

USE OF PYRIMETHAMINE FOR THE PREVENTION OF ABORTIONS AND FOETAL DEFORMITIES

(Caused by Virus Infections during Pregnancy)

by

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Pyrimethamine (sold under the trade name 'Daraprim' in India) was originally introduced for the prevention and treatment of malaria, and is still used for the prevention of malaria in endemic regions, especially for children.

Myatt reported that of twelve male volunteers given 25 mg. of pyrimethamine daily for forty-nine days, six developed a mild to moderate anaemia of macrocytic normochromic type at about the thirtieth day; the bone-marrow picture was of the megaloblastic type similar to that seen in folic acid deficiency and extrinsic factor deficiency in anaemias. Both the anaemia and the bone-marrow changes disappeared promptly on discontinuation of the drug. Isaacs reported that with the dosage adjusted to the needs of each patient pyrimethamine proved useful in six cases of polycythaemia vera in reducing the red cell count and ameliorating the characteristic symptoms. A 25 mg. dose was given once daily and was reduced when the red cell count fell to 4,000,000 per c.cm. Under controlled conditions there were no toxic reactions during the treatment lasting 10 to 12 months. Klein-Felder and Bracharz reported five

cases of polycythaemia with myelofibrosis treated with 50 mg. of pyrimethamine daily. The haemoglobin value and erythrocyte count fell to normal in two to three months. They reported that smaller doses proved ineffective.

Kulshreshtha reported that spectacular response was obtained with the administration of pyrimethamine in cases of mumps and measles.

V. D. Kopp and M. A. Fadeeva reported 40 full-term deliveries out of 45 women who were treated for toxoplasmosis during pregnancy with pyrimethamine in combination with sulphonilamides and vitamins. Of the thirty cases followed up for periods ranging from 3 months to 3 years 9 showed developmental disorders which could be attributed to congenital toxoplasmosis. Five of the children in whom slight pyrexia, digestive disorders refractory to orthodox treatment, convulsions and progressive hydrocephalus were the main clinical features, improved in response to treatment with pyrimethamine and sulphonilamides with vitamins.

E. J. Parrott has suggested that all available measures for the prevention of viral diseases in pregnant women should be used since it is not yet definitely known which of the viral infections act like the virus of German measles.

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Pyrimethamine has definite action of reducing the virulence of virus infections, as is proved by the observations of Kulshreshtha in measles and mumps and of Kopp and Fadeeva in toxoplasmosis. Care is necessary during the course of pregnancy in the use of a potent folic acid antagonist like pyrimethamine. E. J. Hickl, U. Mohr, and G. Martius report that when pyrimethamine was administered to rats prior to implantation and continued over the major part of pregnancy resorption of foetus occurred in 74.6%. This shows that indiscriminate or prolonged use of pyrimethamine is to be avoided. S. S. Zakharchuk reported the use of pyrimethamine and sulfadimidine given in a 10 day course in 76 cases of pregnant women in whom the data obtained were suggestive of latent toxoplasmosis, and of these 76 patients 64 were discharged home with perfectly normal infants. In some cases pregnancy ended prematurely and in these cases pregnanediol levels were low, possibly as a side effect of the drugs used. They used, therefore, progesterone therapy in these cases and gave also multivitamin preparations and iron and vitamin B₁₂ in cases of anaemia.

These reports make out a case for the use of pyrimethamine in all pregnant women who have a virus infection during the first trimester or a recent history of a virus infection. A ten day course of 25 mg. of pyrimethamine is given twice a day supplemented with the administration of a progesterone preparation and multivitamins by mouth. The action of pyrimethamine in virus infections like mumps, measles and toxo-

plasmosis shows that use of this preparation in virus infections in the first trimester of pregnancy will reduce the virulence of the infection sufficiently to prevent foetal deformities due to viraemia.

Nausea and even vomiting is likely to develop during the administration of pyrimethamine and it can be controlled with the administration of meclozine hydrochloride and pyridoxin hydrochloride.

Summary

1. Recorded observations of the action of pyrimethamine in virus infections provide a basis for the use of this drug in virus infections during the first trimester of pregnancy for preventing foetal deformities due to viraemia.

2. Evidence of the likelihood of a lowering of pregnanediol level during a course of pyrimethamine during pregnancy indicates the need of administering simultaneously a potent progesterone preparation.

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