A broad view of a prenatal public health is presented in this paper. Almost limitless frontiers for research and practice appear before one, and one feels that public health work is only in its very beginnings.

PRENATAL HUMAN ECOLOGY

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I DOUBT THAT ten years from now sessions like this will be held on the subject of "pregnancy wastage." The challenge is less that of salvaging waste than of developing a prenatal public health. There are at least three reasonable objectives of this public health of pregnancy: to reach demographic equilibrium before it is forced on future generations by famine or the mass slaughter of war; to understand and adapt to genetic laws; and to control adverse environmental factors that may cripple our descendants before they are born.

For over a century thoughtful scientists, such as Geoffrey St. Hilaire, Camille Dareste, Charles Stockard, Franklin Mall and many others, labored to gain that practical understanding of the origin of acquired deformities which in part is ours today. One discovery after another has come tumbling out of the field and the laboratory since the role of German measles in causing congenital anomalies of the infant was first detected in Australia. Yet we are still far from that theoretical and practical knowledge which is necessary before tangible and effective measures can be developed to improve the health at birth of future citizens. Almost two decades after the teratogenic effect of maternal rubella was established, the indications are that there is more, not less, rubella among young adults and, hence, among young mothers. Many other infections have not even had cursory evaluation. No one can say, for example, whether or not the 1957 Asian influenza has left an impact on many lives then unborn.

Realization that most congenital defects may have their genesis during prenatal life and may be preventable is of recent origin. The idea is an old one, but today's proof that controllable maternal illness may distort fetal development stems in most part from clinical observations made all over the world in the 1940's concerning the impact of German measles on the conceptus when the infection is acquired by the mother during the first trimester of pregnancy.

Epidemiologic confirmation was slow because of the impossibility of observing abnormalities develop in utero after a specified maternal-fetal disorder. Case finding was the bottleneck, for post-rubella congenital defects cannot be diagnosed until birth, at the earliest; for years after birth, as with hydronephrosis; or perhaps not until autopsy, as with aneurisms of the circle of Willis. Not only are the clinical manifestations of deforming disease in the embryo or fetus hidden from view, but the final pathological consequences seem to be of relatively nonspecific nature. For example, congenital cataract, deafness, heart disease, and dental defects are not pathognomonic of rubella. To be sure, they frequently occur as lifelong marks

on the baby of the mother's brief infection, but these stigmas may be observed in babies after other maternal disturbances or in babies with no history of an antecedent illness whatsoever. The obstacles to case finding are truly formidable and indeed many structural and functional congenital defects are just beginning to be systematically classified, recorded, and correlated with maternal factors.

For some years now I have been in correspondence with Dr. Vilm Jonsson, Director General of Health in Iceland (population circa 160,000), to see whether some kind of mass correlation between rubella and any of its congenital sequelae could be developed in this isolated community. Dr. Jonsson has furnished me with vital statistics on reported cases of rubella for the 20-year period from 1935 through 1954 and with some figures indicative of the occurrence of congenital deafness in that interval. In Figure 1, the solid lines indicate cases of rubella in Iceland, the heavy blocks the approximate number of admissions to the State School for the Deaf and Dumb, by different years of birth. And the cases that occurred following the 1954 epidemic are not yet all declared. As Dr. Jonsson puts it, "The harvest of the rubella years 1954 and 1955 is not as yet gathered, but the superintendent of the Deaf and Dumb School has already met with eight cases born in 1954 and later." It seems hardly profitable to transpose these data in terms of rates because of the small numbers involved.

Perhaps this kind of experience in Iceland affords a model which might be used to examine human populations epidemiologically for congenital defects in relation to a suspect agent. With respect to rubella, for example, there is no difficulty in demonstrating epidemics in the years 1940-1941 and 1954-1955, although it would be helpful to have the age and sex distribution of cases, because this would indicate the extent of immunity among young adults. The missing statistic, and it amounts almost to a void, is the case finding and reporting of post-rubella anomalies by year of birth. However, an approximation of the incidence of congenital deafness was arrived at by a survey made of the birth years of pupils actually residing in the State School for the Deaf and Dumb in 1952, as well as of those admitted since. Assuredly, cases of partial deafness are missed, and cases of cataract and other post-rubella defects are ignored in this simplified scheme. The link between maternal rubella and defect should also have been authenticated by a physician in order to demonstrate scientifically the relation that is suggested, but not proved, by the data shown in Figure 1.

