*Although a comparatively large number of strabismus cases occur in child populations, little is known of the etiology. A retrospective study of the relationship of perinatal factors to strabismus was therefore undertaken. The findings show an association with prematurity and lower birth weight, as well as length of gestation. A significantly higher proportion of major abnormalities at birth was encountered.*

# PERINATAL FACTORS ASSOCIATED WITH STRABISMUS IN NEGRO CHILDREN

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STRABISMUS or squint, essentially a childhood problem, is a fairly common oculomotor disorder resulting in a "manifest deviation in which binocular fixation is impossible."[1] The two most common forms of strabismus are esotropia (convergent strabismus) and exotropia (divergent strabismus) and are classified by whether the strabismic or squinting eye turns inward or templeward.

Although the fact that many larger hospitals provide special clinics for children with strabismus indicates that this condition is common, a search of the literature failed to reveal any large-scale, ophthalmologically conducted surveys of incidence or prevalence of strabismus in young children in this country. The foreign literature proved to be somewhat more productive in this regard.

A study[2] of 16,046 children ranging from infancy to seven years of age, in Copenhagen from 1952 to 1957, revealed a 5 per cent prevalence rate. Among infants the prevalence rate was about 1 per cent and it increased progressively to about 7 per cent at seven years. There were no significant sex differences. A crude measure of relative incidence by age in that study can be deduced from the following facts. Fifteen per cent of all cases were observed before the second year of life. The author stated that no new cases had been recognized during the second year of life. However, about 25 per cent of the strabismic children demonstrated the condition during the third year, another 25 per cent during the fourth year, and 12 per cent each during the fifth, sixth, and seventh years of life.

In a study[3] of 891 strabismic children in Amsterdam, ranging in age from infancy to 12 years, 81 per cent had their onset during the first four years of life. There was an overwhelming preponderance of convergent, as compared with divergent, strabismus.

A survey[4] in Norway of some 53,000 children aged 9-10 years, examined during the period 1949-1959, revealed a prevalence rate of convergent strabismus of 2 per cent. In Czechoslovakia a survey[5] of almost 3,000 children of pre-

school age (between six months and six and one-half years of age) examined over a five-year period indicated that 4.7 per cent had strabismus.

In spite of the comparatively large number of strabismus cases in child populations, relatively little is known of the etiology. A search of the literature failed to reveal any study in this country of the relationship between perinatal factors and the occurrence of strabismus. The studies referred to below are from the foreign literature.

The Amsterdam study, mentioned above, found birth trauma in the history of some 10 per cent of strabismic children. Where birth trauma was reported, there was usually an early appearance of strabismus. For instance, birth trauma was present in 15 per cent of the cases where onset of strabismus occurred within the first 18 months of life, in 7 per cent where the onset was between 18 months and the fourth year, and in 5 per cent where onset was during the fourth year or later.

In Czechoslovakia a study[6] was conducted on 159 children born of mothers who suffered from late toxemia of pregnancy and on 148 children whose mothers had a normal course of pregnancy. Strabismus was present in about 10 per cent of the former children as compared with about 5 per cent of the latter. However, based on the data presented in the paper, the difference was not statistically significant.

Reported prenatal and perinatal "traumata" (forceps delivery, prematurity, asphyxia) in 600 children with strabismus and without a family history of strabismus were compared with similar data for 112 nonstrabismic controls.[7] The "traumata" were found to be more prevalent in cases than in controls. In the Copenhagen study, mentioned above, prematurity was more common among strabismic children (11.8 per cent) than among the general population of births (6.1 per cent).

In view of the limited number of well-controlled studies conducted with respect to perinatal causes of strabismus, it is hazardous to speculate on, and difficult to interpret, the reported results.

