SEASON OF CONCEPTION: A NEGLECTED ANALYTIC VARIABLE
(A preliminary report on fetal losses)

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With rare and limited exceptions, seasonal variation with respect to births and factors associated therewith has been examined on the basis of season of delivery. (1-9) It is our contention that seasonal analysis based on date of conception will yield more precise measurement of the effect on the fetus of time-limited exogenous events occurring during pregnancy.

A Hypothetical Example.

Assume an infant mortality rate of 25 per 1,000 live births. Based on the New York City total of 162,911 births in 1964, the standard error of such a rate is 0.39. To demonstrate a significant increase in the annual rate would require a level of 25.8 or an increment of 125 infant deaths. We now suppose that all babies are conceived and delivered equally throughout the year, or, on the annual total given, 12,531 each lunar month of 28 days.

Assuming again that the expected infant mortality among a group of 12,531 births is 25, the standard error of the monthly rate would be 1.39, with 95 percent confidence limits of 22.3 to 27.7. If, then, all the 125 additional deaths that are required to produce a significant increase in the annual rate occurred among a single monthly group, the rate for that month would obviously be affected to a highly significant degree. Actually the rate would be 35.0 compared to the 25.0 expected, or a 40 percent rise, well beyond the 27.7 upper limit of the stated confidence interval.

In this example, the increase of infant deaths is presumed to be the result of a single exogenous event (an epidemic, for example) that lasted four weeks. Its effect is exerted only on those fetuses that reached a gestational age of high susceptibility during the period when this exogenous event was operative. Therefore, the only fetuses that could be affected are those conceived during a specific lunar month. Thus, if we identify the live births deriving from that cohort of conceptions, the excess mortality is easily assessible.

But what happens if we look for this excess among groups of delivered infants? Not more than 46 percent of the affected fetuses will be delivered alive within the same lunar month. The remainder will be delivered over as many as six other months. Consequently, the effect of an event exerting stress on one cohort of conceptions will be distributed, to varying extents, among seven monthly groups of deliveries.

Table 1 has been constructed on the basis of the percentage distribution of live births in

Table 1. Distribution of live births for four-week intervals of delivery by four week intervals of conception*

Interval of delivery	All deliveries	Interval of conception								
		A	B	C	D	E	F	G	H	I
All conceptions	-	-	-	-	12,531	12,531	12,531	-	-	-
I	-	-	-	-	38	-	-	-	-	-
J	-	-	-	-	75	38	-	-	-	-
K	-	-	-	-	200	75	38	-	-	-
L	12,531	301	5338	5815	764	200	75	38	-	-
M	12,531	-	301	5338	5815	764	200	75	38	-
N	12,531	-	-	301	5338	5815	764	200	75	38
O	-	-	-	-	301	5338	5815	-	-	-
P	-	-	-	-	-	301	5338	-	-	-
Q	-	-	-	-	-	-	301	-	-	-

* Estimated from New York City 1964 data, assuming an equal distribution of totals by lunar month.

New York City in 1964. The columns portray the number of deliveries in specific lunar months that derive from conceptions in specific earlier months. The rows indicate the distribution of deliveries according to the month of their conception. Only the numbers pertinent to this illustrative example have been inserted.

The infant loss rate (whether computed vertically or horizontally) equals $\Sigma w_i r_i$, where the r_i's are gestation-specific rates and the w_i's are the proportion of the total live births delivered at that gestation. These w_i's are the same whether we deal with conception cohorts or delivery cohorts, as long as the number of conceptions and the distribution of live births resulting from those conceptions remain constant over time. Obviously, the r_i's for affected conception cohorts are uniformly increased, while for delivery groups only those r_i's referring to the affected conception cohorts contribute to an increase in the total rate.

Table 2. Estimated excess deaths* contributed to various groups of deliveries assuming the total excess of 125 deaths is limited to conceptions during a specified number of months.

Affected delivery groups	Estimated distribution of 125 excess infant deaths if increase limited to conceptions during		
	One month (D)	Two months (D,E)	Three months (D,E,F)
Total excess deaths	125.0	125.2	124.8
I	6.1	6.1	4.2
J	26.1	16.2	10.8
K	19.2	19.8	17.3
L	18.4	19.0	19.3
M	31.9	25.3	23.4
N	21.9	26.7	24.0
O	2.1	11.8	18.5
P	-	1.1	7.8
Q	-	-	0.7

* Estimated from New York City distribution of 1964 infant deaths by duration of gestation.

