AUDITORY FUNCTION IN PATIENTS WITH SICKLE CELL ANEMIA

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This study investigated the incidence of peripheral hearing loss in sickle cell anemia and the possibility of central auditory nervous system involvement.

Nine Black subjects with sickle cell disease and nine with normal hemoglobin were administed an auditory test battery. There appeared to be no correlation between number of crisis episodes, duration of symptoms, severity of symptoms, and audiologic manifestations. Acoustic reflex testing suggested the possibility of impaired neural function in the sickle cell group. Whether impaired function was due to peripheral VIIIth nerve or to central brain stem involvement could not be determined. Results of the central auditory test battery suggested the possibility of impaired or reduced central auditory function in subjects with sickle cell anemia.

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CHAPTER I

INTRODUCTION

Sickle cell disease was first noticed in 1910 by James B. Herrick who reported an abnormal blood condition characterized by severe anemia and by sickle-shaped cells. It is now known that sickle cell disease is the result of a hereditary abnormality of the hemoglobin molecule. The role of the hemoglobin molecule is to transport oxygen through the body under many varied conditions; during physical exertion, pregnancy, high altitudes, and low oxygen concentrations. It consists of two chemical substances: protein and heme. The protein portion of the hemoglobin molecule (globin) is determined by genetic inheritance. Globin is composed of two polypeptide chains--two alpha and two beta. In sickle cell disease, a valine residue in the beta chain is substituted for a glutamate residue. This expression of genetic mutation interferes with the hemoglobin's ability to adapt to the intracellular environment. Under oxygen deprivation the valine substitution causes the cell to take on a sickle shape.

The abnormal hemoglobin which produces sickle cell disease is called S. There is evidence that hemoglobin S is a protector against malaria. The gene for hemoglobin S operates under Mendelian law. Thus, an individual can inherit the gene from one or both parents. If the individual inherits one normal gene (Hb A) and one abnormal gene (Hb S), he will have sickle cell trait. If he inherits an abnormal gene (Hb S) from both parents, he will have sickle cell anemia. If both parents have the abnormal gene, there is a statistical possibility that 25 percent of their children will have normal hemoglobin (AA), 25 percent will have sickle cell anemia (SS), and 50 percent will have sickle cell trait (AS).

There are rarely any clinical manifestations in sickle cell trait. Sickling may occur in AS under such conditions as high altitude flying in unpressurized cabins, severe pneumonia, and during anesthesia. Oxygen levels, however, must be greatly reduced before sickling can occur.

Sickle cell anemia is characterized by two main features. First, it is a hemolytic anemia. The abnormal cells are destroyed by the spleen so rapidly that the individual cannot manufacture new cells fast enough to prevent anemia. As a result, chronic hemolytic anemia interspersed with crisis episodes exists despite compensatory marrow hyperplasia. Second, the sickle-shaped cells tend to impede blood flow in the smaller veins and capillaries. The clinical manifestations can be explained by the process following oxygen

deprivation in the cells. Under deoxygenation, hemoglobin S becomes less soluble, resulting in the formation of a semi-solid gel. If the gelling occurs within the cell, the cell becomes distorted or sickle-shaped. Blood viscosity increases. The slower the blood flows, the greater the deoxygenation. This in turn increases sickling of the cells and results in greater stasis. Second, sickling cannot occur when the blood pH is within the alkaline side of the normal range. It requires slight acidosis. Acidosis occurs because oxygen in the blood is utilized by the surrounding tissue during stagnation and acid metabolites cannot be carried away. Sickling follows acidosis, causing further stagnation as the sickle cells block the blood vessels. The tissue then suffers anoxia, and depending upon the duration and amount of the sickling, infarcts or death of the tissue may occur. This process may occur in any part of the body and is accentuated by decreased oxygen, lowered blood pH, and increased body temperatures.

The distortion of the red blood cells produces severe and painful symptoms. Jaundice, chronic leg ulcers, priaprism, and neurological disorders such as blindness, strokes, facial weakness, nystagmus, paralysis, and psychotic episodes are all clinical manifestations of sickle cell anemia. If the heart or lungs are involved, death may occur.

Hemoglobin S occurs in people of African and Mediterranean descent. However, in the United States, it is most prevalent in Black Americans. Sickle cell trait occurs in 6-9 percent of Black Americans; sickle cell anemia is present at birth in approximately 2 percent of Black Americans. The ratio at birth between the heterozygote and the homozygote is 44:1. The ratio increases after the first decade of life because of the high mortality rate of children with sickle cell anemia.

The human hearing mechanism is almost completely dependent on its vascular system for a continued supply of oxygen. The cochlear venous system is characterized by a low oxygen tension (Koide, et al, 1964). Functional changes are noticed almost immediately after blood flow is impaired. Experiments by Perlman (1966) on the venous stasis of the cochlea indicated the chronic changes resulting from occlusion of the cochlea aqueduct and its tributaries include atrophy of the stria and spiral ligament, and degeneration of the organ of Corti, particularly the outer hair cells. Functional changes of the organ of Corti associated with venous stasis were reflected in the cochlear microphonic output (Tsunoo and Perlman, 1964; Perlman, 1966).

Very little is known about sickle cell anemia and its effect on hearing. It is known that hearing loss in patients with sickle cell anemia is characterized by a sensori-neural loss of varying degree. The loss may be of gradual onset as noted by Todd (1973) or of sudden onset as observed in an

unpuslished report by Orchik. It was suggested by Serjeant (1975) that the hearing loss resulted from the chronic sequel of sickling and sludging of red cells in the cochlear venous system without clinically recognized episodes. Perlman and Kimura (1957) noted that occlusion of the cochlear aqueduct initially affected the basal turn of the cochlea, then the apical turn, and finally the entire cochlear duct was affected. The basal turn reflects high frequencies and the apical turn reflects low frequencies, indicating that hearing loss would occur first in the high frequencies, followed by the low frequencies and the complete reduction in hearing acuity at all frequencies. This pattern seems to be similar to that found in Todd's (1973) sickle cell patients.

It is well documented that interruption of blood supply can result in hearing loss (Jerger, 1961; Jaffe, 1967; Schuknecht, 1962). Because of the nature of sickle cell anemia, an increase of hearing loss in these patients might be assumed. However, because sickle cell anemia affects the central nervous system as well, the hearing loss may not be confined solely to the peripheral hearing mechanism. Therefore, this study was designed to provide, in addition to information on the incidence of peripheral hearing loss in sickle cell anemia, data concerning possible central auditory nervous system involvement.

CHAPTER II

REVIEW OF THE LITERATURE

The following chapter is a review of the literature pertinent to this investigation. The areas of discussion include: 1) blood and circulation, 2) sickle cell disease, 3) sickle cell crisis, 4) blood supply of the auditory system, 5) sudden deafness of vascular origin, 6) sickle cell anemia and hearing loss, and 7) audiological assessment of the auditory system.

Blood and Circulation

The blood is a fluid that circulates through the heart and blood vessels carrying nutrients and oxygen to the tissues in the body. It consists of a liquid called plasma, red blood cells, white blood cells, and platelets. Plasma acts as a vehicle for the blood cells and also serves as a medium through which the nutrients and products of metabolism are carried. The white blood cells travel along the walls of the blood vessels acting as phagocytes. The function of the platelets is essentially that of coagulation. The primary role of the red blood cells is to transport oxygen to the tissues of the body.

The role of the red blood cell is extremely important in sickle cell disease. Red blood cells are biconcave discs shaped like a donut with an incomplete hole. They constitute between 44 and 48 percent of the total blood volume. The life of a red blood cell is approximately 120 days. The development of the red cells takes place in the bone marrow cavities of the flat bones such as the ribs, skull, sternum, pelvis, and vertebrae (Maximow and Bloom, 1942). Under certain conditions there is a compensatory increase in the formation of blood cells resulting in the appearance of immature red cells into the blood stream. Any abnormal red blood cells are destroyed in either the liver or the spleen.

The chief component of the red blood cell is hemoglobin, a combination of heme and globin. Its main function is to transport oxygen to the tissue. In the lungs, oxygen diffuses through the vessel walls and combines with the hemoglobin. In the tissues, where the oxygen concentration is lower, the process of diffusion releases the oxygen.

In humans, there is a difference between the hemoglobin of the fetus (Hb F) and that of the adult (Hb A). Globin is composed of two apha chains and two beta chains in a genetically determined sequence. Thirty-six of the amino acids found in the beta chain of Hb F are different from those found in Hb A. Hb F remains in the system for four to five months after birth. At that time it is replaced by adult hemoglobin.

There are many varieties of abnormal hemoglobin. One abnormal variety is Hb S. Hb S is the result of a substitution in the beta chain; a glutamate residue is replaced by a valine residue. Hb S has the effect of changing the structure and solubility of the hemoglobin.