Untreated strabismus may involve the risk of impaired vision or blindness in the strabismic eye. For example, there may develop a potentially blinding condition, amblyopia ex anopsia, which is "a reduction in the acuteness of vision which cannot be relieved by glasses and is not dependent upon visible changes in the eye."[1] Furthermore, "very often amblyopia ex anopsia develops in an eye which has squinted from early life on account of its exclusion from the visual act, the retinal image in this eye being suppressed."[1]

A number of investigators[3,8-11] have stated that amblyopia ex anopsia occurs frequently with strabismus. On the other hand, at least one investigator[12] has indicated that one-third to one-half of strabismic eyes show no amblyopia after ten or more years, from which he concludes that factors other than failure to use the eye must also be involved. The results of the treatment of amblyopia have demonstrated that this condition occurs secondarily in a great majority of strabismus cases.[3] Apparently, the longer the strabismus exists, the more often amblyopia is found, and probably the more deep-seated it is and the more difficult to correct.[11] There would appear to be sufficient evidence to believe that a study of the etiology of strabismus is pertinent to an understanding of amblyopia ex anopsia.

It was decided to undertake a study of the relationship of perinatal factors to strabismus in children for the following reasons: (1) strabismus is highly prevalent in children, is related to amblyopia ex anopsia, and may be related to psychological trauma; (2) little is known of its cause. The study undertaken was retrospective in nature.

The retrospective approach to de-

termine associations of specific neurological and psychological disorders in children, with prematurity, and with maternal complications of pregnancy and delivery, has been an accepted technic for many years.[13-21] Due to the association of strabismus with amblyopia, it is evident that a retrospective study of strabismus, even though approached by the method of statistical association, may have much to offer in the area of prevention of blindness and severe visual impairments.

## Objectives and Study Design

The major objectives of the present study were to determine: (a) whether the distribution of birth weights of Negro children with strabismus is different from that of children selected as controls, and (b) whether the pregnancies of mothers of Negro children with strabismus are characterized by an excess of selected perinatal disorders.

For purposes of this study, strabismus was defined as an extraocular muscle imbalance characterized by esotropia or exotropia.

It was decided to limit the study to Negro children to avoid the bias that can be introduced in selecting children as birth certificate controls whose mothers were delivered as private patients. The great majority of Negro births occur on the ward service in Baltimore, Md., where the study was conducted.

In Baltimore, Negro children with strabismus, depending principally on place of residence, generally are referred to the Wilmer Eye Clinic of the Johns Hopkins Hospital; the Baltimore City Eye, Ear, Nose, and Throat Hospital; the Eye Clinic of the Presbyterian Hospital; or the University of Maryland Hospital Eye Clinic—either through well-baby clinics or through the school system. Because of this referral system, these eye clinics serve essentially similar Negro population groups. Most of the cases (66.3 per cent) in this study were obtained from the Wilmer Eye Clinic which serves a majority of Negro strabismic children seen in Baltimore clinics.

The case study group included 406 children with a diagnosis of strabismus made in any of the eye clinics mentioned above. There was no attempt by study personnel to make a diagnosis from hospital records. To be included in the study, a child must have been born in a hospital within the state of Maryland on or after January 1, 1950, and diagnosed with strabismus before October 1, 1964. Only single-born children, as confirmed from hospital records, were included. The child did not have to be a current clinic case or even alive at the time of the study. No child with another diagnosed neurological disorder was eligible for the study.

In selecting the case group from the four eye clinics mentioned above, a search of all records of children alleged to have strabismus provided 1,026 unduplicated names for review. Of these, 620 children were excluded for the following reasons. Birth or hospital records were not available for one reason or another for 229 cases; 188 cases failed to meet the definition of strabismus used in this study; 120 cases were unable to meet other case criteria, such as year of birth, race, single birth, and so on; and 83 cases were excluded because from the records they were found to have additional conditions, such as cerebral palsy, mental retardation, or others, known to be associated with maternal complications of pregnancy and delivery.[13-20] It may be noted that the sex distribution of children included in the study was not significantly different from that of excluded children. A group of 406 cases met all criteria for inclusion in the study.