In Table 2 we show how 125 excess deaths in a single conception cohort (Col. D), two such cohorts (Cols. D and E) or three (Cols. D,E and F) would be distributed among subsequent groups of deliveries (Rows I through Q). The deaths are distributed by duration of gestation according to the 1964 New York City distribution. The figures for two and three cohorts assume the deleterious influence was spread over several months rather than limited to a single month.

Table 3. Infant mortality rates per 1,000 live births by month of delivery assuming an increase of 125 deaths limited to conceptions during a specified number of months.

Delivery months	Mortality rates if increase limited to		
	One month	Two months	Three months
I	25.5	25.5	25.4
J	27.1	26.3	25.9
K	26.6	26.6	26.4
L	26.5	26.5	26.6
M	27.6	27.0	26.9
N	26.7	27.2	26.9
O	25.2	26.0	26.5
P	-	25.1	25.6
Q	-	-	25.1

The resulting infant mortality rates for the delivery cohorts are shown in Table 3. It is clear from the upper confidence limit previously cited (27.7) that the infant mortality rate in not one of these delivery months reveals a rise sufficient to suggest that a time-limited exogenous event was responsible for the significant increase in the annual rate. Seasonal analysis of deliveries could therefore lead to inappropriate conclusions. On the other hand, whether the 125 excess deaths affect only one cohort of conceptions, or even if they are distributed among two or three such cohorts, the infant mortality rate among such cohorts would in each case be significantly raised to 35, 30 or 28.3 per 1,000 live births.

<u>Source of Data</u>.

The substantive data in this discussion derive from routine reports of live births and fetal deaths registered with the Department of Health of the City of New York. While we shall be investigating seasonality of infant losses, complications of pregnancy, congenital malformations, birth weight and duration of gestation according to season of conception, we concentrate in this paper on fetal losses.

In New York City, all fetal deaths are required to be reported regardless of period of gestation. It is recognized that underreporting exists particularly of very early losses where the woman herself may not have been sure of pregnancy and even losses of longer duration, especially where no medical attention was sought. Nevertheless, the sum of live births and fetal deaths reported represent the best estimate we have of total conceptions. From the annual patterns of both total reported conceptions and of live births, we conclude that underreporting is consistent by month over the three years covered in this paper, and that patterns based on conceptions throughout the three years are therefore factual representations of what happened even though the rates for early fetal deaths may be understated because of greater underestimation of numerators than of denominators.

It is also known that inaccuracies exist in reporting of the initial date of the last menstrual period (LMP), through carelessness, ignorance, or simple error. In a study of pregnancy losses made by the senior author some years ago, LMP dates reported by physicians at first prenatal visit were later compared with dates on corresponding certificates filed with the Department of Health. Errors in both directions were discovered but were found to be almost exactly compensating, with agreement as to date by far predominating. Hence, there is reason to believe that patterns will not be seriously disturbed by such errors. It must also be considered that we are here assuming that the date of LMP indicates the beginning of pregnancy, whereas in actuality conception usually does not occur until a couple of weeks after the LMP date. This factor has the effect of distributing the data about a half month earlier than conception actually occurs.

This study became possible because one item on the New York City certificates requests the initial date of the LMP. Its purpose on these documents is to permit calculation of the duration of gestation. On live birth certificates it is rarely unreported (1.6% of total live births in 1964) but more frequently is omitted on fetal death certificates (4.7% in 1964). Distribution by month of delivery of the cases where LMP date was not reported suggests there is no marked seasonal variation in failure to report this fact.

The month and year of LMP have been included on the statistical punch card prepared for all vital records. These cards were converted, beginning in 1960, to magnetic tapes as a space saving measure for future use even though EDP equipment had not yet been installed in the Department of Health. This study was made possible by the availability of these tapes, and this format also made possible editing that was not previously feasible. For example, the month and year of the LMP were checked against the month and year of delivery. For unreasonable combinations (such as LMP more than a year earlier than delivery or after delivery), the original records were checked and appropriate corrections made.

Fetal Losses.

One aspect of pregnancy problems is represented by casualties at various stages of pregnancy. If it could be determined that women whose pregnancies start at specific seasons were at higher risk than others of loss of the baby, special attention could be centered on women conceiving during those intervals. Moreover, the identification of unusually high losses among pregnancies starting during a specific period of time might lead to identification of environmental factors coincidental with the terms of these pregnancies that are implicated in the losses.

In the interest of time, we are not presenting the detailed tables here but this audience will want an approximation of the numbers involved. There are about 15,000 total reported conceptions monthly, more than 13,000 live births and nearly 2,000 fetal deaths. About one half of the fetal deaths are of less than 12 weeks gestation; another 30% occur at 12-19 weeks; the remainder (about 20%) is almost evenly split between 20-27 weeks and 28+, with slightly more in the latter group.

