shedding cells into the bladder. In fact, we didn't see a bladder lesion other than the one in the diverticulum. This diverticulum surprised me because the patient did not have an obstructive voiding history. He was voiding satisfactorily without getting up at night or straining to urinate. After the IVP, we performed a cystoscopy and found the bladder tumor within a diverticulum on the left side. This is what, for us, made the case an interesting challenge. It was a relatively low grade, superficial bladder tumor, but it was within the confines of the diverticula.

Our guidelines for therapy of bladder tumors are based on the depth of infiltration into the bladder wall as well as on the histological grade of the tumor. It is also important to establish whether the tumor is invading the muscle itself. In this case, the tumor lay in the diverticulum with no muscle to protect it from further infiltration into perivesical or extravesical tissue outside the bladder. We biopsied and fulgurated it, but we were still not really sure we had treated him adequately. There was no good way to know whether or not the tumor had gone to regional nodes.

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Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg

Please consult complete prescribing information, a summary of which follows:

Indications: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Glaucoma; prostatic hypertrophy, benign bladder neck obstruction; hypersensitivity to chlordiazepoxide HCI and/or clidinium bromide.

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As with all anticholinergics, inhibition of lactation may occur

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship not established.

Adverse Reactions: No side effects or manifestations not seen with either compound alone reported with Librax. When chlordiazepoxide HCI is used alone, drowsiness, ataxia, confusion may occur, especially in elderly and debilitated, avoidable in most cases by proper dosage adjustment, but also occasionally observed at lower dosage ranges. Syncope reported in a few instances. Also encountered: isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent, generally controlled with dosage reduction; changes in EEG patterns may appear during and after treatment, blood dyscrasias (including agranulocytosis), jaundice, hepatic dysfunction reported occasionally with chlordiazepoxide HCI, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy, constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.



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We could have gone several different directions with this patient, but we chose to do a bladder diverticulectomy because the lesion was isolated and relatively small. It was also located so that we would not have to transplant the ureter. The pathology report showed tumor in the musculature, but the muscle was very thin and attenuated. There was no evidence of metastasis or spread of the tumor at the time of surgery, but we were still not sure that he had been adequately treated. We elected to give a course of pelvic irradiation. Discussion with the P. family was important at that time, since pelvic irradiation can cause proctitis, cystitis, future bladder irritation symptoms, and loss of continence. It is not a form of treatment to be undertaken lightly.

As for future monitoring we will rely on repeat cystoscopy and IVP. There is another test that will probably be very helpful when it becomes more readily available. It is known that urinary epithelial cells have "red cell" antigens that are present in tumor tissue. If you do a hemagglutination test on the tumor tissue and the test remains positive, the tumors will probably be low grade and not metastasize. But if you lose this reactivity, the tumors will probably be far more aggressive. Thus, we hope eventually to screen him with this type of test along with urine cytology, cystoscopies, random bladder wall biopsies, and IVPs. If this is a simple superficial urothelial tumor, he has a five-year survival rate of 70 to 80 percent with chance of recurrence at around 50 percent. But I think he is staged a little low, so the figures for a five-year survival are probably a little lower. That is why we added the x-ray treatment to the surgery.

DR. SMITH: How often do you follow with cystoscopy and IVP?

DR. DIMLICH: I do cystoscopy every four months and get an IVP every six months. I would do this for five years. If the pattern changes after that, though, I would go back to the previous schedule. Once a bladder tumor is diagnosed, I do a cystoscopy at least once a year.

DR. SMITH: Do you do cystoscopies and IVPs on patients who present with two to three red blood cells per high powered field on several urinalyses?

DR. DIMLICH: Yes, particularly the young

patient. The cost of the workup may be a problem though. After I have done an IVP, a urinalysis, a urine culture, and a cystoscopy and still have found no cause, I request additional studies such as antinuclear antibody, immunoglobulin studies, a 24-hour urine, and arteriosclerosis obliterans. This can become quite expensive.

