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Ref #2612

MALNUTRITION, BRAIN DEVELOPMENT, LEARNING, AND BEHAVIOR[1]

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1993

ABSTRACT

Three widely prevalent nutritional deficiencies are recognized to have the potential for permanent adverse effects on learning and behavior: protein-energy, iron, and iodine.

Supplementation with adequate protein and calories during the first two years of life improves the cognitive performance of poorly nourished children, and the benefits may be even more robust years later when the children become adolescents and young adults.

Iron deficiency is the most common global nutritional problem; among the earliest functions to be affected are those associated with the brain enzymes involved in cognition and behavior. The effects of iron deficiency during infancy appear to be irreversible. At older ages iron deficiency is intellectually and educationally disadvantageous independently of ethnicity and of physical and social environment.

Even in areas where cases of cretinism due to iodine deficiency in the mother are few, the linear growth of the infant, its intellectual capacity, and

[1]Developed from a lecture originally presented at Lady Irwin College, New Delhi in 1993 as the 20th Memorial Lecture in remembrance of Kamala Sabharwal who contributed importantly to nutrition in India.

261

certain other of its neurological functions are permanently compromised to varying degrees.

In addition to these three most prevalent forms of deficiency, recent evidence suggests that cow's milk and infant formulas may lack sufficient omega-3 fatty acids for optimal development of the preterm infant and the neonate. Nutritional deficiencies are also potential contributors to impaired cognition in the elderly. Investments in education and community development would be more effective if the physical and cognitive capacity of underprivileged populations were not impaired by malnutrition.

Key Words: behavior, cognition, iodine, iron, malnutrition, protein

INTRODUCTION

Three widely prevalent nutritional deficiencies are recognized to have the potential for permanent adverse effects on learning and behavior, those of protein-energy, iron, and iodine. In 1962 when the first international conference on "Malnutrition, Learning and Behavior" was held at the Massachusetts Institute of Technology (1), there was no real understanding of the extent to which brain development, learning, and behavior were susceptible to the kind of subclinical undernutrition and malnutrition that affects over a billion persons in the world today. Experimental animal studies by behavioral psychologists, largely unknown to the human nutritionists at that time, indicated that both sensory deprivation and malnutrition affected learning and behavior. While the two sets of factors could be distinguished in experimental animal studies, the few human field studies available at the time were hopelessly confounded.

Soon after this conference a number of now classic field studies clearly demonstrated that protein-calorie malnutrition in young children significantly impairs learning and behavior, and that under the social and environmental conditions responsible, it continues to affect them as school children and adults. Completely unsuspected at the time of the conference at MIT was the extent to which the widely prevalent micronutrient deficiencies of iodine and iron also can significantly affect the cognitive performance of young children in ways that may become permanent.

The lasting effects of iodine deficiency began to be recognized in studies conducted in the 1960s. Although feeble-minded dwarfs have been associated with iodine deficiency for more than 50 years, convincing evidence of lesser degrees of neurological damage due to iodine deficiency during pregnancy was first presented only in the 1970s. Recognition that iron deficiency, with or without anemia, could affect cognitive performance is even more recent. These three types of deficiency are of the greatest importance to public health. However, there are other nutritional deficiencies which, when experienced at an early age, may induce neurological deficits that become permanent. These deficiencies include B-vitamins, zinc, and a new concern: omega-3 methyl fatty acid deficiency in the infant.

EFFECTS OF PROTEIN-ENERGY MALNUTRITION

Interest first focused on the lasting effects of severe protein-energy malnutrition on cognitive performance both after recovery and at later ages. The damage seems to come from chronic, severe undernutrition. A short, acute episode of superimposed kwashiorkor does not necessarily have a lasting effect; it depends on the degree to which it is superimposed on the chronic lack of sufficient food that is responsible for marasmus. Severe cognitive effects of marasmus and marasmic-kwashiorkor have been reported from many countries including Chile (2), India (3), Jamaica (4), Mexico (5), Peru (6), Yugoslavia (7), and Uganda (8).

In Mexico, as in most developing countries, nearly all cases of kwashiorkor are superimposed upon some degree of marasmus. Under these circumstances the term marasmic-kwashiorkor is more appropriate. The lasting effects of marasmus or marasmic-kwashiorkor on the cognitive development of underprivileged children have been demonstrated by Cravioto and DeLicardie (9). The differences in language scores were particularly strong for children recovered from marasmic-kwashiorkor matched for weight and length at birth with adequately nourished children in the same social environment. Cravioto and DeLicardie also showed similar differences in intelligence quotients between children who have experienced severe malnutrition and an adequately nourished sibling at the same age. This study helped to confirm that the differences are due mainly to malnutrition at an early age, and not primarily to differences in their psycho-social environment.

Concurrently, in Chile Fernando Mönckeberg (10) was exploring the effects of marasmus during the first few months of life on brain development and performance. He found no overlap between the range of IQs in children who had experienced marasmus as infants and those who had not when they were studied 4 to 7 years after recovery.

Much credit is due the pioneering demonstration in Mexico (11, 12) that subclinical malnutrition manifested only by impaired growth can affect behavior. Among lower socio-economic groups in both Mexico and Guatemala, preschool children in the lowest quartile of weight for age had significantly poorer performances on various tests of intersensory perception than did those in the highest quartile. For children of university faculty and other professionals in middle and upper income groups in the two countries there was no variation in these tests with quartiles of weight for age. The extent to which the differences were due to a lesser degree of sensory stimulation in children from the poorest families rather than to the biological consequences of a poor diet could not be determined at the time.