Total Fetal Mortality.

We have available to us thus far only three years of experience, 1962-1964, derived from events reported from 1962 through 1965. We have chosen to estimate seasonality by accumulating the experience of the three years. Because of aberrations in the observed rates, we are skeptical that the accumulations for this brief period provide a reliable estimate of the seasonality of fetal losses by period of gestation. Definitive patterns of seasonality will have to await the gathering of additional data. However, we do believe it is worth presenting the material analyzed thus far.

From Chart I it can be seen from the solid line based on the aggregate data of the three years that there appears to be a seasonal pattern with low fetal loss rates among conceptions occurring in the summer months and high rates among winter conceptions. However, for none of these three years individually is the aggregate typical. The pattern is followed in 1962 and in the latter half of 1964. From June of 1963 to July of 1964 the rates are uniformly and constantly higher than the monthly means for the three years.

Several possibilities exist. First, the 1962 data may well represent what ordinarily happens although it is also possible that the rates in that year are somewhat lower than might be usual. Second, there seems no doubt that fetal death rates were quite high among conceptions from approximately mid-1963 to mid-1964. Any seasonal pattern in these two years is obscured and yet, despite the variations in these two years, a seasonality appears to persist in the aggregate.

Fetal Deaths by Gestation.

It will be useful to examine separately the seasonal pattern of fetal losses by duration of gestation. Charts II to V present the data respectively for late fetal deaths (28 or more weeks gestation), for intermediate fetal deaths (20-27 weeks gestation) and for early fetal deaths, separately for those 12-19 weeks gestation and those less than 12 weeks gestation.

For each of these gestation intervals there is variation in losses by month of conception. The aggregate data for the three years suggests in each case that seasonality exists and that losses are more likely to be high among winter conceptions than for pregnancies beginning in the summer.

There are, of course, departures from this pattern for each gestation interval and it is our opinion that these departures obscure to some extent the seasonality pattern.

For example, among fetal deaths of 28 weeks or more gestation (Chart II), observed rates were unusually high among conceptions in the spring of 1963, low for those in the spring of 1962 and about average for those in the spring of 1964. These varying specific rates tend to cancel out each other and produce a fairly flat curve in the first half year in the aggregate.

Among fetal deaths at 20-27 weeks gestation (Chart III) a seasonal pattern becomes more evident. The noteworthy features here are the apparently higher than seasonal observed rates in the summer of 1963 and the unusually high rate in March of 1964.

Again, with reported fetal deaths of 12-19 weeks gestation (Chart IV) there appears to be a definite seasonal pattern. Here we seem to have relatively low rates in 1962 and peaks in July, November and December of 1963 and May of 1964.

Fetal deaths of less than 12 weeks gestation (Chart V) do not present as clear a picture. The extraordinarily high rates in early 1964 and the upward trend during 1963 are such that any seasonal pattern is obscured. The data for 1962 suggest the possibility of seasonality in early fetal losses. If this is so, then there appears to have been some factor or factors in 1963 and 1964 that disturbed this seasonality.

Comparison with Estimates.

The general theory on which we are examining variation by month of conception is that such