The control group was selected from birth certificates and was matched with

the case group on the following variables: (1) date of birth (the next registered birth matching on relevant variables); (2) place of birth (same institution and same service); (3) sex; and (4) maternal age (within the following categories: under 20 years; 20-34 years; and 35 years and over). All originally matched controls who died in the neonatal period were replaced by appropriately matched neonatal survivors. It has been shown[21] that in studies of this kind and magnitude, limiting the control to survivors of the neonatal period gives results almost identical to those where the control group is composed of survivors to date of diagnosis of cases with which they are matched. Birth certificates on file at the Baltimore City and Maryland State Vital Statistics Offices were used to obtain matches for each strabismus case. The procedure was to choose the next birth certificate number which represented a Negro single birth of the same sex and maternal age categories and who was also born in the same service of the same hospital as the child with strabismus. This control group included those surviving the 28-day neonatal period and replacements for those who died in the neonatal period. Each replacement was the next child with matching characteristics who survived the neonatal period.

The composition of the study group was such that all cases were born on hospital wards, thus assuring that the cases and controls were relatively homogeneous with regard to socioeconomic status.

The great majority of Negro hospital births in Baltimore occur in only four hospitals, thus reducing problems of bias usually inherent in differences among hospitals. Of the 406 cases (and their matched controls) 356, or about 88 per cent, were born in one of the four hospitals listed below. Of the remaining 50 cases, 31 were born in other hospitals in Baltimore and 19 in hospitals within a 50-mile radius of that city. The hospitals of birth for those in the case group are as follows:

| Hospital | No. | % |
|---|---|---|
| University | 55 | 13.5 |
| Johns Hopkins | 86 | 21.2 |
| Baltimore City | 157 | 38.7 |
| Provident | 58 | 14.3 |
| Other hospitals in Baltimore | 31 | 7.6 |
| Maryland hospitals outside of Baltimore | 19 | 4.7 |
| Total | 406 | 100.0 |

For both the strabismus and control groups obstetrical information concerning the pregnancy was abstracted from hospital records by a physician. Steps were taken to guard against the physician knowing whether the birth was of a strabismic or of a control child. An instruction manual was prepared to describe the process of abstraction and to give definitions used in the study. These instructions are identical with those published in a report of a previous study[21] and are, therefore, not repeated here.

## Results

The type of strabismus in the study cases is shown by sex in Table 1. The most frequent type for each sex was esotropia which accounted for some 62 per cent of male and 74 per cent of female cases. The excess of esotropia over exotropia is in agreement with the findings of other investigators.[2,3,11] The sex distributions for esotropia and exotropia were significantly different ($P<0.025$).* This is difficult to evaluate

* The 0.05 level is used for statistical significance. The probability indicated by P is the chance probability of obtaining a difference as rare or rarer than that observed. In this paper the paired t-test was applied for testing differences in birth weight and duration of gestation. The standard chi-square test with continuity correction was used for all other tests except where expected numbers were small, in which case Fisher's exact test was used.

**Table 1—Type of strabismus by sex and eye affected for the case group**

| Eye affected | Esotropia | | | Exotropia | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|
| | male | female | both sexes | male | female | both sexes | male | female | both sexes |
| Left eye | 59 | 79 | 138 | 30 | 27 | 57 | 89 | 106 | 195 |
| Right eye | 54 | 76 | 130 | 39 | 28 | 67 | 93 | 104 | 197 |
| Alternating | 4 | 5 | 9 | 3 | 1 | 4 | 7 | 6 | 13 |
| Not stated | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 |
| Total | 117 | 161 | 278 | 72 | 56 | 128 | 189 | 217 | 406 |

in the absence of information on the sex-specific incidence of these conditions in the general population. However, where deemed pertinent, comparisons of the esotropic and exotropic cases were made for factors studied in this investigation, and no differences were found. These comparisons are noted later.