Sickle Cell Disease

The abnormal hemoglobin variety characterized by Hb S is called sickle cell disease. Normal adult hemoglobin is replaced by the abnormal hemoglobin. In 1910, James B. Herrick, a well-known cardiologist, reported an abnormal condition characterized by severe anemia and the appearance of long, sickle-shaped cells. Not until 1927 was the relationship between oxygen level and the shape change of the red cells known. Hahn and Gillespie (1927) demonstrated that the cell changed as the level of oxygen was reduced. In 1930 Scriver and Waugh reported that the number of sickle cells increased as oxygen decreased and carbon dioxide increased during venous stasis. Hahn and Gillespie also found that cells from patients with Hb SS were more susceptible to oxygen deprivation than patients with Hb AS. Thus, in addition to demonstrating the relationship between sickling, oxygen saturation, and stasis, the distinction between Hb SS and Hb AS was made.

The role of the hemoglobin molecule was first demonstrated by Pauling in 1949. According to his investigations, patients with sickle cell anemia are anemic because the hemoglobin

molecule causes structural changes within the red blood cell which twists the cell into an abnormal shape. The spleen then destroys the abnormal cells so rapidly, it is impossible for the bone marrow to manufacture new cells fast enough to prevent anemia. He also noted that the deformed cells were sticky and would clamp together in such a way as to clog the capillaries. This interference with blood flow caused damage to different organs from anoxia.

There are two main forms of sickle cell disease; sickle cell trait and sickle cell anemia. Other forms of sickle cell disease include such double heterozygous hemoglobinopathies such as Hb SC, Hb SD, and S-thalassemia. The clinical features of the double heterozygous hemoglobins are similar to Hb SS. These forms are genetically determined by Mendelian law. If an individual inherits Hb S from each parent, his blood cell will contain no Hb A and he will have sickle cell anemia. An individual inheriting normal hemoglobin from one parent and abnormal Hb S from the other parent will have sickle cell trait.

In sickle cell trait neither hemoglobin has real dominance. The survival time of the cells with the highest concentration of Hb S is reduced so that less than 50 percent of the total circulating Hb is S. The proportion of Hb A and Hb S is usually 60 percent and 40 percent, respectively (Song, 1971).

Under certain conditions sickling can occur, but overt symptoms are not common. A pO_2 of approximately 10mm mercury is required for sickling to occur in sickle cell trait. An individual with sickle cell trait should avoid any situation that can drastically lower oxygen levels in the blood, reduce the pH level[1] of the blood, or cause the blood to suddenly concentrate. High altitude flying in unpressurized cabins, exercise at high altitudes, pregnancy, and heaving drinking can bring on a sickling crisis in these patients. The symptoms are generally less severe if they do occur. Pains in the hips, abdomen, and the joints of the arms and legs have been reported. Sometimes symptoms occur involving the kidneys such as blood in the urine, excessive amounts of urine, and urinary infections. Blood clots may also form causing a variety of complications. A sudden loss of blood from injury or surgery can induce sickling. Problems can also be caused by infections, anesthesia, or congestive heart failure.

There are two clinically observed features of sickle cell anemia. First, it is a hemolytic anemia. Anemia results from an insufficient amount of red blood cells in the body. A hemolytic anemia occurs when some agent destroys these cells. Upon deoxygenation a structural change takes

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[1]The pH scale is used to express the blood in terms of its acidity or alkalinity. The range compatible with health in human is from 6.8 to 7.7. The venous blood due to its elevated carbon dioxide content is somewhat more acidic. If the pH becomes too acidic, life is endangered.

place in the hemoglobin. The beta chains loops back on itself forming a bond between the normal valine on the chain and the abnormal valine. This loop then attaches itself to the alpha chain forming a molecular stack. This stack strings together forming long rods of sickle-shaped cells. The cells are recognized by the spleen as abnormal and are destroyed. The bone marrow responds by producing more red blood cells. The new cells do not have sufficient time to develop normally and upon release into the circulatory system are also destroyed by the spleen. The accelerated activity of the marrow eventually leads to bone marrow hyperplasia. The rate of destruction is increased by any mechanism which produces anoxia or increases the osmolarity of the blood. Therefore, disorders which cause fever or slight changes in the blood pH promote sickling. In order to maintain homeostasis, the body increases cardiac output. Therefore, under normal circumstances, sickling in the venous system rarely exceeds 30 percent. However, even during optimal health, sickling and hemolysis continue and a chronic hemolytic anemia is present.

The second clinical feature of sickle cell anemia is the obstruction of the venous blood vessels with sickle cells. Upon deoxygenation, the Hb S becomes 50 times less soluble. This deoxygenated concentration of Hb S forms a semisolid gel. The resultant distortion of the red cell increases blood viscosity and blocks the vessels. The slower the blood

flow, the greater the deoxygenation. A cycle is set up because the deoxygenation, by increasing the sickling process, itself results in further stagnation. Further, sickling cannot occur when the blood pH is within the alkaline side of the normal range. However, stasis will cause local acidosis. When the stasis occurs, the surrounding tissues utilize the remaining oxygen in the blood vessel. The acid metabolites will not be carried away; thus, local acidosis results. The acidosis causes further sickling which in turn causes further stagnation because it increases the blockage of the vessels.

In summary, the sickling phenomenon which results in chronic anemia and obstruction of the venous capillary vessels can be related to three primary factors. Decreased oxygen levels, lowered pH, and increased body temperature produce the structural changes in the hemoglobin which result in the destruction of the red blood cells and in the thrombotic process in the venous capillary system.

The Sickle Cell Crisis

Sickle cell anemia is characterized by crisis episodes. During a crisis, the rate of sickling and hemolysis is increased. The crisis may last from hours to a few weeks. The period between crises may vary from a few weeks to a few months or even years. Ordinarily, they occur two to four times a year. Usually the attacks are more frequent and severe in

children and become less frequent and severe as the patient grows older. A crisis may be triggered by an infection, any stress on the body, chilling of the body, heavy drinking, vomiting or diarrhea, or excessive sweating.

There are several types of crisis that the sickle cell patient can have. The most common type is the vascular occlusive crisis. This painful attack is caused by the blood vessels becoming clogged and stopping circulation. There is an increase in the number of sickled cells in the blood, a semigel forms, the blood vessels constrict, viscosity increases, and the blood becomes more acidic. This combination of events leads to more sickling which may or may not be accompanied by fever.

A less common type of crisis is the aplastic crisis. The bone marrow stops producing red blood cells and after several days, the patient experiences severe anemia. Blood transfusions must be given immediately to save the life of the patient. This crisis may be caused by a severe viral infection. Usually after seven to ten days, the bone marrow recovers spontaneously.

A third type of crisis is called hyperhemolytic crisis. This crisis is caused by the rapid destruction of the red cells after they leave the marrow. Severe anemia is the result.

The most dangerous crisis is called splenic sequestration crisis. It occurs almost exclusively in childhood. The spleen suddenly becomes enlarged when the sickled cells block

the flow of blood through this organ. The amount of blood to the remainder of the body is reduced drastically, and the patient can go into shock. Death can occur within hours. Once a child has had a splenic sequestration crisis, they tend to occur more frequently. Children under age 5 are particularly susceptible.

The anemia and its clinical manifestations do not generally develop prior to the fourth month of life. Hb F acts as a protector against sickling. The more Hb F in the cell, the less likely the cell will sickle. Approximately four months is required for the adult hemoglobin to replace the Hb F and produce the symptoms seen in Hb SS. Once the anemia does occur, the symptoms can be very severe. The child with sickle cell anemia has only a 50 percent chance of living to the age of twenty. The life expectancy of a patient who reaches the age of twenty is only thirty-nine.

The clinical manifestations of sickle cell anemia vary from patient to patient. The severity of the symptoms depends on the severity of the anemia and the overall health of the patient. Some of the symptoms first seen in childhood include leg ulcers, swelling in the bones, joints and muscles, incomplete growth and development, nausea, vomiting, abdominal pains, enlarged heart and heart murmurs. These patients may also have kidney dysfunction which may cause high blood pressure, priaprism, and blood clots. Enlarged

lymph glands, bleeding in the eyeballs, and shortness of breath related to poor circulation in the lungs are common. After many crisis episodes, the spleen shrinks and the liver becomes enlarged. The liver then overproduces bile and jaundice occurs.

The neurological manifestations also vary. Irritability and headaches are quite common. Facial weakness, nystagmus, dizziness, transitory blindness, droopy eyelids and loss of tactile sense are also seen. Other complications are staggering, twitching of the body, generalized rigidity, and paralysis. Convulsions, strokes, and even psychotic episodes have been reported. Ringing in the ears, hearing loss, and loss of speech can also occur but are reported less often. The neurological symptoms may be accentuated by the occurrence of lipid material in the capillaries and precapillary vessels of the brain which narrows the blood vessels (Linde, 1972; Song, 1971).

