of the mother, the high levels of antibody, and the amniotic fluid measurements were doomed children; saving only 40 out of 150 would have been quite an accomplishment, especially since some of them were already hydropic at the time of the first intrauterine transfusion.

However, beyond that, I fail to see how some of them fit into the category either of death or physical or psychological or intellectual maldevelopment primarily as the result of the intrauterine transfusion. Certainly the myelomeningocele was an unrelated lesion, and possibly the twins, who were both premature and had very low Apgar scores at birth, might have suffered the same sort of damage even if they had never had erythroblastosis or been transfused.

It is difficult to understand how the renal damage in two patients could have resulted from the infusion of dye into the kidney substance on one side (the needle unfortunately poked into this and then gave a diffuse nephritis or nephritislike picture which seemed to involve both kidneys); possibly the swallowed dye could do this, though it seems unlikely.

After such an analysis, one might conclude that 2 or, at the most, 3 of these patients may have suffered some ill effect from the intrauterine transfusion, but 3 out of 40 is only around 7 or 8%, whereas your figures suggest almost 20% trouble in these cases.

I would stress, therefore, that intrauterine transfusion, though a difficult and dangerous procedure, is not nearly as hazardous to the physical or mental development of these infants as this report seems to imply.

Dr. COCHRAN: I would respond to Dr. DIAMOND by saying that I do agree. These infants are jeopardized from many directions, not just from the intrauterine transfusion. Thus, the data have been presented so that you could make your decision as to where you think the jeopardy would most likely lay. Slowly but surely if we publish *all* such data we will be able to make some statistical statements in time. For 34-week gestation infants these particular infants have probably done all right; however, it would be better if we could get them up to 37 weeks before delivery, if possible. We have not succeeded on the average, in doing so. Ideally, it would be best to get them up to 40 weeks.

On another tack, I have always felt mothers who endure high risk pregnancies tend to have problems of any type in greater percentage than mothers who have normal pregnancies as regards infant outcome. Therefore, we have to include babies even with congenital anomalies so that once again, if we collect a large enough series, in time we can see if there is an increased incidence of one or another problem. Maybe Dr. WARKANY could respond to this possibility.

Just to speak again about the kidney lesions, Dr. FELLERS and Dr. CRAIG are in the process of preparing a paper concerning dye injection into rats. In this study, they feel they have shown that if dye is put into the region of one kidney it causes bilateral and comparable kidney lesions. These lesions in the rat are also comparable to those seen in our infants.

LEO STERN (The Montreal Children's Hospital, Montreal, Que.): Like Dr. DIAMOND, I am not quite clear why you would impugn the intrauterine transfusion. You have a group of children who are from 28.5 to 37.5 weeks of gestational age. Is there any evidence that the degree of psychological development malfunction that you estimate is any different than that of any ordinary group of 27.5–37.5-week-old infants?

The other problem is also something alluded to by Dr. DIAMOND. You are dealing with a group of infants, many of whom have had to be sectioned to get them out *ex utero* at that age. A number of them probably had to be induced, and much of this is not so much the song as the singer—who does the induction, who does the delivery, and the section. I am not clear as to why the relationship should be to the procedure of intrauterine transfusion. Maybe it is just the prematurity and how they were delivered.

Dr. COCHRAN: First of all, Dr. STERN, the one factor that brings these infants together is that they all have had an intrauterine transfusion. I agree that some are more premature than others, and some certainly have many problems to conquer than just the intrauterine transfusion, but all have had intrauterine transfusions. Thus, it is the intrauterine transfusion that puts them in a particular category and selects out those infants we have been discussing here. Except for the three with problems fairly definitely associated with the intrauterine transfusion procedure one cannot say specifically that their problem is due to this procedure or due to the threat to their life for which the procedure is incidentally performed. They still are clinically one group that we would like to make as healthy as possible. Once again, if we collect a pool of such infants who have had this procedure, in time we may have enough data to make some statistical tables that they truly are different—or maybe not different. Obviously most of you think they are not different from the normal run of 28–37-week-old infants.