Table 2 shows the comparison of cases and matched controls by weight group. When each case was compared with its matched control, the number of infants in the case group weighing less than their matched controls was 225, while 179 case infants weighed more, and two weighed the same. On the average the cases weighed 143 grams less than the controls, a difference that was statistically significant ($P<0.001$).

Using a weight criterion of 2,500 grams or less for prematurity, there were 82 prematures among the cases (20.2 per cent) and 49 among the controls (12.1 per cent), again a statistically significant difference ($P<0.005$). It is interesting to note that all of this difference was confined to babies under 2,001 grams. Among the cases, 11.1 per cent had a birth weight less than 2,001 grams compared with only 2.7 per cent among controls. At 1,500 grams or less the corresponding percentages were 3.2 and 0.5.

It is interesting to compare these results for Negro children with unpublished data of Knobloch and Pasamanick[22] dealing with 398 children with strabismus in Columbus, Ohio. Data on the latter group, the great majority of whom were white, were secured from

**Table 2—Distribution of birth weights of case and control groups in grams**

| Case group | Control group | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1,001-1,500 | 1,501-2,000 | 2,001-2,500 | 2,501-3,000 | 3,001-3,500 | 3,501-4,000 | 4,001-4,500 | 4,501-5,000 | over 5,000 | Total |
| 1,001-1,500 | 1 | 2 | 1 | 4 | 5 | | | | | 13 |
| 1,501-2,000 | 1 | 1 | 2 | 12 | 10 | 6 | | | | 32 |
| 2,001-2,500 | | 1 | 1 | 13 | 17 | 4 | 1 | | | 37 |
| 2,501-3,000 | | 2 | 12 | 37 | 35 | 17 | 1 | 1 | 1 | 106 |
| 3,001-3,500 | | 3 | 16 | 38 | 51 | 32 | 4 | 1 | | 145 |
| 3,501-4,000 | | | 3 | 18 | 26 | 10 | | | | 57 |
| 4,001-4,500 | | | 3 | 3 | 5 | 3 | | 1 | | 15 |
| 4,501-5,000 | | | | | | 1 | | | | 1 |
| Total | 2 | 9 | 38 | 125 | 149 | 73 | 6 | 3 | 1 | 406 |

the Children's Hospital Eye Clinic and from the private practice of an ophthalmologist in that city. The age range was from four to 12 years. Each case was matched by a control of the same sex and race, born in the same hospital, with both mothers within the same age group. The investigators found that 13.6 per cent of the study group were premature as compared with 7.8 per cent of the control group. This difference was statistically significant ($P<0.02$). Despite the fact that the Columbus study included both white and Negro children, some of whom were private patients while others were clinic patients, the results are in agreement with those of the present study.

In the present study, information on length of gestation, measured from the first day of the last menstrual period (LMP) to the date of birth, was secured for mothers of the two groups, except for some 10 per cent of each group where it was not available. There were 349 instances where gestational information was available for both cases and their matched controls. (In 57 pairs the information was not available for either the case, its matched control, or both.)

Analysis of the 349 matched pairs with known gestational information revealed a significantly shorter duration of pregnancy among the case group ($P<0.02$). On the average, the cases were born five days earlier than the controls.

Birth weight and duration of gestation were used in combination to define immature infants as those of 2,000 grams or less born before 36 weeks of gestation.* There were significantly more immature infants in the case group, 33 or 8.1 per cent, than in the control group, 4 or 1.0 per cent ($P<0.001$). In contrast, there were 12 infants in the case group and 7 in the control group weighing 2,000 grams or less after pregnancies of 36 weeks or longer.

Since cases and controls were matched according to broad maternal age groups, and since maternal age is associated with pregnancy order, no material difference was found in the proportion of cases which were outcomes of first pregnancies, 20.7 per cent, and of controls, 16.5 per cent. Nevertheless, because of the association of birth weight with pregnancy order, it was thought desirable to rule out directly the possible effect of pregnancy order on the observed difference in birth weight among cases and controls.

