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Short communication

Overview: Issues concerning the pharmacology of multiple drug regimens

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A pharmacologic perspective on regimens involving multiple drugs in HIV infected patients focuses attention on the effects of the drug on both virus and host, as well as the effects of the virus and host on the drugs. To the extent that we can understand these processes at a biochemical level, we should be able to understand the consequences of these drug interactions and to predict others. A useful division of the processes is into pharmacodynamic and pharmacokinetic effects. Pharmacodynamics encompasses the relationships between the concentration of the ultimate and active drug and the biochemical effects, be they antiviral or toxicologic. Pharmacodynamics should also be viewed as changing over time and this somewhat novel concept has been called 'time-dependent pharmacodynamics'. Pharmacokinetics encompasses all of the processes affecting the concentration of the ultimate and active drug at and on its way from administration to the site of action and considers these as a function of time. This review emphasizes pharmacodynamic drug interactions of zidovudine with dipyridamole, ribavirin, ganciclovir, several cytokines, and inhibitors of thymidylate synthase and interactions of didanosine with dipyridamole, ribavirin and hydroxyurea. Pharmacokinetic drug interactions that are emphasized include interactions of zidovudine with probenecid, ribavirin, doxorubicin, rifampicin, trimethoprim and chloramphenicol, as well as interactions of didanosine with itraconazole, ciprofloxocin, ranitidine and probenicid.

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