Blood Supply of the Auditory System

The human auditory system may be divided into peripheral and central systems. The peripheral system is subdivided into three areas: the outer ear, the middle ear, and the inner ear. The outer ear consists of the pinna which is attached to the side of the head and the external auditory meatus or canal. The pinna contributes very little in terms of the sensitivity of the ear. The external auditory meatus serves

two functions. First, it serves a protective function for the ear drum. Second, it enhances the sensitivity of the ear by acting as a resonator for acoustic stimuli (Newby, 1972).

The middle ear is a six-walled cavity which consists of the tympanic membrane (ear drum), three ossicles (malleus, incus, and stapes), the opening into the Eustachian tube, and two muscles (stapedius and tensor tympani). The tympanic membrane is a thin, concave, translucent structure located on the lateral wall of the middle ear cavity. The malleus, incus, and stapes form a chain across the cavity by attaching to the tympanic membrane on the lateral wall and the oval window on the medial wal. The tympanic membrane and the ossicular chain act like a transformer. They improve the impedance mismatch between the transmission of sound waves from air to the fluid of the inner ear. The oval window communicates with the stapes on one side and the inner ear on the other. The round window is also located on the medial wall below the oval window and connects to the inner ear. The opening into the Eustachian tube is located on the anterior wall. The Eustachian tube runs obliquely and opens on the lower end into the nasopharynx. It provides ventilation for the middle ear so that air pressure within the cavity is equal to air pressure outside the cavity. The tensor tympani arises out of the anterior wall and inserts into the malleus. It is innervated by the trigeminal nerve (Vth). It enhances the

sensitivity of the ear by drawing the malleus forward and increasing the tension of the tympanic membrane. The stapedius muscle arises from the posterior wall and attaches to the neck of the stapes. It is innervated by the facial nerve (VIIth). It serves as a brake to the action of the ossicular chain when the tympanic membrane receives an intense signal. It protects the inner ear from excessive stimulation (Gardner, 1968).

On a functional basis the inner ear may be divided into two cavities: one houses the organs of equilibrium and the other houses the organ of hearing. The part of the inner ear concerned with equilibrium is called the vestibular system. It consists of three semi-circular canals, the saccule, and the utricle. The part of the inner ear concerned with hearing is the cochlea. The inner ear consists of a bony labyrinth which sits within the petrous portion of the temporal bone. Within the bony labyrinth is the membranous labyrinth. The membranous labyrinth is protected from the bony labyrinth by a fluid called perilymph. Inside the membranous labyrinth is another fluid called endolymph. The bony cochlea, a spiral-shaped cavity, is divided into the scala vestibuli and the scala tympani. The cochlear duct or scala media lies between the two cavities separated from the scala vestibuli by Reissner's membrane and from the scala tympani by the basilar membrane. The scala vestibuli and the scala tympani are connected at the apex of the cochlea by the helicotrema. The scala tympani communicates with the middle ear at the

round window and the scala vestibuli communicates with the middle ear at the oval window. The sensory end organ of hearing, the organ of Corti, is situated on the basilar membrane. The organ of Corti contains an inner row and three to five outer rows of hair cells. The hair cells connect with nerve fibers which course into the central core of the cochlea and unite to form the cochlear branch of the VIIIth nerve. Within the internal auditory meatus, the cochlear branch joins the vestibular branch coming from the semi-circular canals, the utricle, and the saccule. The VIIIth nerve is joined by the VIIth nerve and both proceed to nuclei in the brain stem.

The central auditory system begins with the first synapse of the VIIIth nerve at the cochlear nuclei in the upper medulla and pons of the brain stem. At this point approximately one-half of the fibers cross-over to the contralateral side. Because of this bilateral representation of the nerve fibers, interruption of the ascending tracts above the cochlear nuclei will not cause a loss in the threshold acuity. There is a further progression of at least four neurons and decussations from the cochlear nuclei to Heschl's gyrus in the temporal lobe. Heschl's gyrus is the primary reception area in the cortex. Auditory association is recorded in both hemispheres; however, the left hemisphere reflects a dominance for speech and language functions (Zemlin, 1968; Cullen, 1974). At the level of the pons, the ascending fibers of the VIIIth nerve synapse with descending fibers of the VIIth nerve and form a reflex arc. This synapse occurs above the point of

decussation of the VIIth nerve so that fibers from the VIIIth nerve synapse with VIIth nerve fibers that will go to both ears. Therefore, intense stimulation will cause a contraction of the stapedius muscle in both ears (Zemlin, 1968).

The blood supply is very necessary in order to maintain the structure and function of the neurological connections within the cochlea. The oxygen requirements of the central nervous system are such that loss of function can occur following fifteen seconds of oxygen deprivation. Cochlear potentials are also maintained by the oxygen supplied by the blood (Fernandez, 1955). Reduction in cochlear blood flow can produce drastic changes in cochlear potentials and the action potentials of neural fibers.

Investigators agree that the branches of the arterial vessels to the labyrinth enter through the internal auditory meatus. The cochlear artery proper enters the modiolous running spirally to the apex. Side branches are sent to the spiral ganglion and to the inner parts of the basilar membrane where the vessels form arcades.

There is some disagreement about the venous drainage. Siebenmann (1894) described three veins in the human labyrinth: one adjacent to the cochlear aqueduct (inferior cochlear vein), one along the endolymphatic sac, and one through the internal auditory meatus. Nabeya (1923) was unable to locate the vessel in the internal meatus. The veins originate in the region of the spiral prominence. On their downward course,

they receive branches from the spiral ganglion. The veins then empty partly into the internal auditory vein and partly into the inferior cochlear vein.

The inferior cochlear vein accounts for a large part of the venous drainage in humans (Siebenmann, 1894; Nabeya, 1923). The inferior cochlear vein courses in a minute bony channel from the basal turn to the inferior petrosal sinus. Its course is adjacent to but entirely separate from the bony channel of the cochlear aqueduct (Perlman and Kimura, 1957).

The hair cells in the organ of Corti receive their nourishment from the stria vascularis. In turn, the stria vascularis derives its nutrients from the intricate capillary circulation in the basilar membrane.

Sudden Deafness of Vascular Origin

Sudden deafness of unknown origin has been linked to vascular disturbances in the cochlear vessles. The small blood vessels of the cochlea could easily be affected in part or as a whole by thrombosis, vascular hemorrhage or vasopasm (Hallberg, 1956).

Fowler (1950) reviewed the cases of sixty patients who presented a sudden deafness of unknown origin. In all of the patients there appeared to have been neuritis or degeneration of the VIIIth nerve of unknown origin. Fowler suggested that it was probably that the degeneration was caused primarily by anoxia, ischemia, and altered metabolism.

Because sludging (the clumping of blood) is closely associated with vascular spasm, Fowler examined five patients to see if sluding had occurred. He felt it very probable that the degeneration causing the sudden deafness was in part caused by the sludging phenomena. Although sludging occurs in a variety of conditions, it only occasionally causes recognizable symptoms in an organ. For this reason, Fowler suggested that sludging only causes deafness when there is some hereditary, anatomical, or previous disease which "favors sludge sticking" in the vessels of the cochlea.

Hallberg (1956) made a study of 178 cases of sudden deafness of unknown origin. Eight-nine patients had a hearing loss thought to be of vascular origin. In sixty-two of these patients he noted a relationship between hearing loss and coronary occlusion. The ages of the subjects compared well with the age incidence of coronary occlusion. One patient's hearing loss was related to large dosages of alcohol and bromoquinine. Hearing loss related to the postoperative period and general anesthesia was diagnosed in two cases of sudden deafness. The early postoperative period is characterized by a rise in platelet number and platelet adhesiveness which may account for microthrombi in the inner ear (Jaffe, 1967).

The record of 143 patients with sudden deafness were reviewed by Jaffe (1967). A vascular cause was diagnosed

as the probably cause in nine patients. Of these nine patients, a vascular occlusion was suspected in three patients with hypertension two with arteriosclerotic heart disease, and one with diabetes. Two patients had a hypercoagulation disorder and one had polycythemia. The hyperviscosity related to the number of red cells in polycythemia may account for sludging, reduction in blood flow, and blood clots in the inner ear.

Two patients with sudden hearing loss were examined to see if a relationship could be exhibited between their hearing loss and hypercoagulation. Both patients demonstrated hypercoagulation.