Birth weights were compared between the 26 cases and their matched controls which were all outcomes of first pregnancies. The cases, on the average, weighed 86 grams less than their controls, a difference which was not statistically significant. Also, there was no statistically significant difference between these two groups in the number of premature infants (seven cases and five controls). Similar analysis of data for 49 cases and their matched controls, whose multigravidous mothers had exactly the same number of previous pregnancies, showed the cases to weigh, on the average, 171 grams less than their controls, a difference which was not statistically significant. The difference in number of premature infants among the matched multigravidae was also not significant (seven cases and five controls). The drastic reduction in numbers of pairs available when matches were made on the exact number of previous pregnancies may account for the lack of statistical significance. It should be noted that the difference in each instance was in the direction of average lower birth weight for the cases. A further indication that insufficient pairs might be responsible for the lack of significance is shown by a comparison of 275 cases and their matched controls

* This definition was chosen because it was deemed by the authors to be biologically appropriate for Negro births.

**Table 3—Medical complications of pregnancy and/or delivery**

| Complications | Cases | Controls |
|---|---|---|
| Hemorrhage | | |
| Threatened abortion | 0 | 1 |
| Unclassified vaginal hemorrhage | 7 | 9 |
| Premature separation of placenta | 7 | 4 |
| Placenta praevia | 3 | 2 |
| Other ante-partum bleeding | 5 | 6 |
| Unknown hemorrhage | 5 | 1 |
| Preeclampsia | 18 | 24 |
| Eclampsia | 1 | 1 |
| Toxemia | 1 | 5 |
| Hypertension without eclampsia | 28 | 30 |
| Urinary tract infection | 9 | 12 |
| Heart disease | 9 | 2 |
| Diabetes | 2 | 1 |
| Anemia | 62 | 60 |
| Other medical conditions* | 18 | 12 |
| No. with one or more complications | 131 | 123 |
| No. with no complications | 272 | 283 |
| No. with no information | 3 | 0 |
| Total in study | 406 | 406 |

* The most frequent other medical complications were hemoglobin abnormalities and various infections.

whose mothers had one or more previous pregnancies, without matching for the exact number of such pregnancies. The difference, a lower average weight for the cases of 114 grams, was statistically significant ($P<0.02$). Thus, the data strongly suggest that strabismus is associated with low birth weight regardless of gravidity.

Table 3 summarizes the reported medical complications of pregnancy and/or delivery in the mothers of the cases and controls. No meaningful differences were noted. Table 4 presents similar findings with respect to mechanical* complications of delivery. Here also the two groups did not differ substantially.

In order to determine whether differences between case and control groups had been obscured by the inclusion of relatively unimportant complications, it was decided to carry out the following analyses. For each woman all medical complications of pregnancy and delivery were listed. These complications were reviewed and she was assigned to the class of the most important complication according to the following order of priority: (a) hemorrhage; (b) toxemia, preeclampsia, or eclampsia; (c) hypertension; (d) urinary tract infection; and (e) hyperemesis.

Similarly, all mechanical complications of delivery were listed for each woman, and she again was assigned to the class of the most important complication. The order of priority of major mechanical complications was: (a) cephalopelvic disproportion; (b) dystocia; (c) uterine inertia; and (d) prolapsed cord.

In all, 88 mothers of strabismic children had one or more major medical or mechanical complications as compared

**Table 4—Mechanical complications of delivery**

| Complications | Cases | Controls |
|---|---|---|
| Abnormality of bony pelvis | 16 | 14 |
| Abnormality of birth canal | 4 | 1 |
| Dystocia | 3 | 2 |
| Prolapsed cord | 3 | 2 |
| Uterine inertia | 4 | 6 |
| Other mechanical complications* | 10 | 6 |
| No. with one or more complications | 34 | 29 |
| No. with no complications | 372 | 377 |
| No. with no information | 0 | 0 |
| Total in study | 406 | 406 |

* The most frequent other mechanical complication was precipitate labor.

