

The lessons to be learned

The observations concerning chloramphenicol described above do not justify prohibition of the use of this valuable antibiotic. However, certain limitations are indicated. Similar limitations apply to therapeutics in general.

1. Many modern therapeutic agents are potentially very valuable—but they are also potentially harmful.

2. The indiscriminate use of a potentially toxic therapeutic agent in the absence of a clearcut indication is not justified.

3. A shotgun should not be used when a rifle would be better. An exact diagnosis permits the use of a specific agent instead of a "wide spectrum" therapeutic agent which the physician hopes will bring down the target he cannot see.

4. A cannon should not be used to kill a mouse. The risks involved in the use of a therapeutic agent should be weighed against the seriousness of the disease to be treated and the possibility of treating the condition with another agent which is less potentially toxic should be considered.

5. The physician must at all times be alert to the possible occurrence of an adverse reaction.

6. Specifically, with reference to chloramphenicol, it would seem wise to restrict the daily oral dose to approximately 30 mg. per kg. body weight and to limit the course of therapy to 14 days. It has been suggested, but not proved that, when higher doses must be used, or therapy must be prolonged or repeated, serum iron and iron-binding capacity and reticulocyte counts may be found to give warning of impending trouble.

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DRUG-INDUCED BLOOD DYCRASIAS

I. APLASTIC ANEMIA

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Aplastic anemia is a frequent manifestation of drug toxicity, and is characterized by pancytopenia and a fatty hypoplastic bone marrow.¹⁻³ It seems best to restrict the term aplastic anemia to conditions in which the red marrow has been largely replaced by fatty tissue, although normal or even hypercellular foci occasionally may be present.

A drug or chemical is believed to play an etiological role in about one half the cases reported. Chloramphenicol appears to be by far the most important offender,⁴ but published case reports and those sent to the Registry on Blood Dyscrasias of the American Medical Association attest to the potential bone marrow toxicity of mephenytoin (Mesantoin), sulfonamides, phenylbutazone (Butazolidin), some insecticides and solvents, and many other compounds (Table). However, it is difficult to separate drug-induced from idiopathic cases, and unfortunately there is no test which provides proof of an etiological relationship. Therefore, conclusions must be drawn on the basis of personal judgment and statistics, particularly since everyone in our industrialized society is exposed to potentially toxic chemicals.

The characteristic signs and symptoms of severe pancytopenia are weakness and pallor, hemorrhage and ecchymoses, and a decreased resistance to infections. The demonstration of a pancytopenia in the absence of adenopathy, splenomegaly, bone tenderness, or evidence of an underlying disease strongly indicates a diagnosis of aplastic anemia. The crucial piece of evidence is the demonstration of a hypocellular fatty bone marrow. Bone marrow aspirations should be made

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¹ Huguley, C. M., Jr.: "Drug-Induced Blood Dyscrasias," in *DM Disease-a-Month*, Chicago: Yearbook Medical Publishers, Inc., October, 1963.

² Scott, J. L.; Cartwright, G. E.; and Wintrobe, M. M.: Acquired Aplastic Anemia: Analysis of Thirty-Nine Cases and Review of Pertinent Literature, *Medicine (Balt)* 38:119 (May) 1959.

³ Harris, J. W.: *Red Cell: Production, Metabolism, Destruction, Normal and Abnormal*, Cambridge, Mass.: Harvard University Press, 1963.

⁴ McCurdy, P. R.: Chloramphenicol Bone Marrow Toxicity, *JAMA* 176:588 (May 20) 1961.