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Title: Drug induced Thrombocytopenia - another look

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In the September 2001 issue of *The Platelet*, Dr. Provan described how allergic reactions to some medicines can cause low platelet counts. These reactions are uncommon and not a reason for patients with ITP to avoid essential medicines. However, these reactions can be confused with ITP, and that is an important problem. They are more common in adults, especially in older adults, than in children simply because older adults take many more medicines and have had more years to develop allergies. When a person becomes allergic to anything, whether it is a medicine or a food or pollen, the allergic reaction is caused by antibodies that the person forms against the medicine or food or pollen. Sometimes the reaction can result in sneezing or asthma; sometimes a skin rash; and sometimes in a low platelet count. These reactions occur with platelets because platelets can act like a sponge and adsorb medicines on to their surface. Then when a person becomes allergic and forms antibodies to the drug, these antibodies react also with the platelets to which the drug is bound, and the platelets are destroyed. Some drugs are more likely to cause allergic reaction than others. The problem for physicians is to know which drugs can actually cause a low platelet count. Many articles in medical journals describe numerous drugs causing low platelet counts, but most of these descriptions are difficult to interpret and may not be accurate. To better understand which drugs are most likely to cause a low platelet count, we did a systematic review of all published patient descriptions beginning with the earliest reports over 70 years ago and continuing up through 1999. Using comprehensive computer search strategies, we identified 690 articles describing 921 patients. We excluded 337 patients because the drugs are no longer used or they were taken inappropriately. The remaining patient descriptions were analyzed according to strict criteria to define a definite, probable, possible, or unlikely relation of the drug as a cause of the low platelet count. Most reports presented insufficient evidence, supporting only a possible or unlikely relationship. We identified 52 drugs that had a definite relationship and 17 additional drugs that had two or more reports with a probable relationship. This information was published in two articles in the *Annals of Internal Medicine* (volume 129, p. 886, 1998 and volume 134, p. 346, 2001), but all of the data were too extensive for traditional medical journals. Therefore we have posted the complete data on our Website (<http://moon.ouhsc.edu/jgeorge>) where they can be viewed by everyone who is interested. The most common drugs that can cause a low platelet count are quinidine (used for irregular heart rhythm) and quinine (very commonly used for the very common symptom of night leg cramps). The importance of recognizing the risk for drug-induced low platelet counts was illustrated by the story of a man one of us cared for last year; we published his story in the *Journal of the Oklahoma State Medical Association* (volume 93, p. 519, 2000). He had had ITP requiring a splenectomy in 1992 and had been well since. Then, in December 1999 he had sudden and severe thrombocytopenia with extensive bleeding. He got better with platelet transfusions, IVIG, and steroids. He was told to stop all his medications and he was given only prednisone for his presumed recurrent ITP and insulin for his diabetes. Then over the next month he had three more episodes of acute severe thrombocytopenia, each accompanied by severe bleeding, and each recovering promptly after entering hospital and receiving platelet transfusions and IVIG. This is when one of us saw him. Although ITP was a reasonable diagnosis since it had been clearly present 7 years before, we became suspicious because of the sharp fall of his platelet counts on four occasions followed by recovery to normal just as quickly. Maybe the low platelet count was due to some medicine he was taking, or some food or remedy. When asked if he had stopped all of his medicines, he said, 'Yes, I am only taking prednisone and insulin, just as the doctors told me'. When asked if he had leg cramps at night, and he said, 'Yes, I have them almost every night and they're bad.' When asked if he ever took quinine for leg cramps he replied, 'Yes, I take quinine every week or two. It's the only the thing that helps my cramps'. When asked why he said he was only taking prednisone and insulin, he replied, 'Well, I didn't think these quinine tablets could hurt me.' He was instructed never to take quinine again. But a week later he had severe leg cramps one night and thought perhaps only a half quinine tablet would be OK. Again he was promptly in the hospital with a platelet count of near zero with bleeding symptoms. That was the final proof. He has not taken quinine since.