* Mechanical complications include cephalopelvic disproportion, dystocia, prolapsed cord, uterine inertia, and precipitate labor.

**Table 5—Major medical and mechanical complications of pregnancy and delivery**

| Complications | Cases | Controls |
|---|---|---|
| Major medical complications* | 72 | 74 |
| Hemorrhage (early or late) | 25 | 23 |
| Toxemia, preeclampsia, or eclampsia | 18 | 22 |
| Hypertension (without eclampsia) | 21 | 19 |
| Urinary tract infection | 7 | 9 |
| Hyperemesis | 1 | 1 |
| Major mechanical complications† | 22 | 22 |
| Disproportion or contracted pelvis | 16 | 13 |
| Dystocia | 1 | 1 |
| Uterine inertia | 3 | 6 |
| Prolapsed cord | 2 | 2 |
| Major medical or mechanical complications | | |
| Total with one or more complications | 88 | 94 |
| Total with no complications | 315 | 312 |
| Total with no information | 3 | 0 |
| Total in study | 406 | 406 |

* Each patient classified by the single most significant medical complication recorded. Preferential order of classification: (a) hemorrhage; (b) toxemia, preeclampsia, or eclampsia; (c) hypertension; (d) urinary tract infection; and (e) hyperemesis.

† Each patient classified by the single most significant mechanical complication recorded. Preferential order of classification: (a) disproportion or contracted pelvis; (b) dystocia; (c) uterine inertia; and (d) prolapsed cord.

with 94 mothers of control children (Table 5). Little difference was found for major medical or mechanical complications, either specifically or in total, between mothers of the case and control groups.

Information on duration of the second stage of labor was available for 89 per cent of both cases and controls delivered vaginally. The mothers of the cases did not differ significantly from the mothers of the controls in the duration of second stage of labor. Similarly, no statistical significance was found when comparisons of matched pairs were limited to primigravidae (26 matched pairs), multigravidae with one to four previous pregnancies (152 matched pairs), or multigravidae with five or more previous pregnancies (26 matched pairs).

Information on first stage of labor was not available for about 9 per cent of both cases and controls. An additional 3 per cent of both cases and controls were delivered by elective cesarean section. There was no substantial difference between the remaining cases and controls in the distributions of duration of first stage of labor. This finding still held when comparison of matched pairs was limited to primigravidae, to multigravidae with one to four previous pregnancies, and to multigravidae with five or more previous pregnancies.

No material differences were noted between cases and controls with respect to type of presentation at delivery. Similarly, no meaningful differences were found according to type of delivery and operative procedures used, as indicated below.

| Type of Delivery and Operative Procedures Used | Cases | Controls |
|---|---|---|
| Without assistance | 298 | 313 |
| Cesarean section | 13 | 11 |
| Manual rotation | 2 | 1 |
| Low forceps | 72 | 71 |
| Mid forceps | 6 | 2 |
| High forceps | 0 | 0 |
| Forceps, type unspecified | 10 | 6 |
| Manual rotation and forceps | 4 | 2 |
| Unknown | 1 | 0 |
| Total | 406 | 406 |

Table 6 shows that among case group mothers with one or more prior pregnancies, some 27 per cent had at least one previous pregnancy loss (abortion or stillbirth). For mothers of controls, the comparable figure was about 20 per cent yielding a statistically significant difference ($P<0.05$). The table lists five "previous pregnancy" categories. In all but one of these categories, the

per cent of case group mothers with at least one previous pregnancy loss exceeded that of the control group mothers.