JOHN M. BOWMAN (Winnipeg, Man.): We have transfused 156 fetuses 341 times; 151 have been delivered and we have 80 survivors. Of the 80 survivors, 58 are now more than 1 year old and we have been able to follow 45 of them. Of the 45, we have had 2 severely damaged infants. One was hydropic at delivery, survived 7 exchange transfusions, developed a spontaneous subarachnoid hemorrhage at 19 days of age, had communicating hydrocephalus, has had a shunt, and now has a developmental quotient of 65. The second severely damaged patient was noted to be hydropic at the time of the second fetal transfusion. This hydropic condition was reversed after the third transfusion. This patient was delivered after 34 weeks of gestation, and has been observed to have severe cerebral agenesis. Her parents were not too dissimilar from the parents of the twins that Dr. COCHRAN mentioned because they also were of very low intellect. The remaining 43, as far as we can determine, are well within the normal range.

RONALD J. CANTWELL (University of Miami, Miami, Fla.): Dr. COCHRAN may be interested to know that Dr. BILL LILEY's first case of intrauterine transfusion which I followed up, also had a hemiparesis. Although we did not regard this as a complication of the procedure, I notice that of your 7 survivors who had complications, 1 had hemiparesis. It may be that this is a significant complication of intrauterine transfusion.

10 *Decreased Infant Mortality Rates in a Low Income Population Served by a Comprehensive Community Health Program.* ANDRE CHABOT, Univ. of Colorado Sch. of Med., Dept. of Ped. and Preventive Med., and Denver Dept. of Health and Hosp., Dept. of Ped., Denver, CO (introduced by Henry K. Silver).

MARK RICHMAN (Shaker Heights, Ohio): What statistical evidence do you have that the populations with which your study dealt (in the two different periods compared) were at all similar, in terms of some of the

things you mentioned: socioeconomic status, mean maternal age, and so on?

Dr. CHABOT: We do not have age breakdowns, but we know that the incidence of welfare recipients during the years is about the same.

FRANK ZECHSNER (Germany): As your first example you showed an infant mortality rate for West Germany of about 22%. That is about the mortality rate of Central Africa. We are not that bad, you know; probably your data are derived from statistical publications of our government, and these are usually 100 years behind the present time.

Dr. CHABOT: Thank you. Those were 1967 data, and are presented in the World Health Organization book.

FRED SELIGMAN (University of Miami, Miami, Fla.): Dr. CHABOT, do you have any data on the socioeconomic parameters of the low socioeconomic and more affluent census tracts in 1964 and 1968? In other words, can the changes you ascribe to health care, possibly be ascribed to the fact that the socioeconomic parameters have changed, and that perhaps the narrowing gap in terms of health indices is a reflection of a narrowing gap socioeconomically? Also, do you have any data on population characteristics, especially, birth rates?

Dr. CHABOT: I do not have those data. Hopefully, we will when we get the 1970 census data. As far as the number of children born, our birth rate decreased somewhat in the poverty areas, but not significantly.

JOEL J. ALPERT (Children's Hospital Medical Center, Harvard Medical School, Boston, Mass.): I would like very much to be convinced that the health program was responsible for the changes you have described, but there are many questions one can ask about other possible factors. The infant mortality rate is observed to be falling in other communities as well.

I agree with your final statement, when you say that the infant mortality rate in the low socioeconomic census tracts is approaching that of the more affluent census tract. I was curious as to how you calculated your statistical differences.

Dr. CHABOT: A biostatistician did it on the basis of the sample size and the number of deaths. He has been calculating this on the number of live births and on the number of actual deaths that occurred. It was a chi-square test.

LOIS LYON NEUMANN (New York University School of Medicine): Was there a significant difference in the incidence of low birth weight deliveries between the periods being compared?