Four patients whose hearing loss occurred postpartum and one whose hearing loss developed in the eighth month of pregnancy were reported. Shortly after giving birth, there is an increase in platelet number and adhesiveness, suggesting that microthrombi may be formed in the inner ear and lead to sudden deafness.

Following surgery unrelated to the inner ear, four patients demonstrated a hearing loss of sudden onset. There is a rise in platelet number and adhesiveness in the early postoperative period.

Viral infections causing sudden deafness can also be related to blood flow in the capillaries. Viral particles tend to attach to the red blood cells and cause a clumping of the cells. The virus can also cause edema of the vessel walls. There is a strong correlation between viral infections and hypercoagulation.

Jaffe concluded that vascular obstruction is a common cause of sudden deafness. Obstruction can be produced by arteriosclerosis, hypercoagulation, hyperviscosity, increases in platelet number and adhesiveness, and viral infections.

Jerger et al (1961) looked at twelve patients with a unilateral hearing loss of sudden onset to determine the site of lesion. The following tests were administered: Bekesy audiometry, speech discrimination, SISI, alternate and simultaneous binaural balancing, and vestibular examinations. Four of the twelve patients showed an overall pattern indicative of cochlear lesion. SISI scores were high, Bekesy audiograms were Type II, some recruitment was noted, and PB discrimination was measurable. The other eight patients showed an overall pattern suggestive of retrocochlear lesion. SISI scores were low, Bekesy audiograms were Type III, minimal recruitment was noted, and PB discrimination was not measurable.

Jerger, thus, suggested that there are two separate and distinct sites of lesion, one cochlear, the other neural in sudden deafness of vascular origin.

Histological studies were made by Schuknecht et al (1962) on the temporal bones of four patients who had experienced sudden deafness. Two of the patients had a total hearing loss; the other two patients had severe losses. They noted that the loss of hair cells was most severe at the basal end of the cochlea. Four stages of severity were identified:

1. partial loss of hair cells with retention of supporting structures; 2. loss of hair cells and a flattening of supporting structures; 3. shrinking and clumping together of the organ of Corti; 4. complete loss of the organ of Corti. The stria vascularis was severely atrophied in only one ear. The location and degree of spiral ganglion degeneration was proportional to the damage in the supporting structures of the organ of Corti.

The research on hearing loss of sudden onset indicated the relationship between vascular disturbances and hearing loss. The hearing loss was the result of ischemia and anoxia. The research further indicated that the hearing loss may not be confined to the cochlea, but may also affect the neural connections. The histological evidence of structural changes within the labyrinth following sudden deafness were also consistent with ischemia and anoxia.

Sickle Cell Anemia and Hearing Loss

Morgenstein and Manace (1969) studied the temporal bone of a ten year old patient who died as a result of complications related to chronic sickle cell disease. At the age of nine, the patient was treated for bilateral serous otitis media. Audiometry revealed a mild bilateral sensori-neural hearing loss. Histopathology revealed hyperplasia and congestion of the marrow with sickle cells. Both outer and inner hair cells throughout the organ of Corti were either absent or abnormal,

consistent with hypoxia. The supporting structures were not affected. The stria vessels were engorged with sickled cells. Degeneration of the stria vascularis consistent with ischemia was noted. Morgenstein and Manace concluded that repeated crisis and/or chronic hypoxia in the inner ear were the cause of the structural changes noted.

Todd, Serjeant, and Larson (1973) investigated the incidence of hearing loss in eighty-three Jamaican patients with Hb SS ranging in age from twelve to thirty-nine years. Eighteen patients or fourteen percent of the ears presented a hearing loss of at least 25 dB. No ear difference or sex difference was demonstrated. Hearing loss was demonstrated in fifteen ears at 8000 Hz, eight ears at 4000 Hz, three ears at 2000 Hz, and seven ears at 500 Hz. Because of the ambient noise levels in the testing rooms, 250 Hz was not tested. Hearing loss was most common in the oldest group (30-39 years) affecting twenty-seven percent of the ears. The next group most affected ranged from ten to nineteen years. Fifteen percent of the ears in this group were affected. In the patients who had noticed a hearing loss, the onset was gradual. Dizziness and tinnitus were not reported as symptoms. Todd suggested that a low level continuous thrombotic process without clinically recognized episodes was responsible for the hearing loss in patients with sickle cell anemia.

Sergeant, Norman, and Todd (1975) measured the diameter of the internal auditory meatus to investigate the probability of compression of the VIIIth nerve as the cause of hearing loss in sickle cell anemia patients. No correlation was found between the two. Therefore, Sergeant concluded that hearing loss was probably the consequence of sickling and sludging of the venous system of the cochlea. He felt it unlikely that the hearing loss seen in the Jamaican patients could be the result of a single or repeated major infarct.

Orchik and Dunn (1976) have reported a case of sudden deafness apparently related to sickle cell crisis. The patient, a seventeen year old male, complained of hearing loss during hospitalization for a sickle crisis. Initial audiograms indicated complete bilateral deafness. Subsequent tests indicated some recovery in one ear only, to a pure tone average of approximately 63 dB. This sensorinueral hearing loss, although moderate in degree, was characterized by absent stapedial reflexes and extremely poor speech discrimination. Both findings are somewhat unusual for a pure cochlear loss.

Audiological Assessment of the Auditory System

Auditory disorders are generally classified according to the portion or portions of the auditory system involved. Peripheral disorders fall into three categories: conductive, sensorineural, and mixed. A dysfunction of the outer or

middle ear in the presence of a normal inner ear is called a conductive disorder. The patient with a conductive impairment speaks in a soft voice, hears better in noisy situations that a person with a normal hearing, tolerates louder sounds than a person with normal hearing, and may have tinnitus or ringing of the ears. He may describe his tinnitus as being low-pitched. The audiometric pattern is generally flat with thresholds being about the same at all frequencies. If there is a greater loss, it will be seen in the lower frequencies. When speech is presented at a comfortable level, discrimination ability is unimpaired. Conductive disorders of the outer ear are often caused by excessive wax in the ear canal, congenital atresia of the ear canal or agenesis of the pinna, neoplasms or tumors, or external otitis-an infection or inflammation of the external ear. Middle ear disorders are commonly caused by otitis media-an inflammation or infection of the middle ear, perforation of the tympanic membrane, cholesteatoma-a cystic mass which grows from a marginal perforation of the tympanic membrane, or otosclerosis-a hardening of the bone between the middle and inner ear resulting in the fixation of the footplate of the stapes to the oval window (Newby, 1972).

Sensorineural disorders are due to some pathology in the inner ear or along the nerve pathway to the brain stem.

The outer and middle ear are normal. Sensorineural disorders are classified as cochlear or retrocochlear in origin. Disorders of cochlear origin result from damage to the organ of Corti. Retrocochlear disorders result from damage to the VIIth nerve. Patients with sensorineural disorders speak very loudly, hear poorly in noisy surroundings, and demonstrate diplacusis-a form of pitch distortion in which the same frequency sounds different in each ear. He may experience tinnitus which is generally high-pitched. The audiometric pattern shows poorer hearing in the high frequencies. When speech is presented at a comfortable loudness level, discrimination is poor. Sensorineural disorders are characterized by auditory adaptation, a reduction in responsiveness to a sustained tone. Mild to moderate adaptation is seen in cochlear disorders. Extreme adaptation is seen in retrocochlear disorders. Patients with cochlear lesions demonstrate two features not seen in patients with retrocochlear lesions. First, they demonstrate a keen sensitivity to small changes in the intensity of a tone. Second, they demonstrate a phenomena called recruitment. Recruitment refers to the rapid increase in the sensation of loudness once threshold has been reached. The causes of sensorineural disorders can be congenital or acquired through the aging process, disease, vascular disturbances, the toxic effects of drugs, or through mechanical injury (Newby, 1972).

Mixed disorders demonstrate some degree of conductive and sensorineural hearing loss. A loss is seen by bone conduction (Bone conduction measures inner ear sensitivity.) but a greater loss is seen by air conduction. The etiology can be congenital, mechanical injury, acoustic trauma (eg., hearing loss resulting from an explosion), or any combination of factors which can affect the entire auditory system (Newby, 1972).

Central disorders are caused by any interference within the auditory pathway from the brain stem to and including the cerebral cortex. Central disorders may not involve a sensitivity loss. Central impairment does involve the integrative and associative auditory processes. The patient has difficulty recognizing, integrating, and interpreting sound. Any audiologic symptoms usually will be seen in the ear contralateral to the site of the lesion. Central disorders may be caused by a tumor, an abcess, or prenatal or postnatal trauma (Gardner, 1968).

The audiometric assessment of the auditory system is evaluated through a battery of tests which test either the peripheral or central auditory systems.

Peripheral Auditory Battery

The peripheral battery can include impedance audiometry, pure-tone audiometry, and speech audiometry.