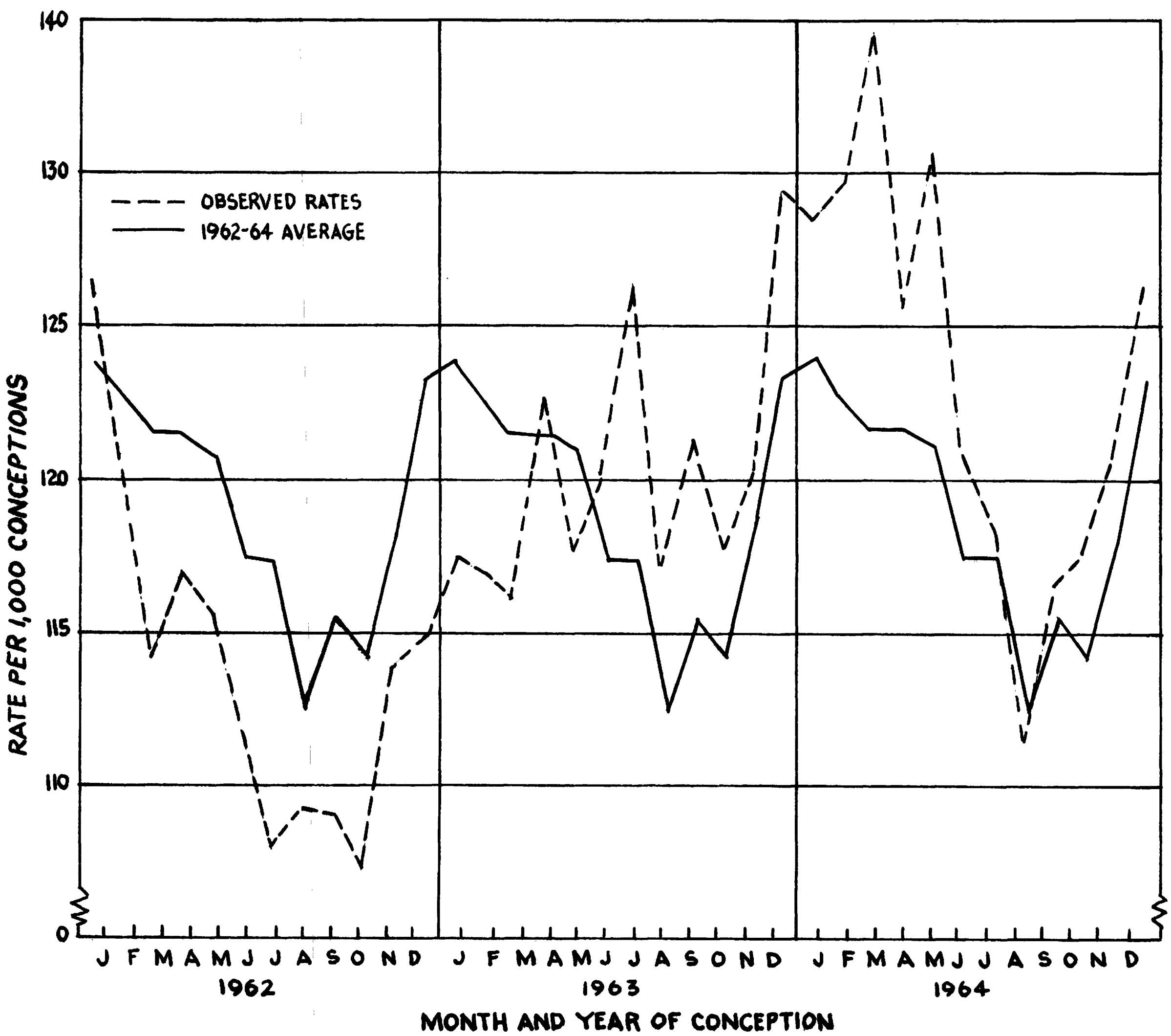

Chart I. All reported fetal deaths per 1,000 conceptions by month of conception: New York City, 1962-1964

