

DEVELOPMENTAL OUTCOME OF CHILDREN BORN FROM EXTRAUTERINE PREGNANCIES

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From 1947 to 1984, 45 advanced ectopic pregnancies were delivered at Freedmen's Hospital and its successor, Howard University Hospital. Four patients of extrauterine pregnancies were contacted to determine their developmental outcome. At the time of the study, their ages ranged from infancy to adulthood. Results are presented of two children who received in-depth interdisciplinary evaluations at the Howard University Child Development Center. The authors reviewed the literature and questioned other authors, who, based on single examinations, reported normal function in children born after extrauterine pregnancies.

In this era of fetal transplants and in vitro fertilization, cerebral and physical growth of infants whose gestation occurred in extrauterine sites is of great importance. Recent reports of extrauterine pregnancy of more than 28 weeks' duration are rare. Only a few articles report on the viability of the fetus and on subsequent survivals.¹⁻³ No articles report on the developmental outcome of these survivors beyond school age. Therefore, the purpose of this paper is to describe the developmental outcome of four persons born at Howard University Hospital as a result of

extrauterine pregnancies, as well as add to the list of physical anomalies previously described by Tan et al.⁴ This article describes the physical and mental growth and development of the survivors and their social, emotional, and academic achievements.

From 1947 to 1984, 45 cases of advanced ectopic pregnancies were encountered in 81,532 deliveries at Freedmen's and Howard University Hospital, an incidence of one in 1,812 deliveries. This incidence is higher than other reports by Beacham and Beacham⁵ of one in 2,081 deliveries; by King,³ of one in 6,600 normal deliveries; by Yahia and Montgomery,⁶ of one in 8,550 viable deliveries; and by Zuspan et al,⁷ of one in 15,000 deliveries. The relatively high incidence at Howard University in the black population compared with that reported in other races (Asians in Singapore and whites in Ware's group) is similar to reports for the total United States and probably reflects the lack of early prenatal supervision in the black population. In the Howard University series, one in 20 cases of advanced ectopic pregnancy resulted in survival of the fetus. Despite a threefold higher risk nationally of death in blacks, the maternal mortality was zero at Howard University. The survival of the fetus depended on gestational age, site of implantation of fetus and placenta, and the maintenance of intact amniotic membranes (Table 1).

MATERIALS AND METHODS

Because of many developmental concerns, case 1 was referred for an interdisciplinary evaluation at the Howard University Child Development Center (HUCDC). The other survivors of extrauterine pregnancy presented in this report were located with the

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TABLE 1. OUTCOME OF FOUR LIVING SURVIVORS OF EXTRAUTERINE PREGNANCY AT HOWARD UNIVERSITY HOSPITAL

Case	Race	Maternal Age (yr)	Birth Order	Gravida	Birth-weight (g)	Gestational Age (weeks)	Sex	Placenta Location	Apgar (1)(5)	Fetal Deformity
1	Black	20	1	1	1619	34 34 Dubowitz	F	Small intestine	(2)(7)	Microcephaly HC 26.5 cm Bilateral talipes valgus Nystagmus Tremors Hyperreflexia Tight heel cords Immature reflexes
2	Black	29	1	2	2386.36	38	M	Small intestine	—	Depressed skull Knee torticollis Asymmetrical upper and lower extremities Asymmetry of skull Cervical muscles Levoscoliosis with pelvic tilt Undescended testes
3	Black	31	3	3	3608	38-40	F	Back of uterus and broad ligament	—	Strabismus Aplastic anemia/ splenectomy
4	Black	32	8	7	4247	40	M	Fallopian tube	—	None known

assistance of the Departments of Pediatrics and Obstetrics and Gynecology and their family physicians. After contact by telephone and letters, the mother of each survivor agreed to participate in the study. Because the mothers of the two older subjects were not willing to reveal the unusual pregnancy to their offspring, they were not evaluated by the HUCDC interdisciplinary team.

The two younger patients and their parents were interviewed by social services, and permission was given for a complete evaluation by the disciplines of psychology, speech pathology, education, pediatrics, and neurology. Special permission was given to obtain medical records from all the facilities where the children received medical care and also to visit the children's schools and homes. All testing was done at the Howard University Child Development Center and at Howard University Hospital.

