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, aspartate, 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.

LYMAN A. PAGE (Stanford School of Medicine, Palo Alto, Calif.): Do you have data on whether the reduced size of other organs is due to reduced cell number?

Dr. KNITTLE: We have no data now. We have organs in the deep freeze, and we will be doing DNA and protein ratios to determine cell number and size.

- 12 *Defective Coenzyme Biosynthesis in B₁₂-dependent Methylmalonicaciduria.* MAURICE J. MAHONEY, MILDRED C. STAMBAUGH and LEON E. ROSENBERG. Depts. of Ped. and Med., Yale Univ. Sch. of Med., New Haven, Conn. (introduced by C. D. Cook).

Chairman GILBERT B. FORBES: Would you like to multiply vitamin B₆ by a factor of 2 and talk about vitamin B₁₂?

CHARLES R. SCRIVER (Montreal Children's Hospital, Montreal, Que.): If only I had half the expertise to attempt it! The authors have presented a beautiful piece of work and there is nothing I can say to add to it.

I would like to ask about something that may be of interest in the future, and which could be one of the legacies of your observations. When these patients respond to the administration of vitamin B₁₂, you are also giving an atom of cobalt for every molecule of vitamin B₁₂. About 3 years ago, in Quebec we had an epidemic of cobalt toxicity with cardiomyopathy. Do you know whether long-term administration of vitamin B₁₂ to your patients will also give them a load of cobalt that may actually be toxic? Do you think this is a danger?

Dr. MAHONEY: I believe we will need a long follow-up period to answer that question. The cobalt atom is held in a tight organic complex in the cobalamine molecule and the cobalamine molecule is rapidly cleared from the blood by renal excretion. Thus we can hope that the cobalt load will not reach a high toxic level.

We have treated the first patient described for over 2 years with twice a week injections of 1 mg of cyano-B₁₂. At times we have substituted the same amount of the coenzyme, deoxyadenosyl-B₁₂.

- 13 *Extending the Evaluation of the Effects of Early Enrichment.* JULIUS B. RICHMOND and BETTYE M. CALDWELL. Upstate Med. Center, Syracuse, NY, and Univ. of Arkansas.

ALEXANDER DRESCHER (Albany Medical College): Do you feel that 0.5 h/week may provide the placebo effect of a caring and concerned adult, rather than any other educational phenomenon?

Dr. RICHMOND: I think this is an important issue. Many of the home 'tutoring' programs that are currently in process, that of WEIKART and several others, stem from the concern over the importance of parent involvement. The impact programs have on parents, and what it does to their attitudes and care of the child, may indeed be the important issues. These are some of the problems that remain to be solved. This suggests that we need alternate programs to explore a variety of approaches.

MARSHALL KLAUS (Case Western Reserve University, Cleveland, Ohio): Historically, it has been of interest to see what is important in pediatrics and how pediatrics has changed over the years. What does the teacher usually do during the half-hour?

Dr. RICHMOND: First, I would suggest that I do not know that we should generalize from this half-hour. Remember, in the program it was the lead teacher who knew these children well and who visited the children at

home. I think that the emotional factors as well as the content of what was presented would be extremely important. I also preface my comments by indicating that our numbers are small and we could rely on only one highly skilled tutor.

Also, I might say that this was a dimension of the program that was not originally planned. In our early days we were not heavily invested in home tutoring. We were rather invested in the group care program, so that at the time we undertook this we did not have an available pool of tutors. We, therefore, used the teacher who was the most skilled and who knew these children, to go into the home.

LEONARD M. LINDE (University of California Medical Center, Los Angeles, Calif.): I have been working this past year with the disadvantaged student as he applies for medical school, and one of the problems that we have encountered is that the tests are made up by advantaged people. I am wondering if the disadvantages student is not learning some other kinds of skills that allow him to cope with his own environment, miserable as it may be, that may be missed in the testing.

In other words, how do you test for what this disadvantaged child has to know to get along? And is it possible that the tests, made up by advantaged people are merely testing something that advantaged children learn?

Dr. RICHMOND: I think this is a very important question, and certainly relates to the whole matter of the testing of cognitive function. Certainly, no one has been successful in developing a test that is free of cultural bias. We use tests that are the best that we have. We do feel, and other data that we have concerning social and psychological functioning of these children indicates, that there are many other gains beyond the cognitive. As a matter of fact, ZIGLER and BUTTERWORTH, in New Haven, and others have become very interested not only in following cognitive function, but also in learning something more about motivation. If we achieve cognitive gains and do not build in motivation for continued learning we have significant losses as a consequence.

As you point out, we are not suggesting that these children are incapable of learning. But they may be incapable of learning what is required of them in the one social institution that we require all of them to attend, the schools. We made that judgement in the middle of the last century, and we are programming some of our children to fail in those institutions.

CHARLES D. COOK (New Haven, Conn.): We have heard a good bit about the interrelationship between nutrition and growth and intelligence. I wonder if you have any information about the growth of these children, so that we could see the relation between the developmental quotient that you measured and their growth.

Dr. RICHMOND: We do have such data. I am not prepared to comment on it at this time, however. The nutrition of our children generally was reasonably good. That is, we have not encountered any striking deviations. Although we are dealing with quite a low income population, nutritionally they seem to in rather good condition.

HANIA W. RIS (University of Wisconsin Medical School, Madison, Wisc.): Are you planning to use the television program 'Sesame Street' as an enrichment program for the preschooler?

This is one of the most creative and imaginative educational programs for children, which is at the same