In the preceding chapters, several of the authors have indicated likely future developments in their respective fields. While the increasing effort in basic and clinical research seems to assure that there will be advances in the chemotherapeutic management of the urological tumors, it is difficult to predict either the rate or the extent of progress. Experience suggests that it will be neither very rapid nor very dramatic: 'breakthroughs' are common in the media but rare in the real world of clinical science.

Caution is also necessary in attempting to predict the avenues of research that will lead to progress. Scientifically, the most appealing approach is that of learning more about the biology of urological tumors, including the intimate details of their cellular chemistry and cell:cell interactions, so that a 'rational' therapy can be devised for each tumor. Further refinement might disclose criteria by which appropriate therapy can be selected for each patient. It must be acknowledged that this approach in cancer research, while contributing much to our understanding of cellular and subcellular processes, has contributed little to practical bedside therapeutics. On occasion, it has explained why certain empirically derived treatments do in fact work, but it has not been notably successful in suggesting new lines of treatment which then are shown to be effective. Therapeutic experimentation, despite an often tenuous rationale, usually has been more productive.

The empirical approach, assessing a whole series of agents in each tumor, is cumbersome, time consuming, and expensive. In some instances — for example renal carcinoma — it has been relatively unrewarding. True, there is always the possibility of a new agent with a high degree of activity 'turning up', but this Micawberish expectation seems less likely to be fulfilled than it did in the 1950s, when chemotherapy was in its infancy. With a few exceptions, notably cisplatin, most of the advances of the last decade have been made by the improved use of existing agents, rather than the discovery of new drugs. Several of the authors have pointed out that for most urological cancers there is a paucity of reliable data concerning the effectiveness even of standard agents that have been available for many years. This deficit is being remedied by the cooperative group studies now in progress, and by the planning of new studies which will examine old and new drugs, and will test chemotherapy both for metastatic disease and as an adjunct to surgery or radiotherapy. Even when the gains from chemotherapy are modest, cooperative group studies offer tangible advantages: (a) the existence of a formal trial tends to
standardize, and to improve, the quality of care; (b) well-designed trials frequently contribute valuable additional knowledge on the natural history of the tumors concerned; (c) a mechanism is created whereby new ideas—often the result of single-institution pilot studies—can be evaluated in a relatively short period, so that genuine advances are verified rapidly and then made available for more widespread use.

In adrenal cancer, improved methods for detecting early disease are needed. The unique properties of mitotane (o,p'-DDD) suggest the desirability of testing further structural analogues of this compound. As in all the rarer urological cancers, cooperative studies should have high priority, to enable the completion of drug trials in a reasonable period of time. A recent report (Tattersall et al. 1980) describes clinical and objective responses in all of four patients with metastatic adrenal cancer who received cisplatin. One of my patients with rapidly progressive adrenal cancer has had stabilization of disease for 7 months with the same treatment. Clearly, cisplatin merits more extensive evaluation in adrenal cancer.

Carcinoma of the kidney has proved remarkably resistant to cytotoxic drugs of any type. The principal contribution of many clinical trials has been to demonstrate the ineffectiveness of both cytotoxic agents and hormones. This has undoubted value, as patients will in future be spared toxic and futile therapy, and a further stimulus is provided for therapeutic research. Because of the capricious nature of renal cancer, studies with cancer chemotherapeutic agents require groups of patients who receive no specific therapy: there is in this tumor no ethical objection to this experimental design, as there is no standard therapy of proved value. Methyl-glyoxal-bisguanylhydrazone appears to possess modest activity in renal cancer, and experience with this drug needs to be enlarged; it is at present unjustified to incorporate it into a multiple-drug regimen, but a surgical adjuvant study should be mounted. Available nephrotoxic agents may be screened in vitro, or against tumor implants in nude mice, for activity against renal cancer, and promising agents might be administered to patients with metastatic renal cancer while their healthy kidney is maintained on an extracorporeal circuit. Unfortunately, the nephrotoxicity of many drugs and chemicals may well depend on the normal physiological activity of renal tissue, and pathological renal tissue may not be similarly susceptible. Thus cisplatin, which is a potent nephrotoxin unless special precautions are taken, seems ineffective in carcinoma of the kidney.

In contrast, Kumar and his colleagues are able to report impressive advances in the management of Wilms' tumor. Further progress is to be expected from more precise clinical and pathological staging, from improved techniques of radionuclide imaging, and from more refined surgical techniques. Wilms' tumor is responsive to a wide range of drugs, but the emergence of drug-resistant tumor cells accounts for a significant number of therapeutic failures. The systematic screening of new agents for activity in Wilms' tumor should have high priority.

Progress in the management of the rarer tumors of the urothelium—the renal pelvis, ureter, and urethra—is likely to be brought about by collaborative studies. No single institution can accrue, in any reasonable time span, sufficient patients to conduct even a simple two-armed study. Fundamental questions, for example the efficacy (or otherwise) of preoperative or postoperative radiotherapy, are unanswered. Adjuvant chemotherapy cannot reasonably be studied, because chemotherapy agents with sufficient activity have not yet been identified.

In bladder cancer, several agents are known to possess useful activity: this opens the way for surgical adjuvant studies. For metastatic bladder cancer, trials of single-agent versus multiple-agent chemotherapy are in progress, and there is a need to continue the screening of new agents. The observation (Falor and Ward 1976; 1978)