CASE STUDIES

Case 1

N. S. was born after 32 weeks' gestation to a 20-year-old primiparous black woman who had only one

prenatal visit. She was delivered by laparotomy following the diagnosis of abdominal pregnancy. At birth, the infant had depressed initial Apgar scores of 2 at 1 minute, 7 at 5 minutes, and 9 at 10 minutes. The infant was admitted to the intensive care nursery with severe perinatal asphyxia and required ventilatory support for nine days. Physical examination revealed microcephaly and bilateral talipes valgus deformities. All Torch titers were negative. Computerized tomography of the brain showed calcification, subependymal hemorrhage, and dilated third ventricles with a small fourth ventricle, consistent with aqueductal stenosis (Figure 1). Further neurologic examination revealed bilateral nystagmus, slight tremors on crying, bilateral sustained ankle clonus, and exaggerated deep tendon reflexes. Throughout infancy, the child showed growth developmental delays. At one month, she showed delayed placing and incurvation. At 19 months, the Moro reflex and tonic neck reflexes were still present (Figure 2). In Table 2 delayed development on the standardized test measures and the Vineland Social Maturity Scales is shown. All inventory test measures that required information from the mother reflected her unusual expectation of



Figure 1. Computed tomographic scan of brain of microcephalic newborn delivered by laparotomy because of abdominal pregnancy

normalcy for her child. On objective tests, the child showed developmental delays in all four major categories.

The patient's developmental pattern is that of a spastic, quadriplegic child with cerebral palsy and mental subnormality (Figure 2). At 21 months of age, she was functioning at the 3- to 5-month age level, totally dependent on support services at home and at a rehabilitation facility. Her progress has remained slow.

When N. S. was aged 2 years 1 month, her mother gave birth to a term female infant by normal spontaneous vaginal delivery. The development of N. S. and this sibling will be followed at HUCDC.

Case 2

E. S., a 15-year-old boy at the time of this study, was born to a 29-year-old gravida 1 woman who, until the fifth month, was unaware of her pregnancy. The mother required frequent hospitalization in the last trimester for continuous gastrointestinal discomfort; she delivered by laparotomy a term male infant weighing 2.386 kg. The neonate's physical examination was remarkable for a skull depression in the right parietal area. Deformities of his distal extremities, bilateral talipes equinovarus, and questionable neck torticollis were managed by the orthopedic division throughout infancy. E. S. continues to com-

plain of intermittent back and leg pains, particularly in both knees. He experienced a single febrile seizure during infancy, which did not recur. Reportedly, his early developmental milestones were delayed: he sat unsupported for a short time at 1 year, stood alone unsupported at 2 years, walked alone at 3 years, said single words at 2 years, and spoke in sentences at 4 years.

At age 15 years, E. S. was enrolled in the sixth grade in a local public school. On physical examination, he was at the 25th percentile for weight (51.81 kg) and 10th percentile for height (158.8 cm). He had total body asymmetry, more marked in the head and neck region (Figure 3). His left leg was shorter than the right, and he wore five socks on the left foot because his shoe did not fit that foot. The left hand was smaller than the right. On neurologic testing, E. S. showed mixed laterality, poor right-left discrimination, fine motor delays with overflow movements, and rostral dominance. He had bilateral undescended testes with a Tanner stage IV and a sexual maturity rating of five. Laboratory investigations showed normal levels of testosterone, luteinizing hormone, and follicle-stimulating hormone. Radiologic examination was negative for other skeletal anomalies and his skeletal maturation was consistent with his chronological age.

A psychological test battery was administered that included the Wechsler Intelligence Scale for Children-Revised (WISC-R), Bender Gestalt Test, Wide Range Achievement Test (WRAT), Human Figure Drawing and the Thematic Apperception Test. His WISC-R profile is shown in Figure 4, and the results of the WRAT are outlined in Table 3. Other test results showed visual perceptual motor delays and impaired social-emotional functioning as a result of family dynamics and environmental difficulties. On scholastic achievement testing, E. S. performed from the second grade level to above the fifth grade level. Scores for grade level on the Stanford Achievement Test were as follows: reading 5.07; vocabulary 5.0; comprehension 4.8; combined reading 5.3; mathematic concepts 2.9; computation 2.5; applications 2.9; and spelling 3.9.