By assessing the function of the middle ear system, impedance audiometry becomes a tool for differentiating conductive and sensorineural hearing disorders. In addition, it is used to determine if a sensorineural hearing loss is due to cochlear or retrocochlear lesions. Impedance is the opposition offered by a system to the flow of energy. The basic components of impedance are mass, stiffness, and friction. The components of the middle ear system accounting for mass are the tympanic membrane and the ossicular chain. Stiffness is accounted for by the flexibility of the tympanic membrane and the ossicular chain. Stiffness and mass are frequency dependent. For high frequencies, mass predominates; for low frequencies, stiffness predominates. Fricition from the movement of the tympanic membrane and ossicular chain results in a dissipation of energy. The conduction of sound waves depends upon how well the system can vibrate (Jerger, 1973).

Clinically, three areas are assessed: tympanometry, static compliance, and acoustic reflex. Tympanometry examines the compliance of the middle ear system by assessing how it changes as air pressure is varied in the external ear. Static compliance examines the compliance or mobility of the tympanic membrane and estimates the volume of air in the middle ear. The acoustic reflex assesses the compliance of the middle ear by determining whether or not a reflex of the stapedius muscle has occurred. Reflex decay is also assessed when a

reflex is observed. Reflex decay is considered a sign of adaptation. The outcome of impedance audiometry leads to the first diagnostic decision of conductive versus sensorineural origin.

In addition, the acoustic reflex measure can help to determine if the sensorineural loss is cochlear or retrocochlear (Jerger, 1973). The absence of the acoustic reflex with a hearing loss of 65 dB or less is a sign of abnormal adaptation (Olsen, Noffsinger, and Kurdziel, 1975). Abnormal adaptation is seen in patients with retrocochlear lesions. Further, decay of the stapedius reflex response would be an additional sign of abnormal adaptation (Anderson, Barr, and Wedenburg, 1969). On the other hand, patients with cochlear lesions tend to show reflexes at reduced sensation levels. Therefore, in patients with cochlear lesions, acoustic reflexes would not be absent unless the hearing loss was severe.

Pure-tone audiometry gives an estimate of the practical consequences of the individual's hearing impairment. It is a quantitative measure of hearing thresholds and identifies certain configurational patterns. Two procedures are used to determine the patient's relative threshold for audiometric frequencies: air conduction testing and bone conduction testing. Bone conduction testing, by assessing the sensitivity of the inner ear, determines whether the loss detected in air conduction testing is conductive, sensorineural, or mixed (Newby, 1972).

Speech audiometry is a tool for assessing the everyday communicative efficiency of an individual. There are two basic aspects of speech audiometry: speech reception testing and speech discrimination. Speech reception is a measure of the threshold sensitivity for speech. It gives an estimate of the degree of hearing impairment by using spondees (two syllable words with equal stress on each syllable). Speech discrimination is a measure of accuracy of speech perception. It assesses the ability to make fine distinctions among similar speech sounds at suprathreshold levels (Jerger, 1973). The deterioration in speech discrimination ability at high intensity levels has been reported as indicating VIIIth nerve involvement (Jerger and Jerger, 1971). The clinical procedure for examining this deterioration is called the PB function and involves an investigation of speech discrimination as a function of increasing intensity.

Tone decay testing is a means of differentiating peripheral disorders into cochlear and retrocochlear. This site of lesion test is an assessment of adaptation. Adaptation in abnormal amounts is observed in retrocochlear lesions. Tone decay tests assess the individual's ability to maintain audibility of a sustained tone at suprathreshold levels.

Central Auditory Battery

A special battery of tests are required to assess central auditory function. A patient with a central auditory lesion

will demonstrate little or no difficulty via pure-tone audiometry (Jerger, 1973). Because of bilateral representation of fibers in the higher auditory pathways and the apparent inability of the peripheral test measures to identify disorders in the central auditory system, the central auditory battery most often involves some altered speech task. As Jerger (1960) states, the higher in the auditory pathway the lesion is located, the more subtle the tasks must be. Therefore, the central auditory battery has included filtered speech, competing messages, and separation tasks designed to reduce the redundancy of the speech message.

One method used to assess central auditory function is time compressed speech. In time compressed speech the message is delivered in less time than is normally required. Sections of the message are deleted at random intervals so that no relevant spectral information is eliminated. Time compressed speech is reported in terms of the percentage of the message deleted. Regardless of the time compression ratio, normal listeners demonstrate improved discrimination as sensation level increases. In addition, at compression ratios up to 60 percent they demonstrate only a slight decrease in discrimination ability. Beyond this point a dramatic reduction in discrimination ability can be observed suggesting that clinical procedures should not employ time compression ratios in excess of 60 percent (Beasley, Schwimmer, and Rintelmann, 1972). Among patients with confirmed temporal lobe lesions,

discrimination ability has been shown to be reduced when time compressed speech is presented to the ear contralateral to the lesion (Calearo and Lazzaroni, 1957; Kurdziel and Noffsinger, 1973).

Summary

The blood and circulation have been reviewed as has the hemolytic disorder of sickle cell anemia. The relationship between vascular disorders and hearing loss appears well established. Cochlear as well as retrocochlear pathologies have been suggested. Audiometric assessment of the peripheral auditory and central auditory systems was described.

Sickle cell anemia as a vascular disorder might be expected to produce a hearing loss as one of its clinical symptoms. Research, however, as to the incidence of hearing loss in sickle cell anemia as well as to site of lesion in the auditory system is surprisingly limited. The only controlled investigation was limited to pure tone acuity and demonstrated a surprisingly small incidence considering the devastation that sickle cell disease can inflict upon other systems. Individual case studies have shown the most dramatic manifestations in terms of degree of hearing loss, but site of lesion data are incomplete.

Auditory disorders do not always present a reduction in peripheral acuity. In fact, some retrocochlear lesions may demonstrate no peripheral hearing loss (Jerger, 1973).

Sickle cell anemia, by its very nature, suggests the potential for involvement throughout the auditory system. The present investigation was proposed to examine, as thoroughly as possible, auditory function in patients with sickle cell anemia. Tests of peripheral acuity were augmented wherever possible by special auditory tests employed clinically to assess cochlear and retrocochlear lesions. In doing so, the following questions were examined relative to sickle cell anemia and auditory function:

1. Is the problem of hearing loss in sickle cell anemia of greater magnitude than previously described?
2. What site of lesion in the auditory system is suggested on the basis of the special test battery?
3. Do patients with sickle cell anemia demonstrate auditory disorders that are not accompanied by an apparent loss in peripheral acuity?

CHAPTER III

EXPERIMENTAL PROCEDURES

Information concerning subjects, instrumentation, test stimuli, and experimental procedures utilized are presented in this chapter.

Subjects

Eighteen Black subjects, nine with sickle cell disease and nine with normal hemoglobin, comprised the sample for this investigation. Of the nine subjects with sickle cell disease, eight had Hb SS and one had Hb SC. The subjects with sickle cell disease were matched in terms of age and sex to the control group.

The sickle cell subjects reported crisis episodes numbering from one a year to twenty-six a year. The severity ranged from mild to severe. The duration of symptoms varied from a few minutes to two weeks. The data regarding the frequency, duration, and number of episodes is presented in Table I. Subjects with many crisis episodes also had longer and more severe attacks. Those subjects with only two to six episodes a year reported mild to moderate symptoms lasting four days or less.

TABLE I

COMPARISON OF SICKLE CELL SUBJECTS

Subject	Age in Years	Number of Crisis per year	Duration of Crisis Episode	Severity of Crisis Episode
A	6.0	2	1 hour	mild
B	7.5	2	3 days	moderate
C	9.9	3	2-3 days	moderate
D	14.5	10	6-7 days	severe
E	15.1	26	4 days	severe
F	16.9	3	2 days	moderate-severe
G	20.8	6	several hours	moderate
H	26.7	3	1 hour	mild
I	28.0	2	3 days-2 weeks	mild-moderate

Test Environment and Instrumentation

The test were conducted in a double-walled Industrial Acoustics Corporation (IAC) test chamber. Instrumentation included a two-channel clinical audiometer with associated tape deck and an electro-acoustic impedance bridge.

Calibration of all test equipment was checked on a daily basis.

Test Stimuli

Stimuli used during the investigation consisted of pure-tone signals ranging from 500 Hz to 8000 Hz as well as speech signals. The speech signals used consisted of spondee words, taped recordings of the Word Intelligibility by Picture Identification Test (WIPI), and taped recordings of the Northwestern University Auditory Test #6 (NU 6) at 0 percent and 60 percent time compression.