An interview with the couple follows:

DR. WILLIAM MERKEL (Behavioral scientist): We are going to be talking today about your reactions to the last few months. I would like to start by asking about your understanding of your problems. What have you had and what caused it?

MR. P.: Well, I had bleeding and I didn't know what caused it at first. I found out it was a tumor. It's eliminated now.

DR. MERKEL: How did you first learn of this? MR. P.: I was at work in the afternoon and went to the bathroom. I started passing blood.

DR. MERKEL: Can you recall some of the things that flashed through your mind at that time?

MR. P.: I wondered what it was and what was causing it. I only had an hour left at work so I went back to my desk and sat down. I didn't go to the bathroom again until I got home, and the same thing happened. I told my wife that I'd been passing blood, and we went down to the toilet and I started passing clots. All of a sudden a big clot came out, and my wife said, "We are going to the emergency room right now!" So, we did, but I had no pain.

DR. MERKEL: Mrs. P., what do you remember of your first reactions?

MRS. P.: I went and got my "doctor book" and read about it. I came to the word "cancer," and I closed it up and put it away.

DR. MERKEL: Why?

MRS. P.: I didn't want to read about it. The book said that when there's bleeding without pain, there is a possibility of cancer, so I closed the book because he didn't have pain and he had a lot of blood.

DR. MERKEL: Had you had previous experience with people who had cancer?

MRS. P.: My father, but he had a colostomy. DR. MERKEL: What do you remember about that?

MRS. P.: I wouldn't let the doctors tell him. DR. MERKEL: What was in your mind when you asked the doctors not to tell him?

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KLOTRIX®

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DESCRIPTION KLOTRIX is a film-coated (not enteric-coated) tablet containing 750 mg potassium chloride (equivalent to 10 mEq) in a wax matrix. This formulation is intended to provide a controlled release of potassium from the matrix to minimize the likelihood of producing high localized concentrations of potassium within the gastrointestinal tract.

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1. For therapeutic use in patients with hypokalemia with or without metabolic alkalosis; in digitalis intoxication and in patients with hypokalemic familial periodic paralysis.

2. For prevention of potassium depletion when the dietary intake of potassium is inadequate in the following conditions: Patients receiving digitalis and diuretics for congestive heart failure; hepatic cirrhosis with ascites; states of aldosterone excess with normal renal function; potassium-losing nephropathy, and certain diarrheal states.

3. The use of potassium salts in patients receiving diuretics for uncomplicated essential hypertension is often unnecessary when such patients have a normal dietary pattern. Serum potassium should be checked periodically, however, and, if hypokalemia occurs, dietary supplementation with potassium-containing foods may be adequate to control milder cases. In more severe cases

supplementation with potassium salts may be indicated.

CÓNTRAINDICATIONS In patients with hyperkalemia, since a further increase in serum potassium concentration in such patients can produce cardiac arrest. Hyperkalemia may complicate any of the following conditions: chronic renal failure, systemic acidosis such as diabetic acidosis, acute dehydration, extensive tissue breakdown as in severe burns, adrenal insufficiency, or the administration of a potassium-sparing diuretic (eg., spironolactone, triamterene).

Wax-matrix potassium chloride preparations have produced esophageal ulceration in certain cardiac patients with esophageal compression due to enlarged left atrium.

All solid dosage forms of potassium supplements are contraindicated in any patient in whom there is cause for arrest or delay in tablet passage through the G.I. tract. In these instances, potassium

supplementation should be with a liquid preparation.

WARNINGS Hyperkalemia: In patients with impaired mechanisms for excreting potassium, administration of potassium salts can produce hyperkalemia and cardiac arrest. This occurs most commonly in patients given potassium intravenously but may also occur when given orally. Potentially fatal hyperkalemia can develop rapidly and be asymptomatic. Use of potassium salts in patients with chronic renal disease, or any other condition which impairs potassium excretion requires particularly careful monitoring of the serum potassium concentration and appropriate dosage adjustment.