Mönckeberg (10), studying groups living under poor socioeconomic conditions and showing low intellectual performance, also observed a significant relationship between growth retardation and lower intellectual capacity. A similar correlation was observed between animal protein calorie intake (FIG. 1) and intelligence but not between total calorie intake and intellectual performance (10). Possibly, the significant variable is not animal protein intake per se, but it serves as an indicator of the overall nutritional quality of the diet.

FIG. 1. Children with progressively lower protein intakes are more likely to have lower scores on the Terman-Merrill test of cognitive performance (10).

The work of Cravioto in Mexico and Mönckeberg in Chile stimulated a number of now classic studies in developing country populations. In Bogota, Colombia selected children from poor families received food supplementation for the entire family, from mid-pregnancy until the target child was 3 years old (13-15). A control group received twice weekly home visits for the same period in order to provide comparable stimulation. At 3 years of age children who received the food supplementation averaged 2.6 cm and 642 grams larger than controls. The supplementation resulted in small but significant improvements in the Bayley test scores compared with the control group. Similar findings were reported from the Bacon Chow Study in Taiwan (16).

The lasting effects of early malnutrition on learning and behavior can be minimized by refeeding and psychosocial stimulation. A study in Cali, Colombia (17,18) provided slum children with 1, 2, or 3 years of nutritional supplementation and stimulation during the day for 6 days a week. Although each additional year of the combined treatment brought about significant improvement in cognitive test performance compared with control children, even after 4 years of the program, test scores were 20% lower than in children of middle and upper income families not enrolled in the program. There have been a very few other studies that have focused on the potential for rehabilitation after malnutrition. Grantham-McGregor et al. have explored this further in Jamaica (4,19,20). A child who, like 16 others, suffered early malnutrition, when adopted into a more favorable environment improved much more in the four years afterwards. Grantham-McGregor et al. (4) also followed up two initially similar groups of children treated for severe malnutrition and a control group of children who were in the hospital at the same time for non-nutritional disorders. One of the malnourished groups received one hour of structured play six days a week while they were in the hospital, one hour a week at home for the next two years, and then every two weeks for a third year.

Children in the three groups were assessed regularly with the Griffith developmental scales. All groups improved in the hospital. The stimulated group maintained their improvement after returning home and achieved developmental quotient scores similar to the control children. However, the unstimulated children were more stunted after leaving the hospital; they were also lighter and had smaller head circumference and lower developmental quotient scores. A more recent study (21) observed 127 stunted 8 to 10 year old children, who had received food supplementation, stimulation, or both. After two years, supplementation and stimulation produced independent benefits on the children's general-cognitive, perceptual-motor, and memory scores. Scores were still lower than for those children who had not been stunted.

Two studies begun in the late 1960s, one in Guatemala by INCAP (22) and the other in Mexico (23) by the National Institute of Nutrition, were well-designed and both strongly confirmed the benefits of supplementary feeding up to two years. From 1969 to 1977 in two villages in Guatemala, INCAPARINA, a nutritionally balanced protein-calorie beverage, fortified further by making it up with skim milk, was offered to the mothers during pregnancy and to their offspring twice daily for two years. In two other villages, a non-protein, low calorie beverage was given as a control to balance the stimulation received by the children in the INCAPARINA group from daily contact with the field workers. Because the volume of the "fresco" consumed was about three times that of the INCAPARINA, calorie intakes were similar.

In Mexico, after the base-line studies, Chavez and Martinez randomly selected half of the children in the village of Tezonteopan to receive a supplement of milk with added vitamins, and minerals. Both groups of the children in this study received stimulation visits and medical care. In both the Guatemalan and

Mexican studies, growth and performance on behavioral tests were significantly better. Figure 2 shows that unsupplemented children in Mexico were much less active (24).

FIG. 2. Non-supplemented rural Mexican children were less active as judged by fewer foot contacts with the support surface. At one year of age, the differences between the two groups are already very significant (24).

Willingness to make policy recommendations based on observations such as these has been limited by uncertainty as to the extent that performance at these early ages is predictive of later functioning. Recent follow-ups of these two studies approximately 15 years later have provided striking confirmation of the lasting benefit of preventing malnutrition in young children. In Guatemala, two of the original investigators and colleagues were able to locate over 2,000 of the original subjects, (comprising 89% of those who had not migrated) and re-examined them as adolescents and young adults (25,26).

Although there had been no further intervention, individuals who had received the INCAPARINA during early childhood had maintained and increased their advantages over the group receiving only the "fresco." On a Central America achievement test that combined tests for literacy, numeracy, reading and vocabulary, and general knowledge with Raven's Progressive Matrices, these individuals performed significantly better per year of schooling. They had also completed more years of schooling. Overall, the cognitive gains that were described as small at two years of age could now be characterized as medium to large (27).

Stimulated by these observations, Chavez and Martinez continued to re-examine most of those who had participated in the original program (24). They found that young adults who had been supplemented as young children continued to perform better in all respects. Figure 3 illustrates the consistent difference in IQ between supplemented and unsupplemented children, both male and female, from 1 to 18 years of age.

FIG. 3. When children who had been supplemented during the first two years of life in a rural Mexican village were re-examined from ages 12 to 17, in comparison with non-supplemented children their IQ levels were considerably higher (24).

