as demonstrated by antibody increases. The virologic events were of particular interest:

A. Virus recovery from pharyngeal swabs. With the daily swab collection, the primary rubella cases were shown to shed virus for an average of 17 days. The range was 9–29 days. The profuse pattern of virus excretion in primary rubella is apparent. In contrast, none of the 17 vaccinees resisting reinfection shed virus. Of the 5 vaccinees with an antibody boost only 2 had virus in their pharyngeal secretions. One of these had antibodies when exposed; this child shed virus in 4 specimens. The other was an apparent vaccine failure who never developed antibodies. When reinfected she had 8 virus-positive swabs.

Each positive specimen was assayed for virus content and the quantitative differences were equally striking. The level of excretion in primary rubella ranged from 200 to 80,000 ID₅₀/ml of swab with an average of 6,000. The vaccinee with antibodies had a peak of 50 ID₅₀/ml of specimen. The vaccine failure was intermediate, excreting a maximum of 100 ID₅₀.

B. Virus recovery from heparinized blood. All persons with primary rubella were viremic. In fact, 83% of blood samples collected in the 11 days preceding the appearance of antibodies yielded virus. Comparable specimens from the 5 reinfected vaccinees and the one naturally immune child reinfected were uniformly negative. Again, all positive specimens were assayed for virus content. The level of viremia in primary rubella averaged 800 ID₅₀/ml with a range in individual cases of 10–10,000 ID₅₀.

None of these observations is particularly surprising since similar findings were made in studies of immunity resulting from live polio and rubeola virus vaccination. In terms of degree of resistance one expects attenuated viruses, in general, to evoke lower levels of antibody than their virulent counterparts. This is true of all the live vaccines—those for polio, smallpox, rubeola, mumps, yellow fever, and rubella. Lesser antigenic differences often exist between strains of the same virus. For example, attenuated rubella viruses are not identical and these variations can be correlated with relative resistance to reinfection.

The important issue is to define what may be reasonably expected in the use of the available vaccines. Summing up the experience to date, we see no basis for altering the practical conclusions reached over a year ago: (1) Challenged vaccinees are protected, rarely shed virus, and are not demonstrably viremic; (2) in relation to herd immunity, vaccinated persons with antibody even if reinfected are not likely to participate in the spread of rubella virus in communities; and (3) concerning maternal-fetal infection, it is reasonable to expect significant fetal protection since vaccine-induced antibodies have been demonstrated to serve as a barrier to viremia.

Dr. HORSTMANN: Some of Dr. MEYER's data, as he pointed out, are similar to ours and to those of others. Our whole concern with the problem is that vaccination against rubella is unique, since it is not the vaccinee who is the main target, but the fetus, some 10 or 15 years hence. It may be that the present vaccination programs will prove effective, but as we gain more experience we tend to be more cautious in predicting an easy victory. The virus turns out to be an unusual agent, virologically and immunologically, and the infection has some strange epidemiologic features. Since there are so many uncertainties, what we need to do at this stage is to follow a number of vaccinated populations closely, and to be alert to the various possibilities that may be in

store for us. I do not think that all of the answers are in by any means, nor will they be for some time to come.

9 *Prognosis of Live Infants Who Have Had Intrauterine Transfusions.* WILLIAM COCHRAN, ANN STARK and CELIA SCHULHOFF, Harvard Med. Sch., Boston, Mass. (introduced by Charles Janeway).

RODERIC H. PHIBBS (University of California, San Francisco, Calif.): You can get an erroneous impression of the outcome of a group of intrauterine transfusion survivors if you only examine each child once during infancy or childhood. We have followed a similar though somewhat smaller group, but have examined them every 6 months.

This slide shows the mean and the range of developmental and intelligence quotients at different ages in this group. At 6 and 12 months, and to a lesser degree at 18 months, many performed at a retarded level. As they grew older an increasing number achieved normal performance. All those who have reached 3 years of age are now performing at the normal or above-normal level. If such a group had been tested only once, as you did, when many were less than 1.5 years of age, you might have erroneously concluded that many intrauterine transfusion survivors were moderately or severely handicapped.

In contrast to your findings, we have not found any evidence of severe physical injury due to the transfusions. The majority of our intrauterine transfusions, however, were done under biplane fluoroscopy where the needle can be guided directly into the abdomen, and this may account for some of the differences in findings.

Dr. COCHRAN: In how many of your group did your intrauterine transfusion team not succeed even with their biplane fluoroscopy?

Dr. PHIBBS: Dr. ALAN MARGOLIS, who does all the intrauterine transfusions at our institution, tells me that with the use of biplane fluoroscopy he has never failed to get the needle into the abdomen of the fetus, although he does not always succeed on the first attempt.

Dr. COCHRAN: I agree that more frequent follow-up might easily have changed our DQ and IQ results. Certainly, as already pointed out, our group went from 6 months to 4.5 years and it is well known that any group tested as early as 6 months of age for IQ puts one on shaky ground.

LOUIS K. DIAMOND (University of California Medical Center, San Francisco, Calif.): I am going to draw on our experience in Boston, not San Francisco, with the same patients reported by Dr. COCHRAN, since our Blood Grouping Laboratory was responsible for the amniotic fluid measurements, all the blood group and blood serum tests on mothers and infants, and the intrauterine transfusion procedure carried out by Dr. EASTERDAY, obstetrician, and Dr. UMANSKY, pediatrician, of the intrauterine transfusion team. These women and their infants, here reported by Dr. Cochran, were, therefore, well known to us up to the time of their delivery.

I think Dr. COCHRAN's paper has merit in pointing out that intrauterine transfusion is neither a simple procedure nor one that is without danger. Therefore, it should only be done when clearly indicated, and the patients should be treated with great care, particularly to avoid infection, which I think has occurred a few times in the 150 or more patients that Dr. EASTERDAY and Dr. UMANSKY have transfused.

As to the patients themselves, it is necessary to realize that almost all these infants, based on the past history

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