Dr. CHABOT: No, there was no decrease.

11 *Cellular and Metabolic Alterations in Obese Rats Treated with Monosodium Glutamate During the Neonatal Period.* JEROME L. KNITTLE and FREDDA GINSBERG-FELLNER. The Mount Sinai Sch. of Med., Dep. of Ped., New York City (introduced by Richard L. Day).

WALTER HEYMANN (Cleveland, Ohio): I think that is a fascinating business. To be obese without weighing too much is a frightening thought, and I wonder if you had any information on blood lipids, cholesterol, total lipids, other lipids.

Dr. KNITTLE: No, we do not. I do not think that it is such an uncommon thing to be obese and weigh the same as a nonobese individual, if one defines obesity as an excessive accumulation of adipose cells and increase in cell size.

H. GHADIMI (Brooklyn, N.Y.): The investigators have prudently avoided extrapolating their results to human infants. Nevertheless, presentation of their data at a pediatric society has the tacit implication that monosodium glutamate (MSG) may have undesirable effects in human infants. To say the least, this conclusion has been repeatedly published following OLNEY's reports [Science *165:* 1028 (1969) and *166:* 386 (1969)].

Completely overlooking the difference between humans and other species, the parenteral administration of any substance cannot be accepted as analogous to ingestion. We happen to consume MSG by mouth. Giving an oral load of MSG as high as 600 mg/kg body weight to a human infant did not cause a significant increase in the plasma level of glutamine-glutamic acid. Even the peak values were rather close to the upper limit of normal. This means that the busy crossroad of glutamine-glutamic acid in the liver has no red light; that is, glutamine and glutamic acid are quickly and efficiently metabolized. Obviously, if the route of administration bypasses the liver, the situation is entirely different.

My comments on the 'fattening' effect of MSG is that alanine and glutamine seem to participate in gluconeogenesis more than other amino acids in rats [PALEOLOGOS, C.; MUNTWYLER, E., and KESNER, L.: Alanine and glutamine levels in rat liver tissue. A direct relationship to gluconeogenic state. PSEBM *132:*270 (1969)].

Dr. KNITTLE: We assiduously avoided not mentioning anything about humans, and I really will not be here to defend either the use or lack of use of MSG, either in baby foods or any other foods. I do not think that merely measuring levels of an amino acid circulating in the blood can give you enough information as to what it is doing on a cellular level. I do not want to imply that the giving of MSG is going to make all our babies fat. I merely present this as a very interesting tool which has shown marked alterations in the fat accumulation, and we have seen now in some studies that we do run into a number of individuals whose obesity, at least in its early stage, is exemplified primarily by an increase in cell lipid content, much higher than others of the same age who are of normal weight.

I think the whole area of growth and development in critical periods has been very difficult to look at in terms of adipose tissue growth and development. Getting a tool that would directly eliminate the problem of large litter size is difficult because one's harvest here is not too good, and one cannot make very clearly defined critical period determinations.

I would like to stress that I think this is a very useful tool. I certainly do not want to extrapolate anything from the rat into people, either in the area of adipose tissue or, for that matter, in the area of the brain.

LAURENCE FINBERG (Montefiore Hospital, New York, N.Y.): Have you fed any animals monosodium glutamate rather than injecting them with it?

Dr. KNITTLE: We are in the process of doing studies with feeding experiments, but I can only refer you to the article in *Science* by OLNEY, who has demonstrated quite conclusively that glutamate, asparatate, and cysteine given orally, in high doses, can produce lesions of the brain. Whether this will lead to obesity, I do not know.

It is of interest, parenthetically, that in the one animal that we have autopsied, we have found no significant lesions in the arcuate area of the brain, as OLNEY described. So it is possible that obesity may be a phenomenon that is quite separate from the problem of brain damage. I think the possibility of the pancreas entering into this is very important. We are going to try to repeat this in the group treated orally.