There are now so many well-controlled studies of the effect of protein-energy malnutrition on cognitive performance that the primary effect is not in doubt. However, the extent to which the adverse effects of early malnutrition on this kind of behavior can be reversed will depend on the circumstances. The Cali, Colombia study (17) fell short of demonstrating complete recovery, but the children returned to an unfavorable environment at night. Pollitt et al. (28) note that the incidence and magnitude of nutritional effects on behavior can be greatly exacerbated by other risk factors and insults; they can also be reduced or even eliminated by buffering factors. The limited observations on undernourished children adopted by more privileged families suggests considerable recovery depending on antecedent circumstances. Unfortunately in developing countries malnourished young children seldom receive a more favorable diet and environment; whether reversible or not, the damage becomes lasting.

Even when there is no biological malnutrition, limited food intake may affect psychomotor development. INCAP researchers Torun and Viteri (29) observed the results of reducing the dietary energy intake by 10% for preschool children in a convalescent home. These children were growing well on an ad libitum diet with adequate protein. Over the following month there was a decrease in their activity that compensated for the reduced dietary energy, but they continued to grow as before. These observations, carried out under controlled conditions, revealed the impact of chronic energy deficiency on millions of children. Reduced activity in children, as long as growth is not affected, might seem to be of little consequence. Reduced activity, however, isolates the child functionally from the environment through lack of the exploratory activity and interaction with family members that are necessary stimuli for normal cognitive development.

EFFECT OF IRON DEFICIENCY ON COGNITIVE PERFORMANCE AND BEHAVIOR

Iron deficiency is the most common nutritional problem in the world today. The earliest functions to be affected by iron deficiency are those of brain enzymes involved in cognition and behavior. There were a number of relevant earlier studies in experimental animals (30-38) that stimulated interest in the possible effect in human subjects. The first clinical study (39) showed an apparent improvement in the Bayley scores of anemic infants given iron supplementation compared to those of a placebo group, but the difference was not significant. Webb and Oski (40-42) later found an improvement in the cognitive performance of iron-supplemented adolescents in Philadelphia, but since there was no control group a practice effect could not be ruled out.

In the past two decades the relationship between iron status and cognitive performance has received increasing attention and confirmation. The first well-controlled demonstration of an adverse effect of subclinical iron deficiency on learning and behavior in young children was in Cambridge, Massachusetts (43,44). On a battery of cognitive and behavioral tests moderately iron deficient 3 to 6 year old children had lower test scores than those with normal iron status. These values returned to normal after 12 weeks of supplementary oral iron (See FIG. 4). However, when Pollitt repeated these studies in Guatemala (43,45) with pre-school children who had iron deficiency anemia, the effects were not reversed by iron supplementation.

FIG. 4. Performance of control and experimental groups on oddity learning tasks before (T_1) and after (T_2) administration of oral iron (44).

The adverse effects of iron deficiency anemia on Bayley scale performance in infancy were demonstrated by Lozoff et al. in Guatemala (46) (FIG. 5) and Costa Rica (47) (FIG. 6) and by Walter in Chile (48) (TABLE 1). When Lozoff returned to Costa Rica to study the same children in school at age seven, lower mental and motor function deficits persisted in those who had moderate anemia even though hematological indicators were now normal (49). In Walter's study (48) performance scores were

FIG. 5. Effects of iron deficiency anemia on Bayley scale performance in infancy—Guatemala (46)

FIG. 6. Bayley psychomotor scores at different levels of iron deficiency—Costa Rica (47).

TABLE 1.

Effect of iron status on Bayley test performance in 12 month old infants (48)

	Normal (n=42)		Anemic (n=32)		Sideropenic (n=95)
MDI*	105 ± 9	p=0.001	98 ± 9	p=0.001	104 ± 9
PDI†	101 ± 11	p=0.0004	90 ± 14	p=0.00003	100 ± 8

*Mental Development Index
†Psychomotor Development Index

significantly lower among infants who had anemia for a longer period or whose anemia was more severe. Studies in Israel (50) and France (51) of children with anemia in infancy also found a lasting effect.

There are two reports of improvement in psychomotor development scores with iron treatment of anemic infants in the UK: Aukett et al. (52) and Idjradinata and Pollitt (53). Iron deficiency anemia effects have also proved at least partially reversible in school children in Indonesia. In 130 rural Indonesian school children near Semerang classified as anemics or non-anemics (54) hematological status returned to normal with supplementation (FIG. 7a). The anemic group markedly improved their learning and achievement scores with iron supplementation (FIG. 7b).

FIG. 7a. Hemoglobin concentration and FIG. 7b. achievement test scores of iron deficient school children before and after iron supplemenatation (54).

No change was observed in the non-anemic groups or the anemic ones given the placebo. The trial was double-blind and all of the subjects were dewormed and randomly assigned. Two other studies near Bandung, Indonesia have provided confirmation: Pollitt et al. (45), Soewondo, Husaini, and Pollitt (55), and Idjradinata and Pollitt (53).

In Egypt there was also an improvement in cognitive test performance in pre-school and school children showing a hematological response to iron supplementation (45). However, in a double-blind study of 1358 children 9 to 11 years old in Bangkok by Pollitt et al. (56) iron supplementation for 14 weeks did not reverse a significant positive association between iron status and performance on the Raven Progressive Matrices used to measure IQ, on the Thai language test, and on a mathematics test. It is noteworthy that even children who were iron-depleted without anemia had significantly lower scores on the Thai language test than did iron replete children. The IQ and mathematics scores were also lower in the iron-depleted children, although the differences were not statistically significant.