However, in a concern with rubella as an example, I do not wish to stray too far from the topic of this paper, which is so much broader—the huge field of prenatal ecology. The point I made with reference to rubella is that this disease-defect relation illustrates, albeit sketchily, how the occurrence of congenital deafness due to German measles is bound up with the broader epidemiology of

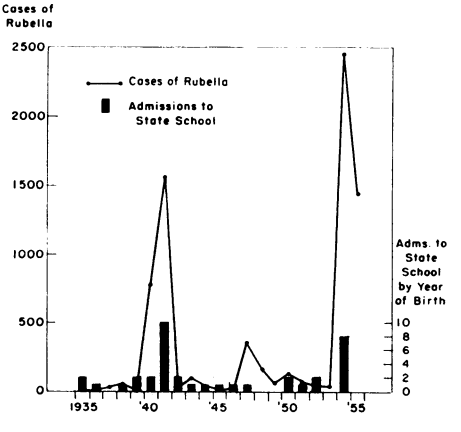

Figure 1—Rubella and Congenital Deafness, Iceland, 1935-1955

the disease. Effects upon unborn cohorts who were in utero at a time of epidemic thus will depend, among other factors, on the degree of susceptibility of the host population and on what might be called degrees of pregnancy. That is to say, the distribution and durations of pregnancy among members of the host population will influence the extent of congenital defect. Direct biological relations between mother and conceptus are also involved in these interrelations, which have virological, immunological, embryological, physiological, and purely obstetrical facets. Hence the field warrants a name of greater depth than that of "pregnancy wastage." If the point has not been made by consideration of this one disease, let us turn to the 1957 outbreak of Asian influenza and its teratogenic hazard about which we know little or nothing.

Influenza is an infection with its own complex epidemiology, and no information exists to show whether it did or did not register a prenatal impact when it was epidemic about October, 1957. With influenza, the obstacles are compounded. Not only do we have all the case-finding difficulties to which I have already alluded, but the maternal infection has no visible pathognomonic signs —no post-auricular adenopathy or pinpoint rash. Yet we have the opportunity of taking a glance at the possibility that the disease does hold a teratogenic risk: In Pennsylvania, thanks to the initiative of Drs. Robert Ivy and Gerald Rice, data have been accumulating for a decade on the occurrence of selected kinds of anomalies as recorded on birth certificates.

This reporting system makes it possible to test provisionally on a state-wide basis the hypothesis that Asian influenza may have a rubella-like impact upon the fetus in utero (Table 1). No evidence is uncovered, however, of a possible cause and effect relation between influenza in the fall of 1957 and congenital anomalies in the cohort of babies born seven to eight months later. Nor, on the other hand, can influenza be acquitted of causing mischief on the strength of such data. Helpful as they are, the data recorded on birth certificates do not give counts on the true extent of congenital heart disease at birth, nor are all cases of Mongolism uncovered in the first days of life. Because there was not a minor epidemic of cleft palate does not mean that cases of partial deafness (as in Iceland) or of cataract will not make themselves known during the preschool years to come. Nor can all anomalies be conveniently lumped together into a single category in order to give numbers that compensate for deficiencies in case finding. If there is one broad principle which emerges clearly from experimental teratology, it is that all anomalies can no more be treated as a single universe than can all rashes or all tumors. So many variable causes produce so many variable effects that some isolation of factors to be studied is desirable and necessary. For example, different pathogenic agents, such as rubella, toxoplasmosis, and syphilis, vary in their capacity to act upon mothers and hence upon babies. Moreover, the manifestations of maternal illness or fetal deformity vary with the stage of pregnancy. Thus, with reference to Asian influenza, it is quite possible that maternal infection may result in congenital deafness of the child, as did rubella in Australia, New Zealand, and Iceland, but that the disease does not measurably influence the occurrence of cleft palate. We just do not have the requisite data to put such speculations to test.

Even for chickenpox, mumps and measles, we do not have the cumulative observations that we have for rubella, and for a simple reason: The limited data which are available indicate mumps, like rubella, to be a real threat when it strikes in early pregnancy. However, like measles

and chickenpox, mumps is so much a disease of childhood that the woman is rarely observed who has managed to avoid exposure past the time of marriage, and who happens to be both susceptible and effectively exposed to mumps in the early stages of pregnancy.

Of course, the problem of congenital defects involves many factors other than those of infectious agents. Recent clinical and experimental studies indicate that testosterone injections of the mother during early pregnancy are capable of inducing major anomalies of the perineal

Table 1—Selected Anomalies* and Groups of Anomalies, Commonwealth of Pennsylvania, 1957 and 1958

(Rates per 1,000 Live Births)