It should be noted that the above analysis of the data presented in Table 6 was not based precisely on matched pairs within each "previous pregnancy" category. There were too few matched pairs within each exact "previous pregnancy" category to permit meaningful analysis for each such group. However, the pattern of higher previous pregnancy loss for the case group still obtained in the comparison of the 49 matched pairs of multigravidous mothers who had exactly the same number of previous pregnancies. In total, for these 49 matched pairs, 18 per cent of the mothers in the case group had at least one prior pregnancy loss compared with 10 per cent of the mothers of the controls.

Similar numbers of case and control mothers had been given prenatal care.

Where available, prenatal information on the serologic test for syphilis, Rh factor, hemoglobin, and hematocrit was obtained. For all of these variables only trivial differences were noted between case and control groups. It should be added, however, that Rh data were not reported in 13 per cent, and neither hemoglobin nor hematocrit in 36 per cent, of the records.

Information was also collected on a number of additional factors, including presentation at delivery, induction of labor, blood transfusions, complete or in-

**Table 6—Previous pregnancy loss among multigravidous mothers of cases and controls, by number of previous pregnancies**

| Number of previous pregnancies | Total number of mothers | Previous unsuccessful pregnancies* | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | number | | | | | | per cent† | |
| | | 0 | 1 | 2 | 3 | 4 | unknown | none | one or more |
| One pregnancy | | | | | | | | | |
| case | 60 | 54 | 6 | — | – | – | – | 90.0 | 10.0 |
| control | 86 | 78 | 8 | — | – | – | – | 90.7 | 9.3 |
| Two pregnancies | | | | | | | | | |
| case | 84 | 67 | 15 | 2 | – | – | – | 79.8 | 20.2 |
| control | 81 | 75 | 4 | 2 | – | – | – | 92.6 | 7.4 |
| Three pregnancies | | | | | | | | | |
| case | 51 | 32 | 15 | 3 | 1 | – | – | 62.7 | 37.3 |
| control | 49 | 37 | 11 | 1 | – | – | – | 75.5 | 24.5 |
| Four pregnancies | | | | | | | | | |
| case | 32 | 25 | 3 | 4 | – | – | – | 78.1 | 21.9 |
| control | 38 | 29 | 3 | 6 | – | – | – | 76.3 | 23.7 |
| Five or more pregnancies | | | | | | | | | |
| case | 95 | 56 | 23 | 10 | 4 | 1 | 1 | 59.6 | 40.4 |
| control | 85 | 53 | 23 | 5 | 1 | 2 | 1 | 63.1 | 36.9 |
| Total with one or more previous pregnancies | | | | | | | | | |
| case | 322 | 234 | 62 | 19 | 5 | 1 | 1 | 72.9 | 27.1 |
| control | 339 | 272 | 49 | 14 | 1 | 2 | 1 | 80.5 | 19.5 |

* Includes abortion or stillbirth.
† Based on mothers with known number of previous unsuccessful pregnancies.

**Table 7—Type of infant abnormality in the presence and absence of recorded maternal complications**

| Type of infant abnormality | Cases | | | Controls | | |
|---|---|---|---|---|---|---|
| | maternal complications | | | maternal complications | | |
| | present | absent | total | present | absent | total |
| Respiratory | 4 | 9 | 13 | 2 | 0 | 2 |
| Central nervous system | 0 | 2 | 2 | 0 | 0 | 0 |
| Erythroblastosis fetalis | 0 | 3 | 3 | 0 | 1 | 1 |
| Severe jaundice | 1 | 1 | 2 | 0 | 2 | 2 |
| Congenital anomaly | 1 | 3 | 4 | 1 | 5 | 6 |
| Birth injury | 2 | 1 | 3 | 1 | 0 | 1 |
| Syphilis | 1 | 0 | 1 | 2 | 0 | 2 |
| Neonatal infection | 0 | 5 | 5 | 0 | 1 | 1 |
| Total | 9 | 24 | 33 | 6 | 9 | 15 |

complete placental delivery, placental anomalies, use and dosage of vasopressor, analgesic and anesthetic drugs, and so on. For each of these factors only minor differences were found between case and control groups.