Four separate studies in India have explored the impact of iron supplementation on school children (57). The first investigated the effects of a 60-day iron-folate supplementation on cognition in 94 boys and girls aged 5 to 8 years. Scores improved markedly in the anemic compared with non-anemic controls. The second study involved the same design for 14 pairs of anemic 5 to 6 year-olds, with one of each pair receiving the supplement and showing significant cognitive benefit. The third study compared the effect of doses of 30 and 40 mg of elemental iron and a placebo in a number of tests of cognitive function on schoolboys 8 to 15 years old. Both doses improved recent memory, attention, auditory memory, auditory sequencing, visual-motor coordination, and visual perception. The fourth study investigated the impact of a prophylactic dose of 60 mg of elemental iron per day or a placebo for 60 days, twice in a school year on underprivileged girls aged 8 to 15 years. Attention, memory, and concentration were improved by the iron supplementation.

The conclusion from these studies was that iron supplementation would improve the scholastic performance of similar children in India's public schools. This is the same conclusion reached by the Indonesian studies cited above and by Pollitt et al. (45) in Egypt. However, anemic Thai school children did not improve their test performance when supplemented with iron, despite recovery from the anemia. Possibly their anemia at the time of the study reflected earlier anemia at a critical period of brain development in infancy. More detailed reviews have recently been published by Pollitt (58) and Lozoff et al. (59) .

In a 1990 study of 9 to 10 year old school children in a rural community in greater Zagreb, 67% of the children were adequately nourished, 20% were overweight or obese, and 14% were slightly undernourished (R. Buzina, Personal Communication, 1996). The variables that best explained the variation in results on the "Revised Beta Examination Test" were transferrin saturation, body height, and vitamin C blood levels. The latter would also be associated with better absorption of iron. Transferrin saturation also best accounted for differences in Wechsler test scores. Ortega et al. (60) described the iron status of a group of high school students (37 males and 27 females) in a Spanish community near Guadalajara. They found significant positive correlation between indicators of iron status and those of attention. Hemoglobin level was also correlated with calculus capability. In general performance on both a capability test and on an intelligence test was low for those with low serum ferritin. Studies have found an improvement in the scholastic test performance of anemic adolescent girls with iron supplementation in Pennsylvania, USA (61) and non-anemic iron deficient adolescent girls in Baltimore, Maryland, USA (62).

It can be concluded that where iron deficiency occurs in infancy and is moderate to severe, there is likely to be permanent neurological damage that cannot later be corrected by iron supplementation. The effects of mild deficiency, at least after infancy, are detectable but appear to be reversible. The cognitive performance was measured in iron deficient adults (young pregnant women) and found decreased. Supplementation with iron did improve their performance although the iron deficiency was mild and without anemia (63). There is no reason to doubt that acute iron deficiency has a reversible effect at any adult age. The overall results of these various studies suggest that iron deficiency is educationally disadvantageous independently of ethnicity and physical and social environment.

There is no direct evidence from human studies for the mechanism of the effect of iron deficiency on neurological function. However, iron deficiency at critical periods may influence both brain development and function. A functional effect can be reversible later. Work in Israel with rats indicates that iron deficiency at an early age results in irreversible damage to developing dopamine neurons (38) and learning ability of rats (64). The decreased number of dopamine D_2 receptors causes a selective diminution of central dopamine neurotransmission (65,66). The result is a modification of dopamine-dependent behaviors and reactions, the most important of which is a reduction in learning processes, a deficit which persists in adult rats (67). It is postulated that interference with iron metabolism at an early age can result in irreversible damage to developing dopamine neurons, with consequences evident in later life, but the dopamine hypothesis has not been tested in humans.

IODINE DEFICIENCY

Although the numbers are decreasing rapidly as the result of the aggressive salt iodization efforts of WHO/UNICEF, a billion persons of all ages have been at risk from iodine deficiency in the current decade. About 6 million of these show signs of cretinism and many more have milder degrees of mental retardation or other neurologic change (68). Until recently, iodine deficiency was identified only with a compensatory swelling of the thyroid gland known as endemic goiter and with cretinism. The latter is a manifestation in the child of severe iodine deficiency during gestation characterized by profound mental deficiency, dwarfism, spastic dysplasia and limited hearing. It is now recognized that, even when cases of cretinism are few in number, they indicate a much larger number of persons who do not have the classic signs of cretinism. However, their linear growth, intellectual capacity, and some other neurological functions are compromised to varying degrees because of iodine deficiency in their mothers (69,70). The difficulty in establishing the correlation between neurological symptoms and endemic goiter was due to the fact that the affected individuals did not show any clinical or biological signs of hypothyroidism when examined several years after birth.

Nevertheless, it had been noted that where endemic rates were high, the prevalence of subnormal intelligence seemed unduly high. The pediatric neurologist Dodge, working in rural Andean Ecuador (71), applied simple cognition tests to school children in such populations who were perceived to be normal and representative of the general population. The test results indicated on average a sharp reduction in both motor skills and formal intelligence. The anthropologist Greene (72,73), working in the same villages, noted that the village perception of the range of normal intelligence shifted downward. His results are shown in TABLE 2.

TABLE 2.