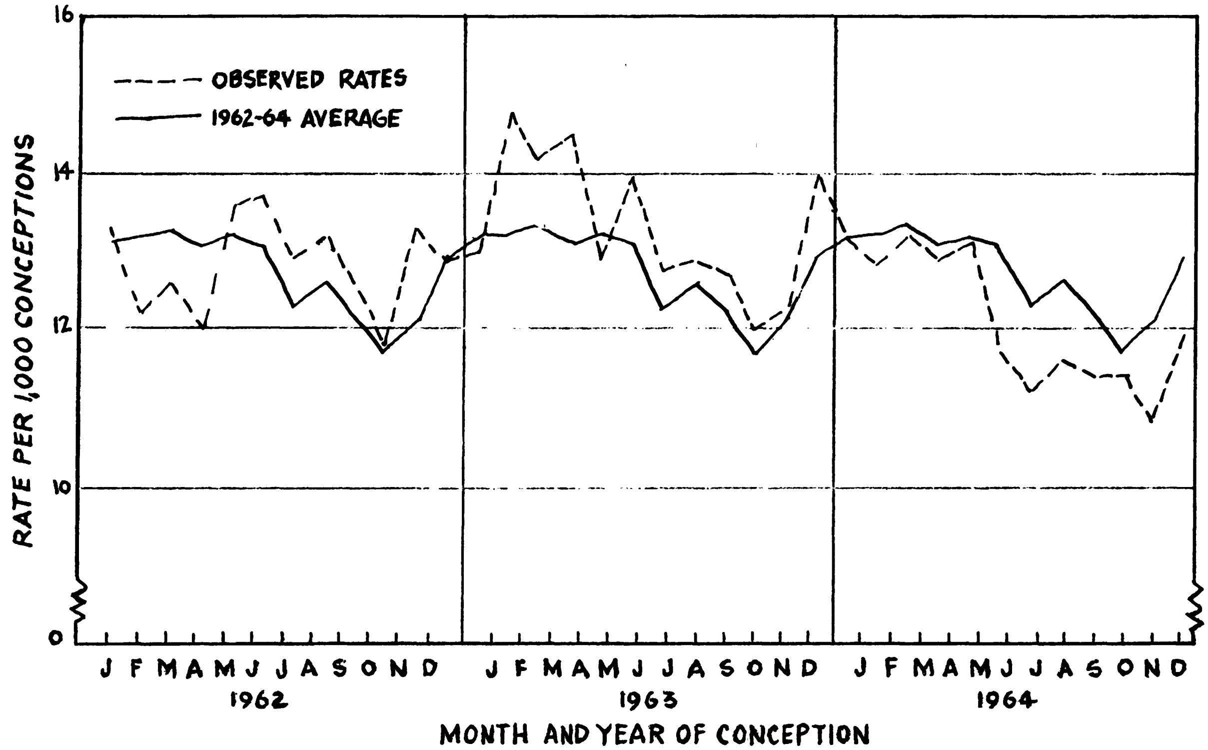

Chart II. Reported fetal deaths 28 and more weeks gestation per 1,000 conceptions by month of conception: New York City, 1962-1964

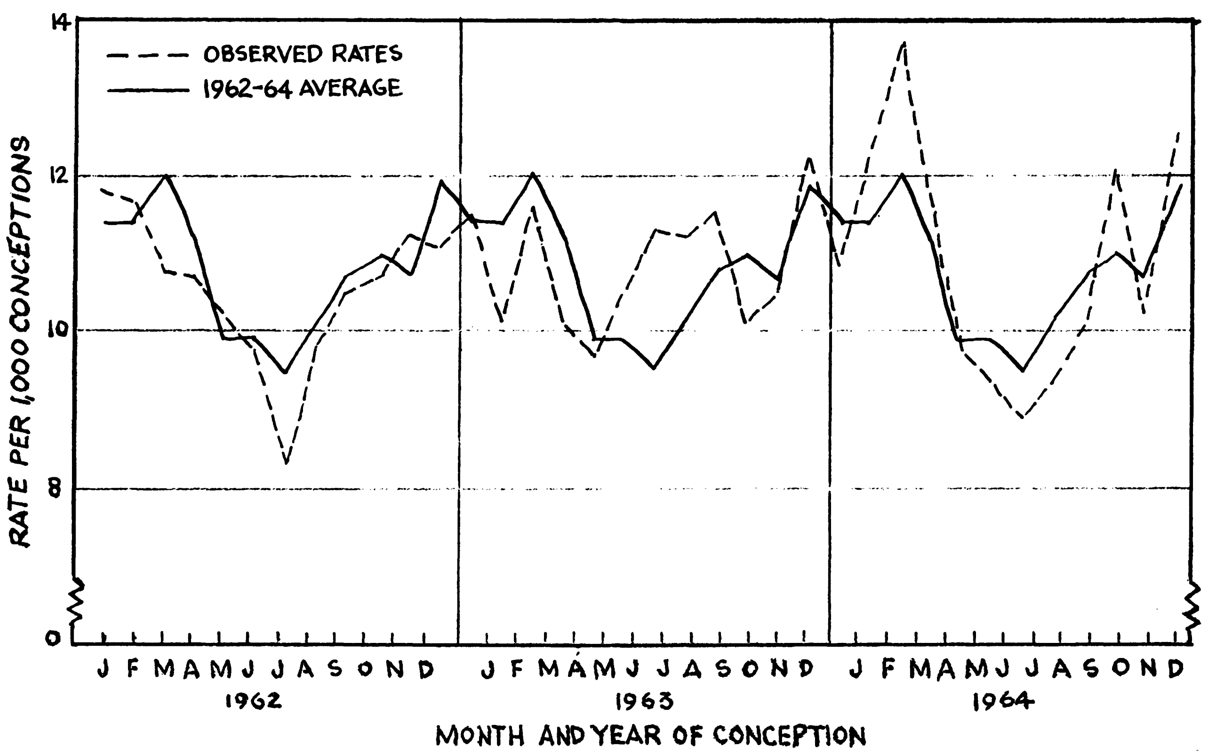

Chart III. Reported fetal deaths 20-27 weeks gestation per 1,000 conceptions by month of conception: New York City, 1962-1964