	1957								1958					
	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	June
Skin														
Birthmark	0.42	0.24	0.09	0.22	0.22	0.31	0.35	0.42	0.65	0.26	0.30	0.25	0.46	0.27
Hemangioma	0.14	0.14	0.18	–	0.27	0.09	0.10	0.48	0.10	0.21	0.35	0.05	0.41	0.09
Nevus	0.05	0.10	–	0.09	0.05	0.04	–	–	0.15	0.21	0.30	–	0.05	0.09
Arms														
Polydactyly	0.56	0.81	0.40	0.54	0.85	0.57	0.80	0.48	0.65	0.68	0.35	0.45	0.41	0.63
Ectromelia	–	–	0.13	0.18	–	0.09	0.30	–	–	0.21	0.15	0.10	0.10	0.18
Malformed	0.09	0.14	0.22	0.18	0.18	0.13	0.10	0.12	0.15	0.01	0.05	0.05	0.26	0.05
Legs														
Ectromelia	–	0.05	0.13	0.05	0.05	0.13	–	0.12	0.05	–	–	–	–	0.05
Polydactyly	–	0.09	0.05	0.04	0.05	–	0.05	0.12	0.15	–	0.10	0.05	0.05	–
Malformed	0.33	0.33	0.22	0.22	0.31	0.40	0.10	0.54	0.25	0.31	0.35	0.25	0.41	0.14
Clubfoot	1.08	1.24	1.31	1.48	1.61	1.58	1.24	1.50	1.17	1.20	1.48	1.16	1.74	1.71
Head and central nervous system														
Cleft lip	0.38	0.24	0.45	0.22	0.37	0.18	0.20	0.30	0.20	0.42	0.45	0.15	0.36	0.09
Cleft palate	0.38	0.48	0.13	0.36	0.18	0.18	0.35	0.48	0.35	0.31	0.40	0.30	0.36	0.23
Cleft lip and cleft palate	0.38	0.19	0.49	0.36	0.37	0.66	0.55	0.72	0.75	0.47	0.70	0.60	0.56	0.32
Mongolism	0.38	0.53	0.40	0.18	0.37	0.40	0.55	0.72	0.40	0.21	0.20	0.15	0.72	0.23
Anencephaly	0.23	0.19	0.13	0.36	0.31	0.26	0.20	0.18	0.30	0.16	0.50	0.35	0.26	0.23
Hydrocephaly	0.28	0.53	0.27	0.18	0.22	0.22	0.25	0.18	0.05	0.42	0.30	0.20	0.26	0.23
Spina bifida	0.61	0.43	0.36	0.54	0.45	0.53	0.40	0.18	0.15	0.21	0.40	0.40	0.56	0.32
Chest														
Tracheal esophageal fistula	–	–	–	–	–	–	0.04	–	0.05	–	0.10	–	0.15	0.09
Congenital heart disease	0.38	0.48	0.22	0.68	0.37	0.49	0.40	0.84	0.65	0.36	0.57	0.50	0.15	0.77
Abdomen														
Intestinal atresia	–	0.14	–	0.13	–	0.09	0.04	0.06	0.05	0.05	0.10	0.05	0.15	0.05
Imperforate anus	0.14	0.19	0.22	0.13	0.10	0.04	0.04	0.24	0.05	0.10	0.05	0.15	0.19	0.09
Hypospadias	0.84	0.76	0.40	0.88	0.85	0.84	0.70	1.20	0.78	0.62	0.77	0.56	0.46	0.86

* Each child is scored under only one category.

and genito-urinary structure. Likewise, the frequency with which antithyroid drug therapy of expectant mothers has induced goiter in the fetus leaves little doubt that congenital thyroid deficiencies may have iatrogenic as well as natural causes, such as environmental deficiencies of iodine. Similarly, time relations of carbon monoxide poisoning in pregnancy to the kinds of congenital defect observed in babies born subsequently indicate that hypoxia of this origin is a teratogenic agent in human beings as it is in animals. I will do no more than allude to the adverse impact of maternal diabetes on the unborn baby. Yet I wish to point out that any woman experiencing diabetic disease while the fetal islets of Langerhans are differentiating may be suspected of initiating a disturbance of sugar metabolism in her unborn baby that may show up in future years. This kind of hypothesis should be tested as seriously as the hypothesis that a metabolic condition which occurs with significant frequency among the children of affected mothers rather than affected fathers is necessarily due to a sex-linked gene.

There are other metabolic, gynecologic, systemic, anesthetic, traumatic, and x-ray induced disorders of the pregnant woman which probably do carry and are at least suspect of carrying a risk for the conceptus. What needs to be done today is to test these suspect influences in the field. The challenge is a difficult one, for the list of agents, combinations of agents and degrees of activity is long and the list of possible consequences is longer still.

As public health and preventive medicine appraise the problem of acquired congenital anomalies in 1958 against the fruitful accomplishments of the past twenty years, the main patterns of causation are emerging. First of all, it is clear that the field embraces a great body of human ecology, not just the produce of pregnancy. For this reason the term "pregnancy wastage" is semantically inspid and, scientifically, a vast understatement.

Matters being treated here come under the "nurture" part of the nature-nurture controversy of yesteryear. The concern is primarily with the prenatal environment, not only with pregnancy itself, but also with prepregnancy—whether the mother herself has congenital heart disease, diabetes, or polycystic kidneys. The challenge is one that faces general medicine as much as preventive medicine and public health. This is so basic that I had at one time settled on the phrase, "Developmental Medicine—the Newcomer to Public Health," as the title for this paper. Perhaps the Japanese come closer still to what I had in mind, with their phrase to be translated as "embryo medicine." Certainly every mother is an incubator for her own baby, and the application of gynecological and obstetrical technics and knowledge is needed for the thorough evaluation of every pregnancy which results in the birth of a deformed child. However, developmental medicine is not inclusive enough. Every mother is also a component part of a population of human beings, old and young, men and women, married and unmarried, pregnant and nonpregnant, and mothers as a group are subject to all the influences that govern the ecology of mass disease. Thus, prenatal human ecology is a concern of all public health as well as of all clinical sciences and specialties.

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