Child mean Bender Gestalt scores (both sexes) (73)

Age (yr)	Ecuador	North America
6-7	11.7	6.4
7-8	8.2	4.7
8-9	6.4	2.5
9-10	6.6	1.6
10-11	3.9	1.5

The pediatric neurologist DeLong has also worked in these villages (74) as have the Ecuadorian physician Fierro-Benitez and his students (75,76). These investigators have found a uniform damping of the scores on both neuromotor and cognitive functions among preschool and school age children in villages with a high goiter prevalence compared with children of similar age in the capital city. In part this difference could show the effect of an urban environment, but the scores improved more in children whose mothers had received iodine supplements. A long-term study of this same population disclosed that when mothers were given iodinated oil prophylactically during or before pregnancy, their children performed better in school, as measured by their grades, the number of years the children remained in school, their academic drop-out rates, and their scores on cognitive tests (77-79).

In several other countries the effect on the child of the administration of iodine in the form of iodinated oil to women of child-bearing age has been determined. Sufficient iodine can be administered intramuscularly to provide enough iodine for approximately three years. Studies in Bolivia (80) and in Peru (81) have indicated beneficial effects of iodinated oil on cognition in regions of severe endemic goiter, but the differences were not statistically significant. The strongest evidence has come from the work of Bleichrodt et al. (82,83) in Central Java and from Thilly et al. (84) in rural Spain and Malawi. Convincing also are studies by Pharoah and Connolly in the Jimi Valley of the Papua-New Guinea highlands (85,86).

In each of these studies there were clear differences both in neuromotor function and cognition scores. Ma Tai (87,88) has reported comparable results from large-scale studies in the People's Republic of China between villages where the salt was iodized and control villages (FIG. 8).

FIG. 8. Difference in distribution of intelligence quotient of 7 to 13 year old students in two socially similar Chinese communities with different iodine nutritional status.

Differences of approximately 10 IQ points were routinely found (88). The shift was in the entire normal distribution curve and not due to a few individuals with very low scores. A meta-analysis by Bleichrodt and Born (89) of 18 studies found scores for the iodine-deficient and non-iodine deficient groups respectively to be 0.9 standard deviations or 13.5 IQ points apart.

The brain of the developing fetus is supplied with thyroid hormone by the mother early in pregnancy, and the fetus is particularly at risk if the mother is deficient in iodine. The reports of Van Wassenaer (90) and Xue-Yi et al. (91) indicate that the damage occurs by the end of the second trimester of pregnancy, when the most rapid development of the neuropile and the cochlea and auditory neurons occurs. This latter observation may explain the vulnerability of the auditory apparatus to iodine deficiency (92).

The damage to the nervous system caused by iodine deficiency is largely irreversible. In the rat, however, some catch-up has been reported (93). The experiences of Dussault et al. (94) and Calaciura et al. (95), who screened for iodine status at birth, indicate that there is sustained and irreversible damage. This is also the finding of Moreale de Escobar et al. (96) in Spain, although non-compliance with the prescribed treatment program may have been a factor in that study. The social and economic implications of these findings is obvious.

ESSENTIAL FATTY ACIDS

Omega-3 fatty acids are essential for mammalian brain function. About half of the decosahexanoic acid required for brain development is obtained in utero and the other half during the first 6 to 12 months after birth, the later half being well supplied by breastmilk (97-99). The offspring of omega-3 deficient non-human primates have a biochemical disorder in the brain lipids that is reversed by feeding omega-3 fatty acids to the deficient animals, but the visual and cognitive changes apparently persist (100, 101). In rats, Yamamoto et al. observed an improvement in brain lipid compositions and learning ability after the rats were fed a diet supplemented with omega-3 fatty acids (102).

The potential public health relevance of these observations is that this fatty acid is present in breastmilk but not in cow's milk, nor is it present in most infant formulas (97,98). Uauy et al. in Chile (103) have compared human infants who received either breastmilk, formula, or formula supplemented with omega-3 fatty acid. Electroretinogram abnormalities were present only in the infants fed the unsupplemented formula. Hoffman et al. (104) found improved retinal and cortical development in premature infants supplemented with omega-3 polyunsaturated fatty acids. A recent study reported significantly high differences in Intelligence Quotients between pre-term children who were breastfed and those who were not (105). This is clearly an area which deserves more research and attention because of the large number of contemporary mothers who do not breastfeed their infants.

OTHER NUTRITIONAL DEFICIENCIES

It is known from classic studies with experimental animals that almost any B-vitamin deficiency during the period of organogenesis, the first trimester in utero, can result in congenital abnormalities. Fortunately, B-vitamin deficiencies during pregnancy substantial enough to produce this effect are now rare in human populations. Only iodine deficiency is known to occur during pregnancy on a large scale. Some of the B-vitamin deficiencies, when severe, can produce cognitive defects at any age. The dementia sometimes seen in pellagra cases is well known. Brozek (106) has described the psychologic effects of experimental thiamine deprivation in normal young men and its reversibility.

In the Mexican Collaborative Research Support Program (CRSP) study (107) lower maternal dietary phytate/zinc ratios during pregnancy, correlated with better attention span, reactivity, social orientation, cooperativeness, and emotional tone on Bayley infant behavior items (108). Higher maternal fruit consumption during both pregnancy and lactation also resulted in better infant Bayley scores. For infants from 3 to 6 months of age, a higher intake of eggs, milk, and fruit was associated with improved Bayley scores. A double-blind, placebo-controlled, 9-month, multiple vitamin-mineral supplementation of school children in Wrexham, Wales found a highly significant effect on the Calvert Non-verbal Intelligence Test but not on verbal cognitive abilities (109), but a similar 16-week trial in Norwich, UK found no effect on tests of intelligence (110). Neither group was considered malnourished. There has been much speculation about the possible effects of zinc deficiency on behavior, but little evidence has been produced in this debate. However, studies on infants by Bentley et al. (111) in rural Guatemala and on children aged 12 to 24 months by Sazawal et al. (112) in northern India report increased activity in supplemented children.