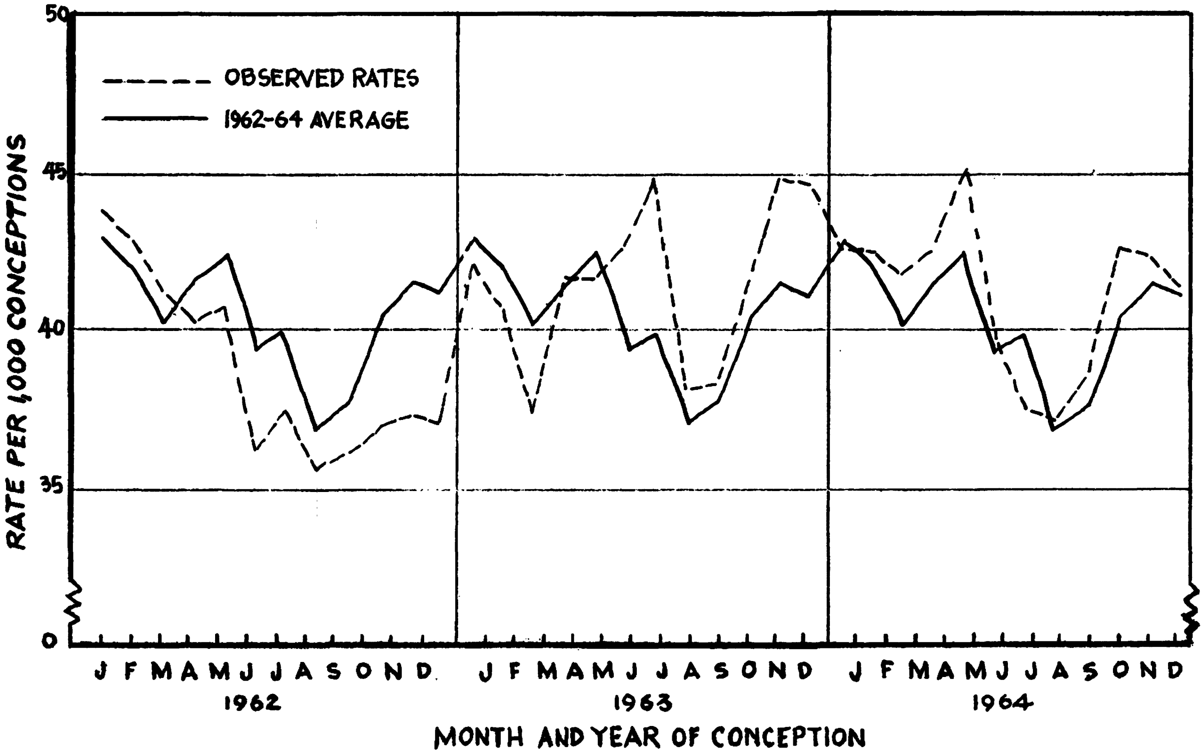

Chart IV. Reported fetal deaths 12-19 weeks gestation per 1,000 conceptions by month of conception: New York City, 1962-1964