Language development was measured, using both formal and informal methods. The Test of Adolescent Language Willeford (TOAL) was administered. Articulation was within normal limits; however, language development was delayed on standardized measures, with weakness related to difficulties with auditory processing and interpreting standard English

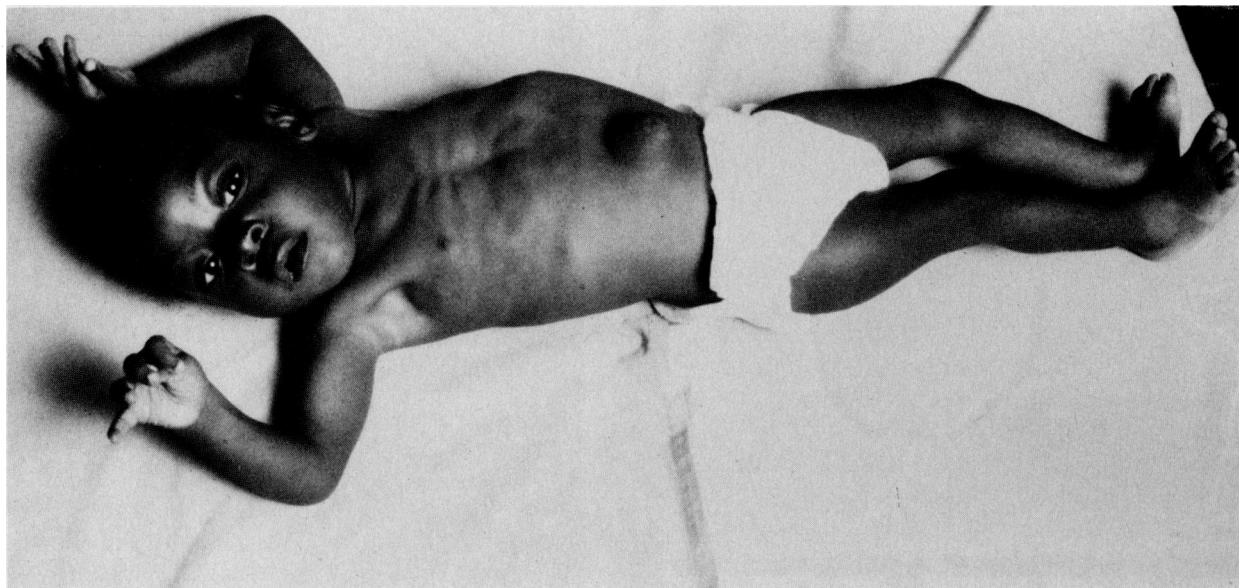


Figure 2. Patient at age 19 months showing an immature startle reflex, spasticity and asymmetrical reflexes, plantar flexion of both feet, and spastic adductor muscles resulting in scissoring of lower extremities

TABLE 2. AGE PERFORMANCE ON TEST MEASURES OF PATIENT IN CASE 1 AT AGE 1½ YEARS

Test	Preterm	Newborn	1 mo	4 mo	6 mo	12 mo	24 mo	36 mo
Dubowitz	×							
Anderson Q-Sort		×				×		
Seashore		×				×	×	
Brazelton	×	×						
Home Baby Scale					×	×		
Bayley MDI					73		57	—
Bayley PDI					71		54	7
Carey					×			

Note: A developmental delay in four major categories: cognitive, speech and language, emotional adaptive, and physical. Developmental pattern of patient is consistent with spastic cerebral palsy and mental subnormality.

forms for listening, reading, writing, and expressing language. These deficits appeared related to learning difficulties, dialectal differences, and the need for greater environmental stimulation.

Case 3

C. G., a 27-year-old woman at the time of this study, was delivered by laparotomy from a utero abdominal pregnancy, which resulted from a tear in the uterus following attempted termination of the pregnancy. The term infant weighed 3,608 g and appeared without physical anomalies at birth. She was found

to have bilateral strabismus. At age 13 months, splenectomy was performed at the National Institutes of Health to treat aplastic anemia of unknown cause. She has been asymptomatic since age 4 years.

Her early motor and language developmental milestones were reportedly achieved within the average range. She was described as an average student in elementary school. However, she required remedial help for mathematics in high school, and she graduated with C and B grades.