MALNUTRITION AND COGNITIVE PERFORMANCE OF THE ELDERLY

Nutritional deficiencies are also potential contributors to impaired cognition in the elderly. Iron deficiency anemia is common in the elderly and can be expected to have the same effects in this age group as are discussed above for younger age groups. It is postulated that B-vitamin status is a risk factor for vascular dementia, an ill-defined but possibly wide-spread form of dementia (113,114). There is also evidence that some elderly patients with symptoms of B-vitamin deficiencies have cognitive, neurological, or affective disorders that improve with vitamin supplementation (115).

EFFECT ON COMMUNITY AND NATIONAL DEVELOPMENT

Developing country investments in education and community development would be more effective if the physical and cognitive capacities of their populations were not impaired by malnutrition. The tragedy is that each month and each year generations on which the future will depend are being needlessly handicapped.

Many developing countries have already successfully eliminated most kwashiorkor and marasmus and have reduced the frequency of undernutrition and retarded growth. As described in this review iodine and iron deficiencies are still causing great damage; however, they are easy and inexpensive to prevent. Salt iodation for the prevention of iodine deficiency disorders is being rapidly adopted. Prevention of iron deficiency should be given an equally high priority in national development plans. In addition, programs that will provide increased stimulation as well as improved nutrition are needed to improve the learning and behavior of underprivileged children and adults.

SUMMARY

Of the deficiencies still common in the developing world, iodine deficiency in the mother during pregnancy is known to be capable of producing permanent neurological damage to the fetus. Iron deficiency anemia in infancy can result in damage, observable in subsequent performance on tests of learning and behavior, that cannot be reversed. At any age iron deficiency anemia impairs cognitive test results. Protein-energy deficiency in infancy and early childhood that is sufficient to cause physical growth retardation is associated with poorer performance on cognitive tests.

Supplementation of the mother during pregnancy and of the child during its first two years of life improves cognitive performance during infancy, and the benefits may extend to further robust years when the children reach adolescence and young adulthood. The most severe forms of protein-energy malnutrition, kwashiorkor, and marasmus are associated with pronounced deficits on behavioral tests. The extent to which the effects of kwashiorkor are reversible by refeeding and stimulation depends upon the degree and duration of the marasmus over which the kwashiorkor is usually superimposed.

Other nutrient deficiencies can also affect cognitive performance, but are in general not current public health problems. Recent evidence suggests that cow's milk and infant formulas may lack sufficient omega-3 fatty acids for optimal development of the preterm infant and the neonate. For the populations of developing countries, high rates of maternal malnutrition, small-for-date babies, and low rates of breastfeeding may be additional factors contributing to impaired cognitive development. B-vitamin and zinc deficiencies may also be sufficient to affect cognitive behavior in some contemporary populations, particularly the elderly and developing country children.

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FIGURE LEGENDS

FIG. 1. Children with progressively lower protein intakes are more likely to have lower scores on the Terman-Merrill test of cognitive performance (10).

FIG. 2. Non-supplemented rural Mexican children were less active as judged by fewer foot contacts with the support surface. At one year of age, the differences between the two groups are already very significant (24).

FIG. 3. When children who had been supplemented during the first two years of life in a rural Mexican village were re-examined from ages 12 to 17, in comparison with non-supplemented children their IQ levels were considerably higher (24).

FIG. 4. Performance of control and experimental groups on oddity learning tasks before (T_1) and after (T_2) administration of oral iron (44).