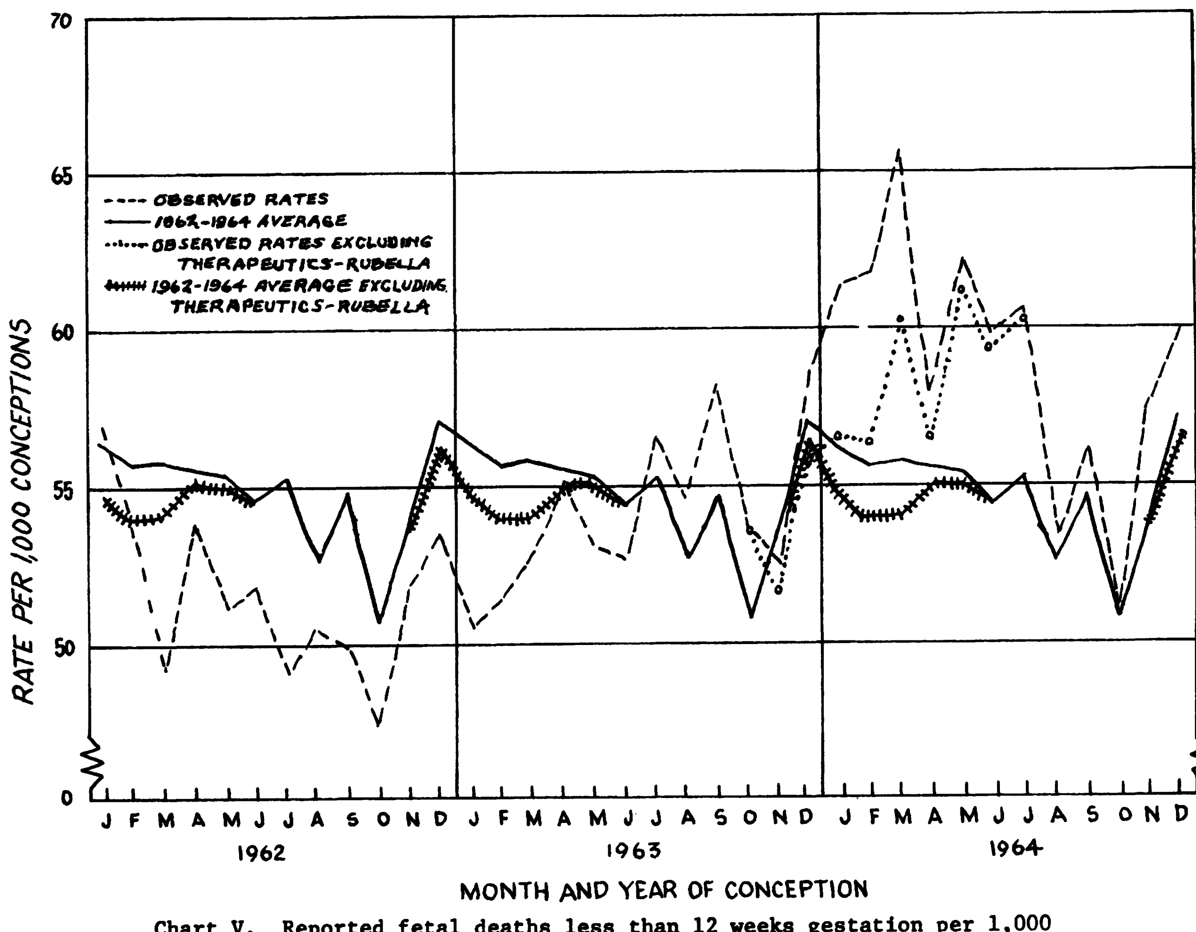

Chart V. Reported fetal deaths less than 12 weeks gestation per 1,000 conceptions by month of conception: New York City, 1962 - 1964

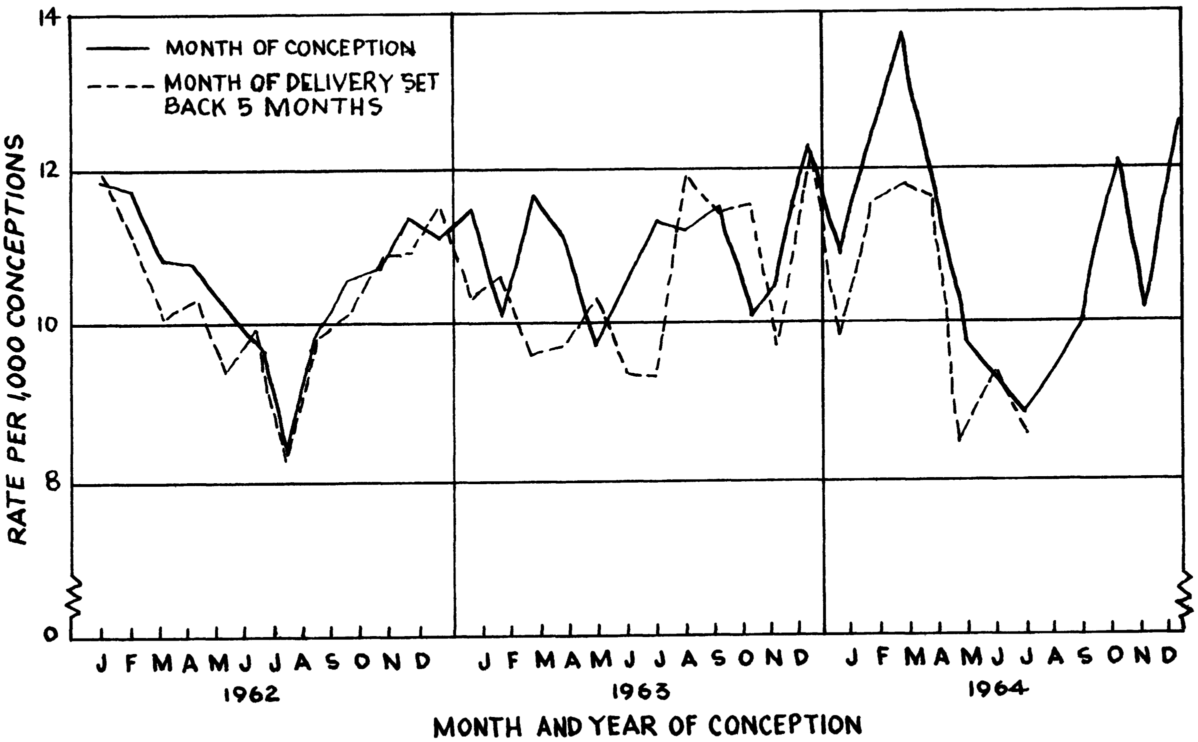

Chart VI. Reported fetal deaths 20-27 weeks gestation per 1,000 conceptions by month of conception and per 1,000 reported deliveries by month of delivery set back five months: New York City, 1962-1964