Experimental Procedures

Each subject was administered an auditory test battery which included, where applicable, each of the following:

1. Impedance audiometry which consisted of tympanometry, static compliance, acoustic reflex assessment, and reflex decay testing.
2. Pure-tone audiograms for the octave frequencies from 500 to 8000 Hz.
3. Speech reception threshold.

4. Speech discrimination test using either the WIPI or NU 6, depending upon the subject's age.
5. Time compressed speech discrimination test at 60 percent time compression using either the WIPI or NU 6, depending upon the age of the subject.

CHAPTER IV

RESULTS AND DISCUSSION

An experimental group of nine subjects with sickle cell anemia were compared to a control group of nine subjects with normal hemoglobin on a variety of auditory tests. In this chapter the results are presented for the comparison of the experimental and control groups. The groups were compared inferentially and descriptively. Inferential analysis consisted of an analysis of variance for repeated measures. The results are discussed in terms of their significance and implications for future research.

Pure-Tone Sensitivity

Pure-tone sensitivity was assessed at 500 Hz through 8000 Hz. A comparison of the mean pure tone thresholds is shown in Figure Ia and Ib. The mean pure tone thresholds in sound pressure level are reported in Table II.

As indicated, both groups showed normal pure-tone sensitivity bilaterally at all test frequencies. In the left ear, the control subjects demonstrated better thresholds than the sickle cell group at all frequencies. In the right ear, the sickle cell population had better hearing at 2000 Hz and 8000 Hz. However, the differences were not significant (df=1, p=0.36).

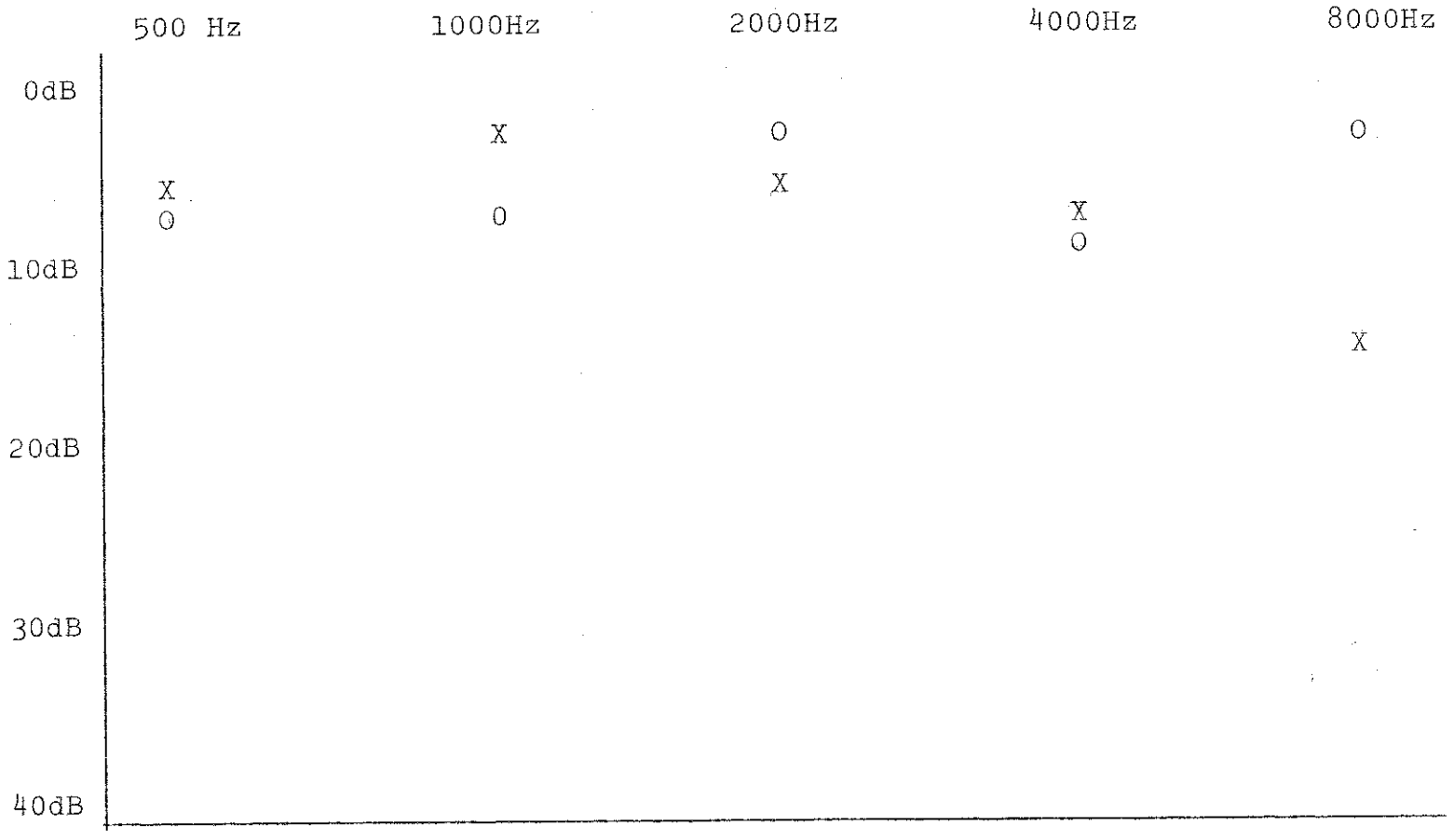

Figure 1a. Mean Pure tone thresholds in the right ear for the sickle cell group and the control groups in dB HL.

0 - Sickle Cell Group

X - Control Group

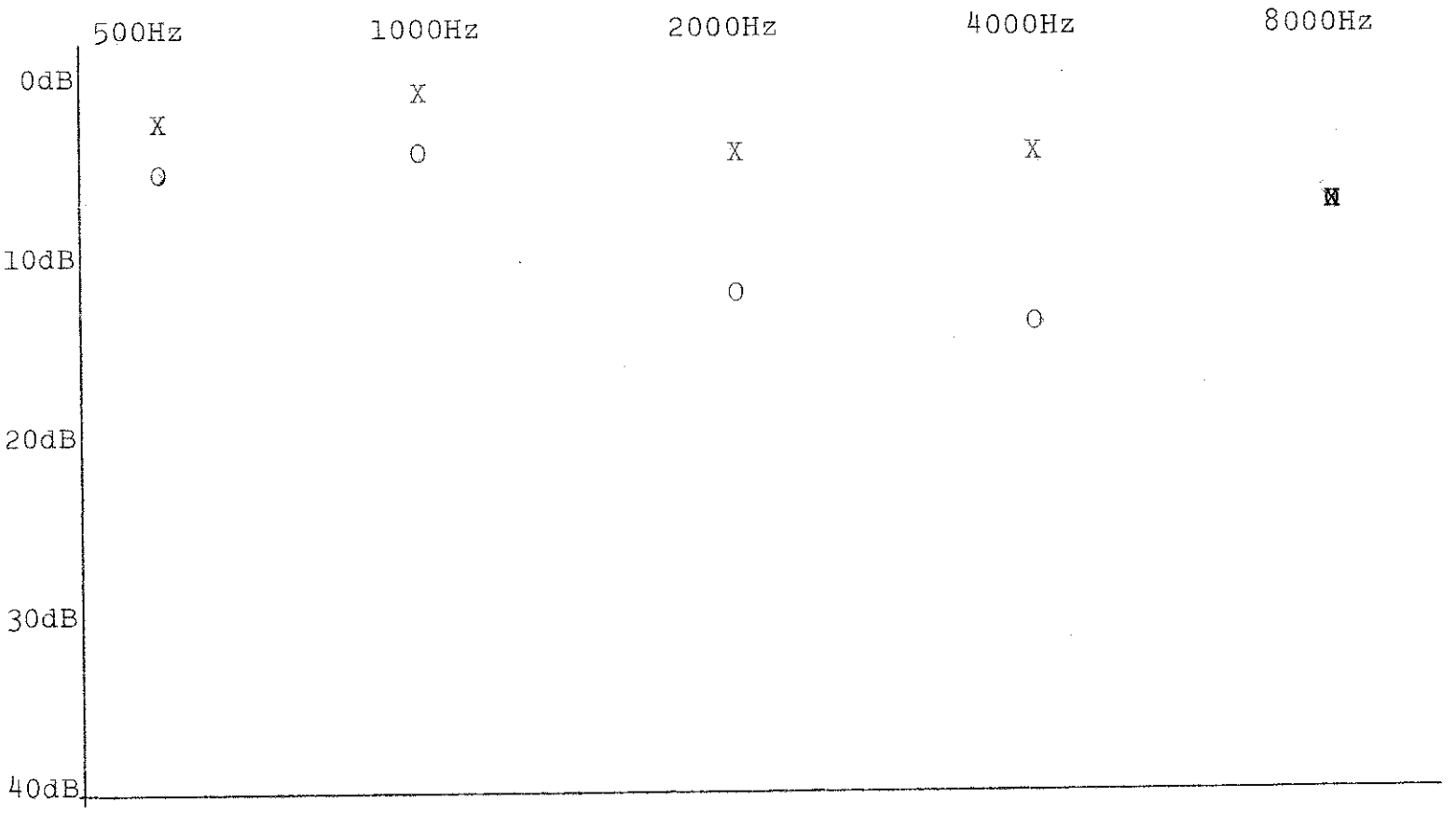

Figure 1b. Mean pure tone thresholds in the left ear for the sickle cell group and the control groups in dB HL.