Interaction with potassium-sparing diuretics: Hypokalemia should not be treated by the concomitant administration of potassium salts and a potassium-sparing diuretic (eg, spironolactone or triamterene), since the simultaneous administration of these agents can produce

severe hyperkalemia.

Gastrointestinal lesions: Potassium chloride tablets have produced stenotic and/or ulcerative lesions of the small bowel and deaths. These lesions are caused by a high localized concentration of potassium ion in the region of a rapidly dissolving tablet, which injures the bowel wall and thereby produces obstruction, hemorrhage, or perforation. KLOTRIX is a wax-matrix tablet formulated to provide a controlled rate of release of potassium chloride and thus to minimize the possibility of a high local concentration of potassium ion near the bowel wall. While the reported frequency of small-bowel lesions is much less with wax-matrix tablets (less than one per 100,000 patient-years) than with enteric-coated potassium chloride tablets (40-50 per 100,000 patient-years) cases associated with wax-matrix tablets have been reported both in foreign countries and in the United States. In addition, perhaps because the wax-matrix preparations are not enteric-coated and release potassium in the stomach, there have been reports of upper gastrointestinal bleeding associated with these products. The total number of gastrointestinal lesions remains less than one per 100,000 patient-years. KLOTRIX should be discontinued immediately and the possibility of bowel obstruction or perforation considered if severe vomiting, abdominal pain, distention, or gastrointestinal bleeding occurs.

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ADVERSE REACTIONS Most common to oral potassium salts: nausea, vomiting, abdominal discomfort, and diarrhea. These symptoms are due to irritation of the gastrointestinal tract and are best managed by diluting the preparation further, taking the dose with meals, or reducing the dose. One of the most severe adverse effects is hyperkalemia (see Contraindications and Warnings). There also have been reports of upper and lower gastrointestinal conditions including obstruction, bleeding, ulceration and perforation (see Contraindications and Warnings); other factors known to be associated with such conditions were present in many of these patients. Skin rash has been reported rarely.

DOSAGE AND ADMINISTRATION The usual dietary intake of potassium by the average adult is 40 to 80 mEq per day. Potassium depletion sufficient to cause hypokalemia usually requires the loss of 200 or more mEq of potassium from the total body store. Dosage must be adjusted to the individual needs of each patient but is typically in the range of 20 mEq per day for the prevention of hypokalemia to 40-100 mEq per day or more for the treatment of potassium depletion.

Note: KLOTRIX® slow-release tablets must be swallowed whole and never crushed or chewed. Following release of the potassium chloride, the expended wax matrix, which is not absorbed, may

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CARCINOMA OF BLADDER

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MRS. P.: Well, my father had lost a dear friend who had stomach cancer, and he had made the statement that he would never linger like his friend did. That worried me, but his doctor said he never lied to a patient. So the doctor used enough big words so that he could tell my dad what he had, but Dad wouldn't really understand. Dad never knew he had cancer until he had the tracheostomy, just a week before he died.

DR. MERKEL: What do you think would have happened if your dad had been told he had cancer?

MRS. P.: I don't know. All I knew was what he had said, and I knew my mother felt that he had everything he needed to take his life.

DR. MERKEL: You were concerned that he might kill himself?

MRS. P.: Right.

DR. MERKEL: Were you worried about that for your husband when you first saw the word "cancer" in your medical book?

MRS. P.: No, but still, I did ask Dr. Dimlich not to tell him

DR. MERKEL: How did Dr. Dimlich handle

MRS. P.: He said, "Don't you think we should tell him?" And then I agreed.

DR. MERKEL: Mr. P., how is your wife doing with all of this?

MR. P.: Well, she does the worrying, and I don't have to.

DR. MERKEL: She does the worrying? That's a pretty good arrangement!

MR. P.: That makes it easy on me.

DR. MERKEL: How do you get her to do the worrying?