Currently, C. G. is reported to be 160 cm tall and to weigh 73 kg, is in good health, and is not receiving any treatment. At the present time, she lives alone and is the mother of a 4-year-old girl.

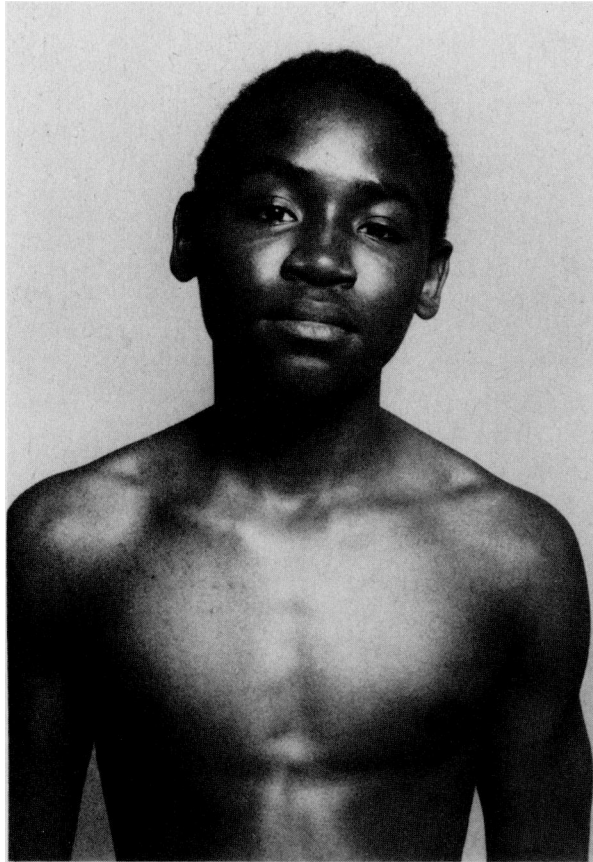


Figure 3. E. S., a 15-year-old boy, with head and neck asymmetry

Case 4

A. C. is a 37-year-old man who was the product of a left tubal pregnancy. He was delivered by laparotomy and salpingotomy and weighed 4,247 g at birth. He had no documented anomalies; his neonatal course was normal. His mother reports that his motor and academic development was slower than his seven siblings. His growth changes were normal. In school, he progressed without repeating any grades, and graduated from high school at age 18. There was no reported past illness of note and no physical deformity; he is currently in good health and is of average stature. A. C. is employed as a civilian in the military, is unmarried, lives at home with his widowed mother, and leads a very active social life.

DISCUSSION

The survival of children from advanced ectopic pregnancy is largely dependent on the site of placental

TABLE 3. RESULTS* OF THE WIDE RANGE ACHIEVEMENT TEST FOR PATIENT IN CASE 2, AGED 15 YEARS

	Grade Rating	Standard Score	Percentile
Reading	7.1	94	34
Spelling	6.7	90	25
Arithmetic	3.99	70	2

* Other test results showed visual perceptual motor delays and impaired social-emotional functioning as a result of family dynamics and environmental difficulties

implantation and the maintenance of an intact amniotic sac. However, the patterns of development are influenced by many factors in the extrauterine and intrauterine environment in addition to hereditary factors. As early as 1904, von Winekel⁸ reported that deformities occurred in one half the fetuses delivered from extrauterine sites. Since that time, several series have reported deformities of fetuses ranging from zero to 100 percent (Table 4).

In the von Winekel series,⁸ 75 percent of the deformities occurred in the head, 50 percent in the lower extremities, and 40 percent in the upper extremities. At Howard University Hospital, 75 percent had physical anomalies and only 50 percent had major deformities. In case 1 and case 2, the placentae were located on the intestinal mesentery, impairing blood supply and compromising fetal nutrition.

Mall,⁹ in 1904, reported that 7 percent of uterine pregnancies contained pathological embryos. However, in his series of 19 tubal pregnancies, 63 percent had normal embryos. By contrast, Brodel found that among 11 specimens of tubal pregnancies, nine contained normal embryos.⁹ The question and answer of normal embryos refers only to the presence of germ cells and is not predictive of normal function.