O - Sickle Cell Group

X - Control Group

TABLE II

MEAN PURE THRESHOLDS IN dB SPL

	Sickle Cell			Control		
	Rt.	Lt.	Avg.	Rt.	Lt.	Avg.
500 Hz	17	16	16.5	16	13	14.5
1000 Hz	14	11	12.5	10	9	9.5
2000 Hz	13	21	17	15	14	14.5
4000 Hz	17	22	19.5	15	13	14
8000	19	22	20.5	29	22	25.5

Speech Reception Thresholds

Table III illustrates the mean speech reception thresholds. The range of thresholds for normal hearing subjects is 20-45 dB SPL. The sickle cell subjects and the control subjects had speech reception thresholds within the normal range. The control subject's thresholds were better by 5.1 dB in the left ear. In the right ear, the sickle cell subject's thresholds were better by 0.1 dB SPL.

Speech Discrimination

Speech discrimination scores for undistorted speech are shown in Table IV. Normal speech discrimination ability using the NU 6 ranges from 88-100 percent. The discrimination scores were slightly better for the control group. However, both groups scored within the normal range.

Acoustic Reflex Thresholds and Reflex Decay

Reported in Table V is a comparision of acoustic reflex thresholds. The acoustic reflex threshold occurs in the normal ear between 70 dB and 100 dB hearing level. Acoustic reflex thresholds for the sickle cell group occurred within normal limits at 500 Hz and 1000 Hz. At 2000 Hz and 4000 Hz the thresholds in the left ear were elevated, averaging 101.6 and 103.8 respectively. For the control

TABLE III

MEAN SPEECH RECEPTION THRESHOLD IN dB SPL

	Sickle Cell Group	Control Group
Rt. Ear	26	27
Lt. Ear	30	25
Mean	28	26

TABLE IV

MEAN UNDISTORTED SPEECH DISCRIMINATION SCORES

	Sickle Cell Group	Control Group
Rt. Ear	90	94
Lt. Ear	93	96
Mean	91.5	95

TABLE V

MEAN ACOUSTIC REFLEX THRESHOLDS IN dB HL

	Sickle Cell Group			Control Group		
	RT Ear	LT Ear	Mean	RT Ear	LT Ear	Mean
500Hz	93.3	93.3	93.3	90.5	91.1	90.8
1000Hz	92.2	94.4	93.3	88.3	87.7	88.0
2000Hz	98.3	101.6	99.9	95.0	91.6	93.3
4000Hz	100.5	103.8	102.1	98.8	100.0	99.4

group the mean acoustic reflex thresholds occurred within the normal range at all test frequencies.

Reflex threshold levels were higher at all frequencies for the sickle cell group (df=1, p=0.16). Threshold differences tended to increase with increasing frequency through 2000 Hz. Four subjects in the sickle cell group demonstrated absent reflexes at one or more frequencies.

Reflex decay was observed in one experimental subject at 1000 Hz. This subject will be treated separately in a later discussion.

Time Compressed Speech Discrimination

The mean discrimination scores for time compressed speech are given in TableVI. In addition, the individual ear scores for the sickle cell group are reported in Table VII.

Both groups demonstrated a decline in performance at sixty percent time compression (df=1, p=0.00). However, the time compressed speech discrimination scores for the sickle cell group were on the average about five percent poorer in the left ear and fifteen percent poorer in the right ear as compared to those of the control group (df=1, p=0.10).

TABLE VI

A COMPARISON OF MEAN DISCRIMINATION SCORES AT 0% and 60% TC

	Sickle Cell Group		Control Group	
	0%	60%	0%	60%
RT Ear	87.4	58.8	93.1	73.7
LT Ear	93.1	77.7	96.0	82.2
MEAN	90.2	68.2	94.5	77.9

TABLE VII

DISCRIMINATION SCORES AT 60% TC

	Sickle Cell Group			Control Group		
Subjects	RT Ear	LT Ear	Mean	RT Ear	LT Ear	Mean
A	36	40	38	56	76	66
B	56	80	68	72	80	76
C	44	80	62	84	68	76
D	80	92	86	56	88	72
E	72	80	76	84	88	86
F	60	92	76	88	92	90
G	64	80	72	76	84	80

DISCUSSION

The difficulties in making generalizations from a small sample are recognized. However, it is felt that several of the findings are worthy of further discussion.

Measures of Peripheral Sensitivity

The two measures of peripheral sensitivity in the investigation were pure tone sensitivity and speech reception threshold. The results indicated no significant differences between groups. This would suggest, at least in terms of the present population, that peripheral acuity had not been significantly affected by sickle cell anemia. This finding is in contrast to the report by Todd et al (1973) in which a significant number of the sickle cell subjects demonstrated thresholds outside normal limits. However, Todd's subjects were generally older than the subjects in the present study. In addition, the reduction in hearing sensitivity he found was predominantly at 4000 Hz and 8000 Hz. Further, the magnitude of the hearing loss was not reported by Todd, but rather the number of thresholds greater than 25dB (ANSI, 1969).

Speech Discrimination Scores

Clinical speech discrimination tests, unlike the threshold measurements employed in this study, examine the ability to make fine distinctions among sounds. The test is commonly administered in quiet at a comfortable listening level. As such, it primarily assesses peripheral integrity.

The sickle cell subjects in the present study demonstrated normal discrimination ability for undistorted speech on the NU 6 and the WIPI. This would imply that sickle cell anemia had no affect on performance using an undistorted speech discrimination task.

Acoustic Reflex Thresholds

Acoustic reflex measurement can provide information concerning both central and peripheral auditory function. Because of the reflex arc, intense auditory stimulation will cause a contraction of the stapedius muscle in both ears. Thus in certain pathologies the acoustic reflex can give information relative to the central (brain stem) and peripheral auditory systems.

Although the acoustic reflex thresholds occurred at normal hearing levels in the sickle cell group at 500 Hz and 1000 Hz, the levels were elevated relative to those in the control group. In addition, at 2000 Hz and 4000 Hz, the average reflex threshold was elevated above normal

limits being 101.6dB at 2000 Hz and 103.8dB at 4000 Hz. It should be noted that the acoustic reflex was absent at several frequencies in four of the nine subjects. The reflexes were absent at two or more frequencies in at least one ear of each of the four subjects.

One possible explanation for elevated and absent reflexes would be impaired neural function that is evidenced only at suprathreshold levels (Jerger, et al, 1974). As all of these subjects had otherwise normal impedance findings, the influence of conductive problems can be effectively eliminated (Jerger, Jerger, and Maudlin, 1972; Jerger, Neely, and Jerger, 1975). Further, the fact that the reflex levels tended to increase with increasing frequency would suggest that middle ear function was not a contributing factor in the acoustic reflex measurement (Jerger, Neely, and Jerger, 1975). Whether the impaired neural function is suggestive of peripheral VIIIth nerve involvement or of central brain stem involvement is difficult to say based upon the limited sample and marginal statistical significance.

Time Compressed Speech Discrimination

Time compressed speech has been previously employed as a measure of central auditory function (Kurdziel and Noffsinger, 1973). Patients with central auditory lesions have demonstrated reduced performance on measures of time

compressed speech. Reduction in performance has been manifested in terms of poorer performance in the ear contralateral to the lesion or in bilaterally reduced discrimination scores (Kurdziel and Noffsinger, 1973; Walker, 1975).

The time compressed speech discrimination scores for the sickle cell group were poorer than the scores for the control group. These findings would suggest the possibilities of impaired or reduced central auditory function in subjects with sickle cell anemia. This is consistent with the previously reported incidence of central nervous system dysfunction (Reynolds, 1965; Song, 1971), but further investigation is necessary.

Isolated Case Findings

Although no significant correlation appeared evident between the number of crisis episodes, the severity of crisis episodes, the duration of crisis episodes, and the audiometric test battery, one subject manifested rather dramatic audiologic findings. The results are shown in Figure 2. It is interesting to note that this subject had hemoglobin levels of 100 percent S and had the longest history of serious crisis episodes. This subject was a twenty-eight year old male with no history of middle ear disease. The history of noise exposure was unremarkable. Moreover, as audiometric findings suggest, the hearing loss was unilateral and did not show the characteristic noise-induced configuration.