MR. P.: I think it just comes naturally. She has always done the worrying. I do the work.

DR. MERKEL: Mrs. P., you mean your husband doesn't worry at all?

MRS. P.: If he does, he doesn't show it.

DR. MERKEL: Mr. P., how is it for you when your wife worries?

MR. P.: Well, I guess I've gotten used to it. I tried to get her not to worry about so many things. I always told her that when she's got one thing she doesn't have to worry about, she just invents something else. She just likes to have something on her mind.

DR. MERKEL: Let's go back to when you first went into the hospital. What changed most at

home when you went to the hospital?

MRS. P.: My biggest problem was my mother. I had to prepare all of her meals and figure out her menus so that she could have her meals on time because she's a diabetic. I did this each night so I could spend all of my time at the hospital. Being able to sit there by my husband's bed helped me a lot. Sometimes I stayed overnight.

MR. P.: It helped me too. I could wake up and see her, and I knew she was there.

DR. MERKEL: What changed the most about your home life since you've been back from the hospital?

MRS. P.: Well, I'm trying to feed him his meals on time, and I'm going by the book the cancer therapy people gave me about what to give him and what not to give him. Other than that, of course, our sex life is down the drain for right now.

DR. MERKEL: What other changes have you noticed at home or in your marriage?

MRS. P.: Maybe I'm nicer to him.

MR. P.: She's always been pretty loyal. She doesn't want to do things without me. I go along with her when she goes bowling, and I sit and do the scoring.

DR. MERKEL: Mr. P., were you working full time?

MR. P.: Oh yes.

DR. MERKEL: Are you back at work now? MR. P.: No.

DR. MERKEL: Mrs. P., what's it like to have him home all day?

MRS. P.: Oh, I love it. It's nice to have him there.

DR. MERKEL: When is he going to go back? MRS. P.: I have no idea.

MR. P.: I had a conflict with some of the people at work. You see, I got caught in some bad political situations. I've been harrassed, but I'm getting used to it now. It's almost to the point where I'm going to seek legal help.

DR. MERKEL: Mr. P., do you have a plan to return to work?

MR. P.: My job is waiting for me.

DR. MERKEL: Thank you very much for joining us today.

Couple leaves.

DR. PERILMAN: There is one thing I would like to add about using words like "tumor" and "cancer" with different families and patients. When I first saw Mr. P. in the emergency room, I

explained that we would be doing an IVP and ultimately a cystoscopy, and that the differential diagnosis included stone, infection, tumor, and congenital problems. Then when it turned out to be a tumor, there was inevitably some difficulty understanding the word. Is a tumor cancer? Is cancer a tumor? Are all tumors cancer? Are there different kinds of cancer? So I have had to rethink the ways I talk about these things with patients and their families.

DR. SMITH: What kind of wording should you use in your initial explanation to patients? There was a recent case here of a patient with an almost certain malignancy on an upper gastrointestinal series. This was the first time the physician had seen the patient. The patient was very unhappy and frightened and refused to come back. She complained about the way the word "cancer" was used in the initial explanation. Maybe some of you have ideas about how to handle this in your encounters with patients. Perhaps it is better to just answer their questions instead of volunteering too much information initially.

DR. DIMLICH: If I'm thinking bladder tumor, I say that there may be a small growth in the bladder that we want to try to take care of. Frankly, I don't use the word "cancer" at first because I don't want to spend the next 30 minutes explaining it. If I say "cancer" in the initial interview or when I am trying to explain a surgical procedure, all kinds of questions and problems arise. I tend to refrain from using it until a definite diagnosis has been made.

DR. SMITH: Dr. Merkel, what are your thoughts?