analysis will provide more precise measures than examination by season of delivery. We should then compare our observations with data routinely produced that might be used to estimate what happens among conception cohorts. Chart VI reproduces the observed data from Chart III for fetal deaths at 20-27 weeks gestation. Here we have also charted (dashed line) rates per 1,000 total deliveries reported as occurring in the same month as the fetal deaths of this gestation interval. The curve has then been shifted five months earlier to approximate the time of conception of the 20-27 week fetuses.

Limitation to fetal losses at a specific gestation interval in itself serves to minimize the effect of the estimation process. The close conformity of the two curves for 1962 suggests to us that during periods when no unusual extraneous factors are operating, the simple estimation process works quite well. However, from Spring, 1963, to April, 1964, when, as we have already commented, the course of the fetal loss rate seems to be aberrant, the two curves frequently are out of phase. Moreover, the sharp increase in March, 1964, is more clearly seen in the date of conception series.

Discussion.

Until further data become available we cannot say with certainty that there is a fundamental seasonal pattern of fetal losses by time of conception. Data in this paper suggest that such seasonality exists, but that, for at least a year of the three years under observation, any such pattern was suppressed by unusually high rates. Were there any events that might explain such aberrations?

Weekly mortality rates from influenza and pneumonia were unusually high in New York City, from late January to early March of 1963. In July of that year, a prolonged heat wave raised mortality rates in New York City to 13.4 and 13.7 per 1,000 population for the weeks ending June 28 and July 5, compared to an expected rate of about 10.2. An epidemic of German Measles built up during the Fall of 1963 with the peak number of case reports to the Department of Health reaching 5,720 in March and 5,731 in April of 1964. (Allowing for delay in reports, the epidemic peak in terms of onset of disease undoubtedly occurred somewhat earlier.)

In connection with the rubella outbreak, it is pertinent to mention that the number of early fetal losses counted in this paper for early 1964 includes therapeutic abortions. Starting with November, 1963, therapeutic abortions with reported indication that the mother had contracted German Measles increased substantially in New York City. Such abortions reached a peak with 78 reported among conceptions in each of the months of February and March, 1964. To indicate the effect of these therapeutic abortions, we recomputed the rates after their exclusion. The result is shown by the dotted line on Chart V for monthly observed rates and by the crossed line for the three-year aggregate. These reductions in the rates do not entirely remove the apparent excess for the period.

Any and all of these environmental events may have had an effect on fetal losses. Further work needs to be done to establish the facts epidemiologically and pathologically. It does not stretch credulity, however, that influenza virus, excessive heat or rubella virus may have been factors in producing higher than expected fetal loss rates among conceptions during 1963 and early 1964. We have not yet been able to investigate other possible influences, such as Widelock's series of infectious agents in the community (10) or even to examine carefully enough those we have cited.

While monthly analysis of fetal losses by date of occurrence would have indicated that fetal loss rates behaved strangely in 1963 and early 1964, we believe that analysis by date of conception points more directly at the time periods that require investigation for association with environmental conditions.

Summary

It is shown, by a hypothetical example, that a 40 percent increase in infant mortality among infants conceived during a one month period could not be detected as a significant increase in the annual rate nor in monthly rates computed in the usual way. It is concluded, therefore, that analysis by month of conception will yield more precise measures of the effect on the fetus of exogenous (environmental) factors during pregnancy.

In this paper are presented fetal loss rates by period of gestation according to month of conception for 1962, 1963 and 1964. The data suggest that fetal losses are low among summer conceptions and high among those in winter. Definitive seasonal patterns cannot be determined from these three years of observations, mainly because rates were almost continuously high throughout 1963 reaching a peak in early 1964.

Some conjectures are offered at this time that such events as high prevalence of influenza and pneumonia as evidenced by mortality in Spring, 1963; prolonged heat in July, 1963, and the German Measles epidemic from Fall 1963, to its peak about March, 1964, may have had a bearing on the relatively high loss rates among fetuses conceived during this period.

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