

drug accelerate its own metabolism, but it may affect others. The administration of drug A may stimulate hepatic enzymes which accelerate the metabolic breakdown of drug B. If this phenomenon is not appreciated and anticipated, it may result in lower than expected blood levels of drug B.

I would like to show a slide at this moment to illustrate this point, if I may.

The point is this. Here we have a patient who comes to see a doctor. The diagnosis is made, and the patient is started on a conventional dose of this drug. He is given one gram a day. Over a period of time over the next few days the patient gets the desired therapeutic effect, and the patient is going quite well.

However, by the fourth day the patient is seen by another doctor or by the same doctor and is then given drug B for some other complaint.

Now, drug B happens to be a drug capable of causing induction of drug A. In other words, it accelerates its metabolism, and the blood level of drug A rapidly falls off. So you see we have now a lack of effect. The patient comes back to the original doctor and says, "Doctor, I am certainly not getting the same response that I got from that drug (A) you gave me." But she neglects to tell him that she is also taking drug B; so he increases the dose of the first drug (A). After a few days she gets back up to the same therapeutic level, and then for one reason or another drug B is stopped, and this was the drug which was inducing and accelerating the metabolism of drug A. It is gone and suddenly we have a patient who becomes toxic from drug A. And if the physician does not know about this mechanism, he will become very confused and may think that the drug is no longer effective. And this is why enzyme induction is dreadfully important to us.

The cardinal principle involved is that individual doses of drugs may be required that are quite toxic in an effort to maintain blood levels that were achieved with much lower doses earlier in the course of drug therapy. And the corollary is equally as important. One may consider that a drug is ineffective, when the actual fact is that the blood levels are too low, despite the administration of proper doses.

ENZYME INHIBITION

Now, the next phenomenon, one that is more familiar to physicians, that is antithetical to the concept of enzyme induction and accelerated drug metabolism. This is inhibition of the metabolic breakdown of one drug by another with a potentiation of its effect.

And we have another slide to illustrate this.

Now, here we have exactly the reverse situation. The patient comes in and is given drug A (drug A becomes more notorious as we proceed) and gets a therapeutic effect as anticipated.

At this particular time drug B is given by someone else. Drug B in this situation, rather than accelerate the metabolism of drug A, as occurred previously, now inhibits the metabolism. Therefore, drug A remains in the blood stream longer than was anticipated, begins to accumulate, and suddenly the patient develops toxic effects from drug A.