Infant abnormalities described in the hospital records were abstracted for analysis. There were seven groups of major neonatal conditions: (1) respiratory conditions causing anoxia; (2) erythroblastosis fetalis; (3) neurological disorders; (4) positive tests for syphilis; (5) congenital abnormalities; (6) mechanical birth injuries; and (7) neonatal infections. A number of other children were reported to have severe jaundice.

The frequencies of the seven groups of disorders and of severe jaundice in case and control infants are shown in Table 7. Of the infants who later developed strabismus, 33 had abnormal conditions at birth or shortly thereafter compared with 15 of the control infants, a difference which was statistically significant ($P<0.025$). The greatest difference was in the number of respiratory conditions. Most of the reported abnormalities are those usually associated with prematurity. This is evidenced by the fact that 19 of the 33 cases and 7 of the 15 controls with infant abnormalities were premature. Table 7 also shows that the excess of abnormalities reported in children who later developed strabismus was not associated with maternal complications of pregnancy or delivery.

As noted earlier, comparisons were made between the esotropic and exotropic cases for various pertinent factors under study. For both types of strabismus, the case-control comparisons yielded similar results for birth weight, length of gestation, complications of pregnancy, and previous pregnancy loss. Further, no significant differences were found between the esotropic and exotropic cases in the proportion with birth weights under 2,001 grams or in the proportion with infant abnormalities.

## Discussion

Although the ophthalomological and obstetrical data were collected retrospectively from eye clinics and obstetrical clinics, respectively, there is no reason to assume a bias affecting cases or controls selectively in recording such data. The abstracting of the data involved procedures designed to avoid bias.

As concerns the two objectives of this investigation:

(a) Negro strabismic children are generally characterized by low birth weight. In this case the low weight is associated with short pregnancies and the authors believe that these are immature rather than undersized infants. Strabismic infants are not undersized relative to control infants born after the same gestational periods.
(b) The mothers of strabismic children had no more complications of pregnancy and delivery than control mothers. These were women who delivered premature infants without recognizable cause. It is important to note that the case infants were still lighter even when gravidity was controlled, suggesting a direct association of strabismus with birth weight.

Mothers of cases suffered more previous pregnancy loss than control mothers of similar gravidity. Women with a previous history of pregnancy loss have an increased risk of prematurity, particularly prematurity without specific clinical cause. This again points to nonspecific prematurity as the direct association with strabismus.

Lilienfeld and Parkhurst[13] have hypothesized a "continuum of reproductive wastage" which Lilienfeld and Pasamanick[18] have called a "continuum of reproductive casualty." If such a continuum does in fact exist, the data of this study would reflect that continuum to the extent that strabismus is associated with prematurity and infant abnormalities.

## Summary

A total of 406 Negro single births, born since 1950 in Maryland and diagnosed with strabismus before October 1, 1964, were studied retrospectively. A birth certificate control was selected for each case, matched according to race, sex, plurality, hospital of delivery, age of mother, and date of delivery. Children with other diagnosed neurological conditions were excluded from the case group.

The case group was found to have a significantly lower average birth weight and a significantly higher prematurity rate. Significantly shorter durations of pregnancies were noted for mothers of cases than for mothers of controls. Using birth weight and length of gestation in combination to define immature infants (i.e., under 2,001 grams and less than 36 weeks gestation), there were found to be significantly more immature infants among the cases.

Hospital records showed that the pregnancies of mothers of the cases were similar to those of mothers of the controls in the frequency of specific medical and mechanical complications of pregnancy and delivery.

A significantly greater proportion of mothers of the cases had at least one previous pregnancy loss (abortion or stillbirth) when compared to mothers of the controls.

A significantly higher proportion of cases than controls had major abnormalities at birth or shortly thereafter. The difference was confined principally to respiratory conditions causing anoxia.

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