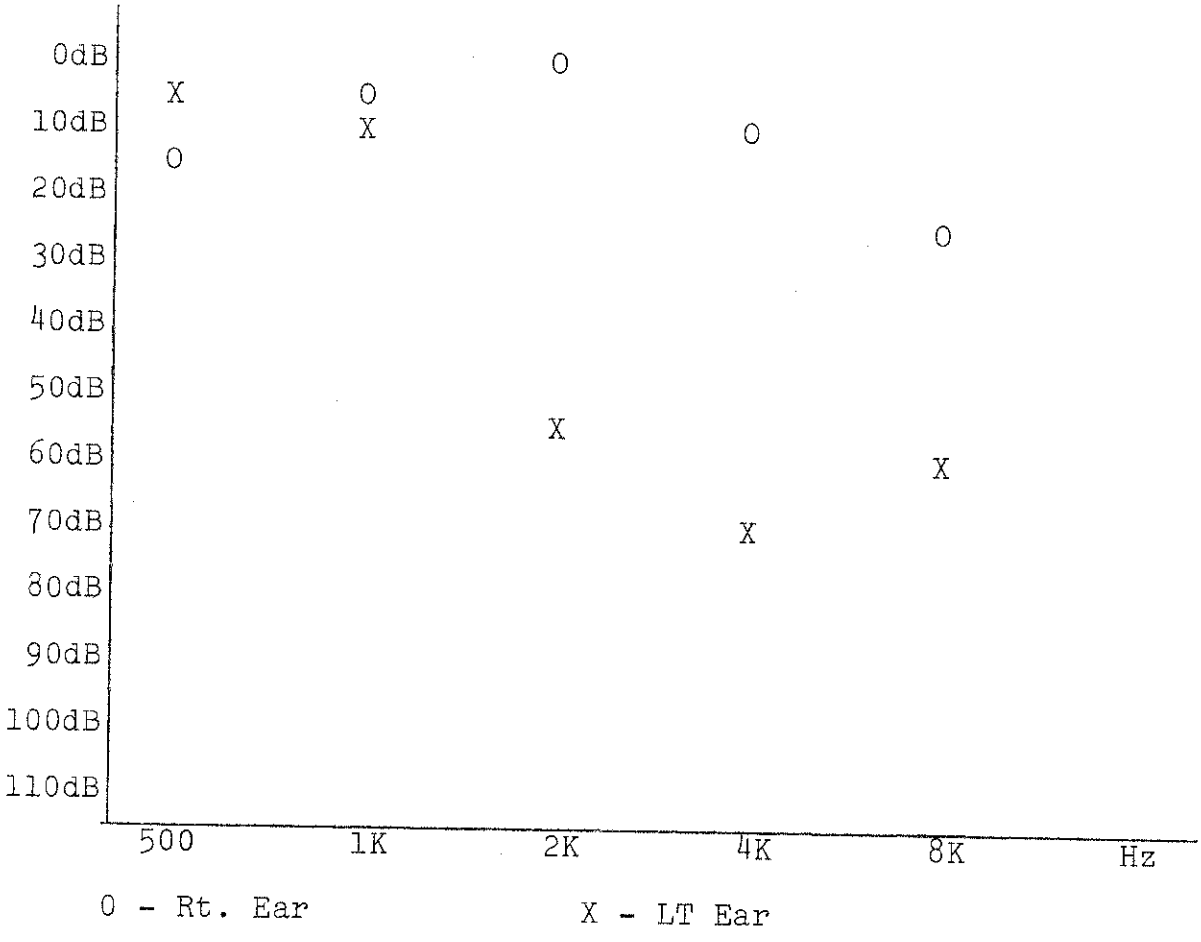

Figure 2. Air Conduction Thresholds in dB HL for Sickle Cell Subject I.

Pure-tone audiometry revealed essentially normal hearing in the right ear at 500 Hz through 4000 Hz. In the left ear the hearing was within normal limits through 1000 Hz. At 2000 Hz through 8000 Hz the subject demonstrated a moderately severe hearing loss. Bone conduction audiometry indicated the hearing loss in the left ear was predominantly sensorineural. The speech reception thresholds were within 2 dB of the pure tone thresholds bilaterally.

Impedance audiometry indicated Type A tympanograms bilaterally. Reflexes in the right ear were obtained at normal hearing levels at 500 Hz, 1000 Hz, and 2000 Hz. The reflex hearing level was elevated at 4000 Hz in the right ear. In the left ear reflexes were obtained at normal hearing levels at 500 Hz and 1000 Hz. Reflexes were absent at 2000 Hz and 4000 Hz in the left ear. Acoustic reflex decay was negative at 500 Hz and 1000 Hz in the right ear. In the left ear, reflex decay was negative at 500 Hz and positive at 1000 Hz. Reflexes are noted in Table VIII.

The Suprathreshold Adaptation Test (STAT) was administered at 500 Hz and 2000 Hz in the left ear. Jerger and Jerger (1975) developed this test as a means to differentiate cochlear and retro-cochlear lesions. The STAT is an assessment of adaptation. Adaptation in abnormal amounts is usually indicative of VIIth nerve lesions whereas minimal adaptation is observed in cochlear lesions. With this subject the result at each frequencies was negative.

TABLE VIII

REFLEX HEARING THRESHOLDS FOR SUBJECT I

	500 Hz	1000 Hz	2000 Hz	4000 Hz
RT Ear	100	95	95	110
LT Ear	100	95	absent	absent

Speech discrimination was assessed at several sensation levels and a performance-intensity function was plotted bilaterally. The right ear showed no significant reducation in discrimination ability as a function of sensation level. The left ear showed a deterioration of discrimination ability of approximately twenty-five percent at high intensity levels. The scores are shown in Table IX.

TABLE IX

DISCRIMINATION SCORES FOR SUBJECT I WITH UNDISTORTED SPEECH AS A FUNCTION OF SENSATION LEVEL

	35 dB SL	50 dB SL	70 dB SL
RT. Ear	100	100	96
LT Ear	88	76	64
Mean	94	88	80

The audiologic results in this single case suggest the possibility of cochlear and neural involvement. A similar finding has been reported in the case of sudden deafness in a sickle cell subject (Orchik and Dunn, 1976). Pure-tone audiometry indicated the hearing loss in the left ear was sensorineural. Several of the test results would support neural findings whereas others would indicate cochlear as well. Absence of the acoustic reflex at 2000 Hz in the presence of a 55 dB hearing loss could be interpreted as an indicator of retrocochlear involvement (Jerger, 1974; Olsen, Noffsinger, and Kurdziel, 1975). In addition reflex decay at 1000 Hz may be considered a retrocochlear sign although it has been reported in cochlear lesions (Olsen, Noffsinger, and Kurdziel, 1975).

The reduction in speech discrimination ability of approximately twenty-five percent at high intensity levels is a somewhat equivocal finding. The magnitude of the performance decrement is larger than expected in a pure cochlear loss. However, it is less than that originally described by Jerger and Jerger (1971) as being indicative of retrocochlear involvement. Further, the suprathreshold tone decay test did not support retrocochlear involvement.

The subject reported tinnitus in the left ear several months prior to the onset of the hearing loss. Further,

he reported that he had begun to notice a gradual decline in hearing in the left ear in the past three years. The cause of the hearing loss is unknown. The subject experienced frequent severe crisis episodes until recently. They now occur once or twice a year. The symptoms are mild to moderate ranging from three days to two weeks. The subject did not report a crisis episode just prior to the onset of the tinnitus or the hearing loss.

Without medical assessment it was not possible to suggest a probably cause for the unilateral hearing loss. Otological examination was advised. As yet, no follow-up information on the subject has been received.

Implications

In summary, the measures of peripheral sensitivity showed no real differences between the sickle cell group and the control group with the exception of one subject. There was, however, evidence suggesting reduced eighth nerve and central auditory function.

Based on the results of this investigation, the following recommendations are made:

1. Central auditory function in patients with sickle cell anemia should be investigated more extensively. The investigations should include both a larger population with sickle cell anemia and an expanded

test battery. The use of measures like the Staggered Spondiac Wordlist and other dichotic listening tasks would be of interest.

2. It would appear that further investigation is needed in terms of the correlation between the number of crisis episodes, the duration of crisis episodes, the severity of crisis episodes, and the audiologic manifestations observed in subjects with sickle cell anemia.

3. The inter-relationship of other environmental factors with sickle cell anemia should be investigated. For example, would a person with sickle cell anemia be more susceptible to noise-induced hearing loss than a person with normal hemoglobin?

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