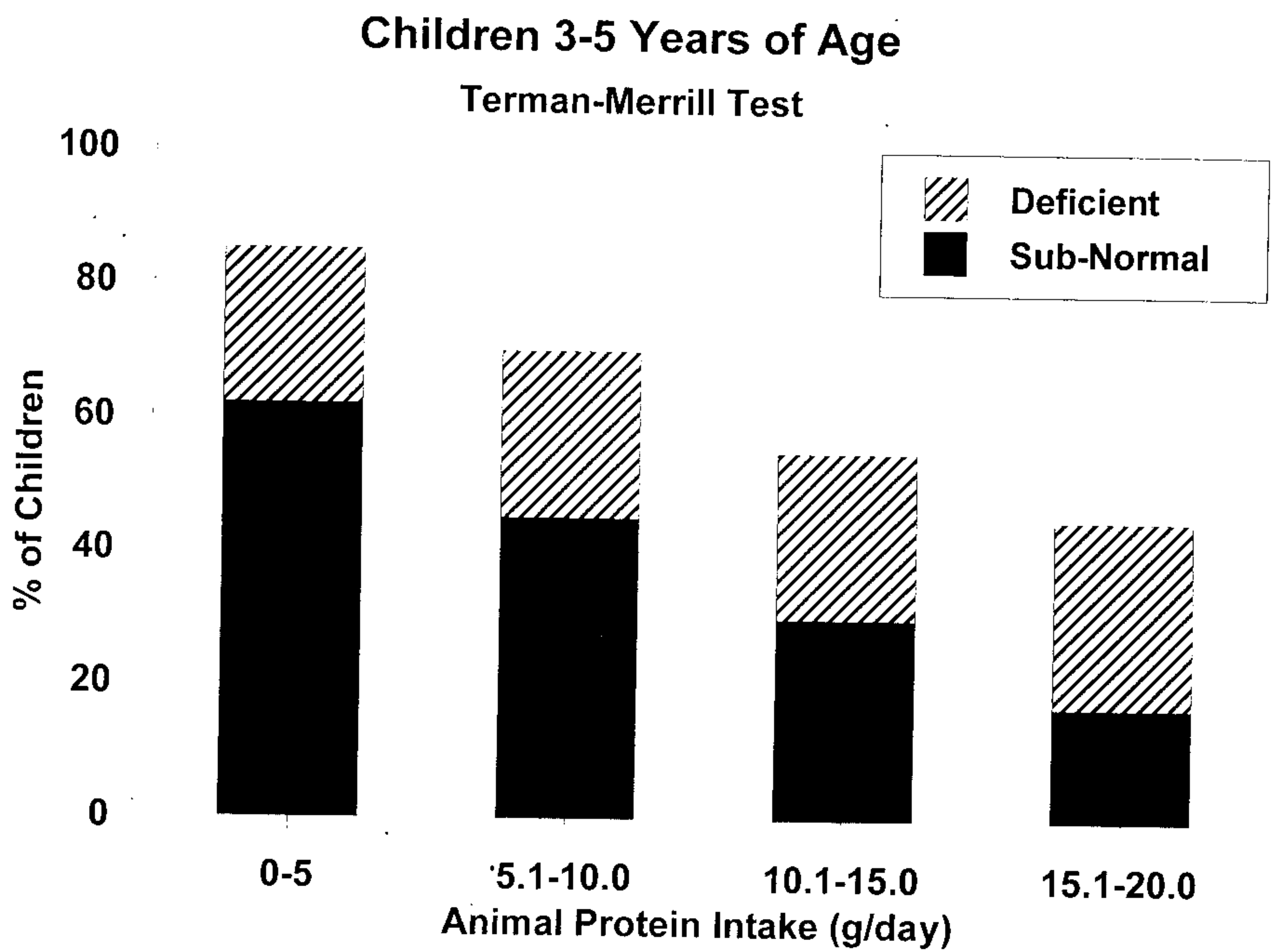
FIG. 5. Effects of iron deficiency anemia on Bayley scale performance in infancy–Guatemala (46)

FIG. 6. Bayley psychomotor scores at different levels of iron deficiency–Costa Rica (47).

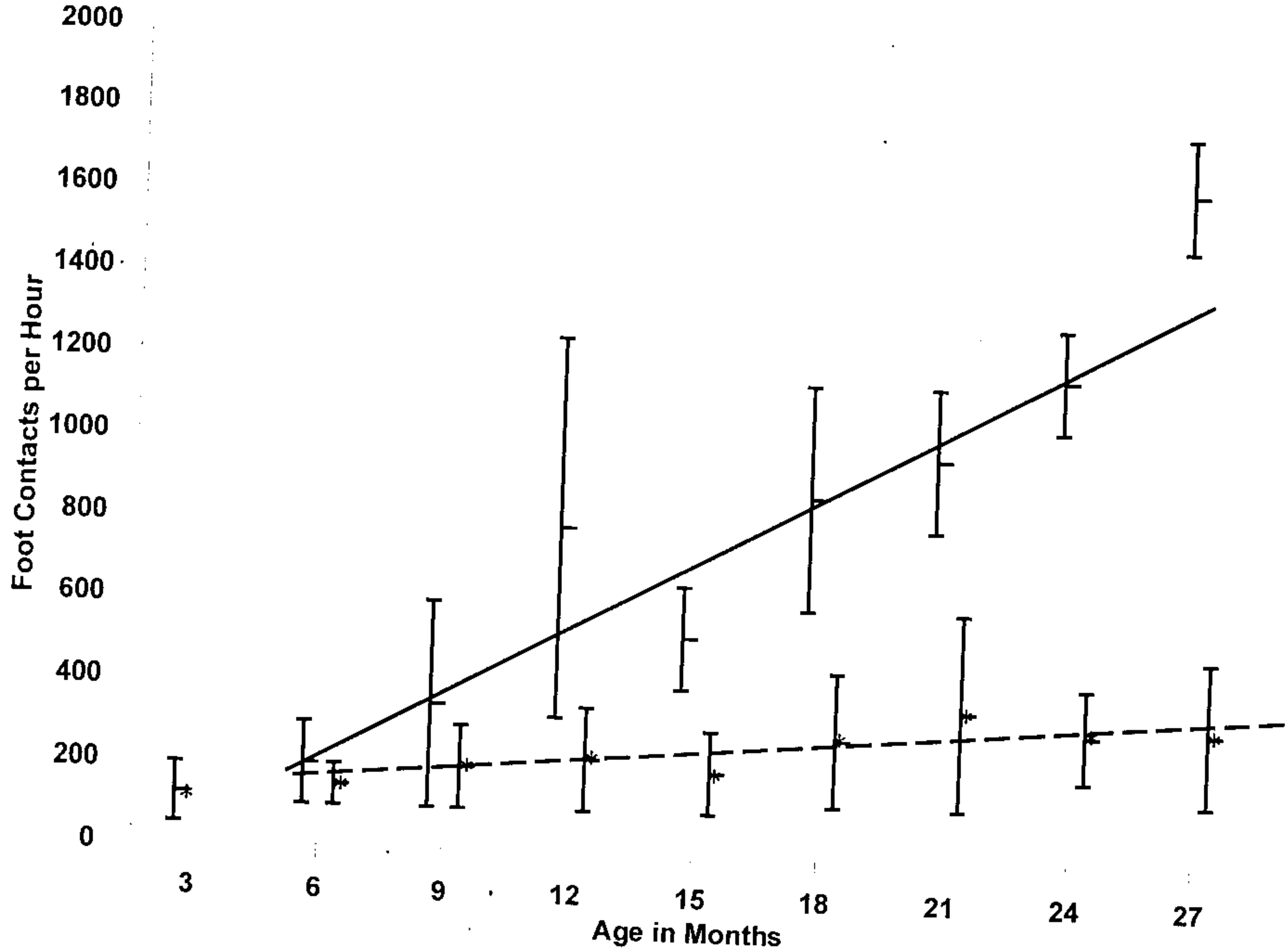
FIG. 7a. Hemoglobin concentration and FIG. 7b. achievement test scores of iron deficient school children before and after iron supplemenatation (54).

