

Discussion:

Professor Hadad: As a matter of fact in our last conference, I read a paper on Malaria In Pregnancy, and being ignorant of the effects of these drugs on the foetus, I mentioned that Chloroquin is the usual drug of choice in the treatment of malaria, but for some resistant cases we give Quinine. I came to the conclusion that the dangers of quinine had been over emphasized. I would like to ask Professor Brimblecombe to what extent these ill effects have been demonstrated. Because hundreds of thousands of pregnant women have received Chloroquin and Quinine and unless a prospective study is done on the hundreds of thousands of babies born to these mothers to see how many suffer from mental retardation or hearing impairment, we shall not know.

Professor Brimblecombe: Thank you Professor Hadad. I accept what you say and it is most important to get this into perspective. I think the evidence, for Chloroquin, for example, comes from those mothers, who have not been treated with prophylactic doses of Chloroquin, but for women with very complex diseases, who are given very high doses. It may well be that the people that put the blame on Chloroquin should put the blame on to the other diseases from which these women suffer.

I would agree with you; we must all use our clinical judgement in dealing with cases. Of course it is important that a mother should be prevented from getting malaria during pregnancy, or if she does get it then it should be treated. If the drug is given judiciously and carefully and not on excessive doses, then the baby is unlikely to suffer. As you know it is possible to get a complete list of drug reactions and in particular those effecting the neonate. I confess to not having personally studied the evidence upon which the original statement on Chloroquin was made.

Dr A. Moneim El Seed: Thank you Professor Brimblecombe for a most interesting talk. I would just like to make three points. Taking the last point first; I think that the deafness reported in association with Chloroquin and Quinine is rather difficult to check because we tend to see the child in the first few weeks of life and in the reports the deafness was recorded at a much later age when it became possible to observe the infant more closely. Certainly it was not the malaria that caused the deafness because I know of reports where deafness in infants developed when the mother was taking Chloroquine for Rheumatoid arthritis, during pregnancy.

Another point in this respect, is that of drug interaction, particularly of those which cause deafness. One that I came to know about is that between Quinine, Chloroquin and Aminoglycosides. These are all known

to cause deafness in association with noise from the incubators and from the surrounding environment. It seems that there is an increased incidence of deafness if a high threshold of noise is maintained, when giving these infants such drugs.

The second point is the possible effects of drugs, even before pregnancy. Some drugs have been reported to have caused change in reduction-division so that exposure to the drug or toxic agent might have occurred even before pregnancy. This was noticed in people, technicians and female doctors working in radiation units and to a lesser extent in those working with anaesthetics. What is interesting is that exposure before pregnancy has been reported to be associated with an increase in congenital anomalies.

The last point that I would like to make is this; I would like to ask Professor Brimblecombe whether he would like to add one more drug to his list and that is Formula milks. Someone has said, in the past, that the introduction of Formula milks is the most radical experiment on which mankind has embarked without a controlled study. We are seeing more and more problems relating to Formula milks. Laterly I was interested to read about some controlled studies done at the Institute of Child Health London, by professor Soothill and others, on the prevention of allergy. They did a careful prospective study on the incidence of Eczema in infants born to mothers who were known to be allergic. It was found that there was a significantly higher incidence of Eczema in children that were fed on Formula milks in the first few weeks of life over those that were fed on breast milk; and the same applied to other forms of Atopy. Thus, one wonders, when one is introducing the child to Formula Milk in the first few weeks of life whether one is not introducing a drug.

Professor Brimblecombe: Just while we are talking on this subject I have shown you a list of the drugs that come through in the mothers' breast milk. To come to your question; Yes, I think that this is very important. I think that the evidence is very good that allergies in general are more common in those babies that are given artificial feeds in the first few weeks of life. I think this is almost certainly true. And I think that this is very much bound up with the Immune System. We are currently doing quite a lot of investigations into the quality of breast milk, how far the immunoglobulins are preserved in breast milk. Obviously, if the mother is feeding the baby directly this is fine, but if the milk is kept for any time and then given to the baby, certainly if it is heated, then the immunoglobulins are destroyed. All these factors come into the equation. This is a very

complicated subject and an important one. Certainly everybody in the U.K. is extremely anxious to repair the damage that has been done over the last thirty years in the encouragement of artificial feeding and the reduction of breast feeding, especially in the first six weeks of life. Because the evidence is not only about allergy but also about infections and in many other matters where we believe that there is a great advantage to the baby in being breast fed.

Dr Ahmed Karamala: Is there any relation between Syntocinon and Neonatal jaundice?

Professor Brimblecombe: I must immediately say that I do not know. The purpose of my talk today was to show how little we all know about the effects of drugs given in pregnancy, and about drugs given to the newborn, and how much more we need to know. We are often forced to prescribe for the newborn, but it is something we should do after the great thought, because of some of the effects that I have been talking about today.

Dr. Mufti: We all know that there is a difference in the rate of transport of different drugs across the blood-brain barrier in disease and health, I wonder whether this applies to drugs passing across the placenta or whether this applies to the medical conditions of the mother on the placental side.

Professor Brimblecombe: I shall try to make two points. Obviously the mother's state is important. If there is vasoconstriction on the maternal side the transport across the placenta will be effected, but I also tried to point out the very selective action of the placenta the way that it handles, on the one hand, water that is transferred across by simple osmosis, and on the other the very selective diffusion of sodium, most of the other basic salts, and most amino acids. There is also a preferential diffusion of some of the lipids. So it depends very much on what one is talking about. There is a great variability. Some substances cross the placenta and others do not. This does not depend entirely on molecular size. The placenta is a complex organ about which there is still a great deal to know. Unfortunately what we learn has to be from animal experiments and there is always a danger of applying what happens in one species to that of another.

Dr. Mohamed Ibrahim: Unfortunately we are pressed for time and although I would have liked to have prolonged the discussion, we must move on. If I may just take up my prerogative as chairman and make some final comments on the discussion that has been going on. I would like to take up first the point about those drugs that effect the newborn. I would like

to say that I do not know of the relationship between Syntocinon and jaundice. There is no doubt that there are a number of drugs which do effect the excretion of bilirubin and its metabolites in the neonatal period. This is a very important aspect that has to be taken into consideration when we are prescribing drugs to the mother during labour and to the baby after birth. The problem of jaundice in particular is of great importance because of the effect of this metabolite on the future development of the child. There are many drugs but one must remember in particular the sulphonamides, Novobiacin, commonly prescribed drugs which are known to have an effect on the excretion of Bilirubin.

The other comment that I would like to make is on the Formula Milks. It is not only the problem of allergy, but in our country, the effects of Formula milks are much more devastating than that. It is probably one of the biggest killers in the Sudan, particularly in the second and third years of life. It predisposes to the causes of the highest mortality and that is malnutrition. Dr. Moneim has rightly said that man has embarked on the biggest prescription of a drug even without a control and nobody really knows the real effect of the Formula Milks in the future health and development of children throughout the world. But we are sure of the devastating effect of bottle feeding on the health and lives of our children in the Sudan.