It is easy to conceptualize that a normal embryo that develops in a constricted environment may have skeletal deformities, eg, asymmetric parietal depression or neck torricollis. However, strabismus, cerebral palsy, and learning disabilities indicate insults prenatally to the cerebral motor cortex.

It has been reported that brain development is normal in survivors of extrauterine pregnancies, however, the samples have been both young in age and small in numbers. This long-term follow-up study not only challenges current research data, but also questions earlier reports of the normal functioning of these same

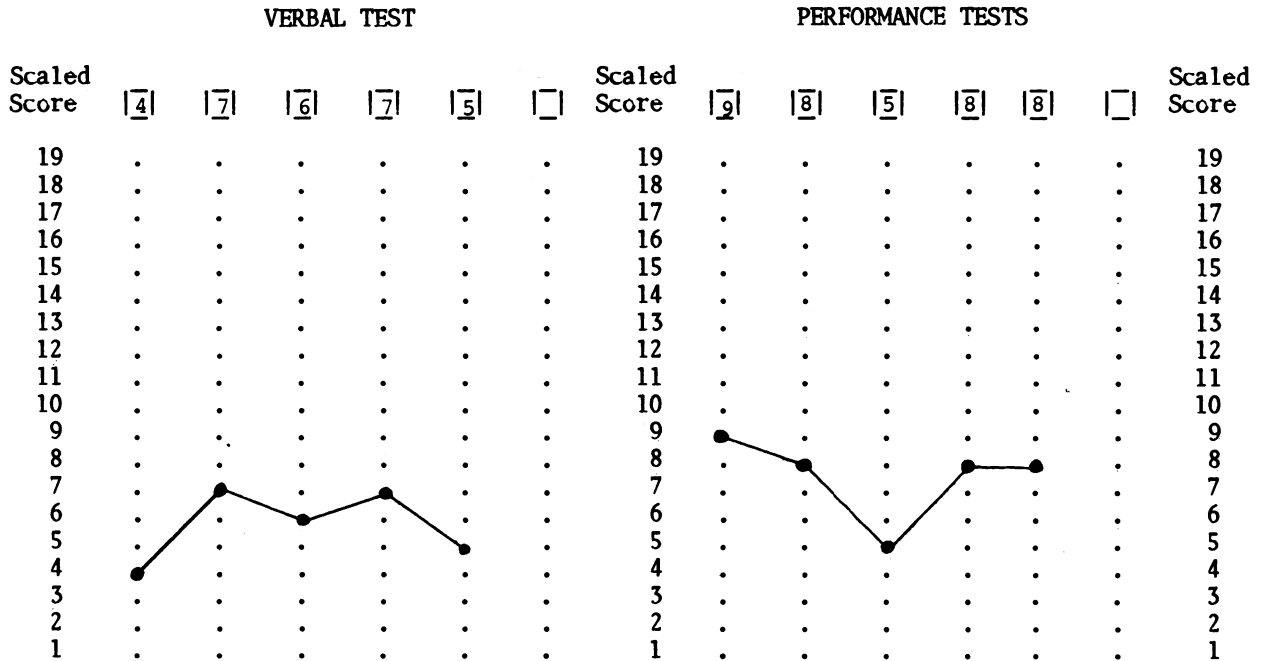


Figure 4. The Wechsler Intelligence Scale for Children-Revised profile of male adolescent with academic difficulties

TABLE 4. DEFORMITIES IN VIABLE FETUSES FROM ADVANCED ECTOPIC PREGNANCIES

Author	No. of Viable Babies	No. of Deformed Babies	Percent	Deformities Noted
Mundell (1933)	49	8	16.3	Talipes equinovarus Webbing of the neck
Hellman and Simon (1935)	64	30	46.6	Torticollis
Suter and Wischer (1948) ¹	31	12	38.7	Facial asymmetry
Ware (1948) ²	5	0	0	Webbing of the elbow
Yahia and Montgomery (1956) ⁶	4	3	75	Webbing of the knee
Beachan et al (1962) ⁵	9	9	100	Talipes calcaneovalgus
Tan (1969) ⁴	5	3	60	Microcephaly, undescended testes, levo scoliosis, umbilical hernia

children. Therefore, each child should have the benefit of a total developmental assessment in all major categories at each stage from birth through adulthood.

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