DR. MERKEL: This couple has an interesting arrangement: she does the worrying and he does the work. One of my concerns is that this arrangement makes it hard for Mr. P. to worry and even harder for him to worry out loud. He surely has some emotional reaction to what he is going through, and I wonder if it's possible for him to get much support from his wife since she doesn't want him to worry. He may be feeling very alone with this in spite of his professed nonchalance or refusal to worry. There is another thing that struck me about these two: Mrs. P. enjoys having her husband home and she wants to do everything with him. Furthermore, Mr. P. is in a stressful job. This all suggests that Mr. P. may be a little slow in getting back to work, and part of his care now might well be directed toward helping him get back on the job if he is physically able to do so. Without some attention to this, his convalescence may be longer than necessary. This couple demonstrates another interesting point. The family is often the first contact for symptom assessment and the primary referral source to the health care system. When Mr. P. had a problem, he went to his wife. She went to her medical book, looked up his symptoms, and then *they* decided to come to the emergency room. Rather than seeking immediate professional care, most people go first to their family and further triaging becomes a family decision.

DR. SMITH: It is curious to me why some families or physicians feel that it's best not to tell patients they have cancer. Some physicians feel that telling patients just makes their remaining days more miserable. In today's case, Mrs. P. said that she didn't want her husband to know the diagnosis, but she wanted to run out of the room when she was told what his diagnosis was. I suspect that if people don't want to tell relatives that they have cancer, they are probably having their own difficulty in handling the issue.

DR. MERKEL: She seemed to have had some difficulty with her father's diagnosis.

A PHYSICIAN: Is it better to discuss the diagnosis of cancer with the patient who seems reluctant to talk about it?

DR. MERKEL: I personally feel that it is better to explore it. Patients' fears and fantasies are often much worse than the reality. In spite of all the publicity, most people do not really know much about cancer, which kinds are treatable, what recovery rates are, and so on. Particularly in a case in which there is a good prognosis, the patient will probably fare better than his wife's anticipation; her fantasies are most likely based on her father's fatal illness. If the disease is not discussed with the patient, a conspiracy of silence develops in which people won't talk about anything that might reveal the presence of cancer. The patient quickly learns not to talk about these things and is left alone with high levels of anxiety and many questions that cannot be asked. So one consequence of not saying the dread word cancer is progressive emotional isolation of the patient, who needs more support than ever.

DR. DIMLICH: Not only does communication break down initially in a family of a cancer patient, but the whole family becomes troubled. They can no longer function at their previous level of interaction, and that can be devastating.

A PHYSICIAN: Dr. Merkel, once in a while an elderly person has an operation to remove a cancerous growth, and the family will come to me and say: "Please don't tell him that he has cancer. He doesn't need to know that." What do you suggest in a case like that?

DR. MERKEL: The patient often gets caught between the health care team and the family, both competing to define what is in the patient's "best interest." In this case, the physician is caught between the patient's family and the other hospital staff; I doubt that is going to benefit the patient's health care. To answer your question, I would try to explore with the family what they thought would happen if the diagnosis of cancer were disclosed to the patient. Those fantasies may be much worse than the facts. I don't think you necessarily have to hammer bad news into people. Clearly there are times when families and patients are more or less ready to listen. When you first make a frightening diagnosis and the patient's anxiety is high, he is not likely to absorb much, particularly if the information is complicated. As a family physician, though, you can work with the family over time, and their resistance to accepting the diagnosis is likely to decrease as they become more trusting of you.

A PHYSICIAN: Dr. Dimlich, what do you explain to the family if you find a cancer? Do you take one family member to a room and leave the other relatives outside or do you speak with the whole group?

DR. DIMLICH: Generally I speak with the spouse and the other members of the family as well. I believe in repetition because so often the things I say are not initially clear. I may say something two or three times to help the family understand. I talk to anybody in the family—together, alone, or however they want to do it.

DR. MERKEL: This is a time when people try to combat their anxiety by asking for more information, but that same anxiety makes it harder to integrate and really understand what you tell them. It's a real bind for the physician.

DR. SMITH: Many interesting points have been raised about approaching patients with tumors and I would like to thank Drs. Merkel, Dimlich, and Perilman for their contributions to this Grand Rounds.