FIG. 8. Difference in distribution of intelligence quotient of 7 to 13 year old students in two socially similar Chinese communities with different iodine nutritional status.

Scrimshaw Fig. 1



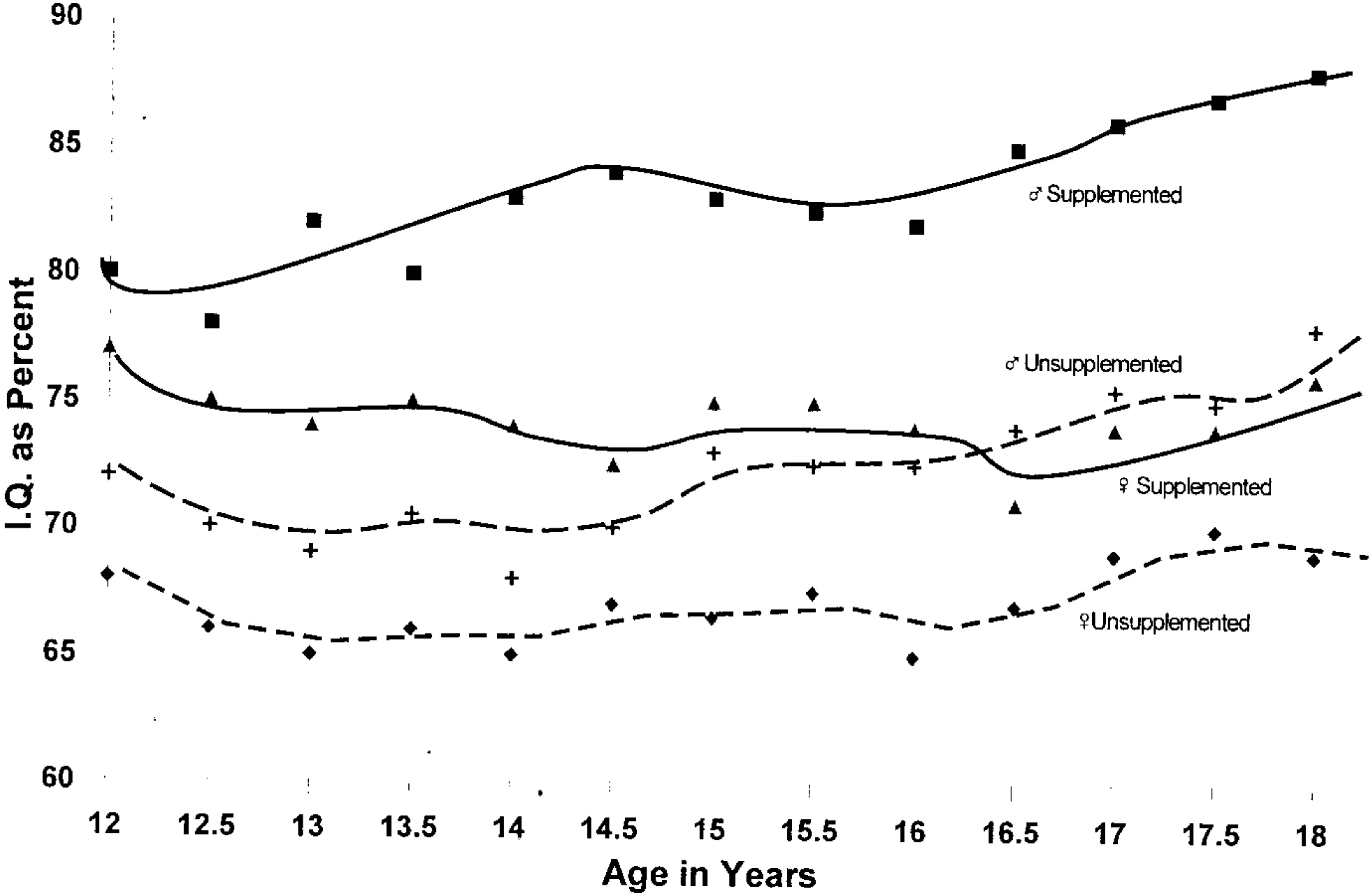
Scrimshaw - Fig. 2



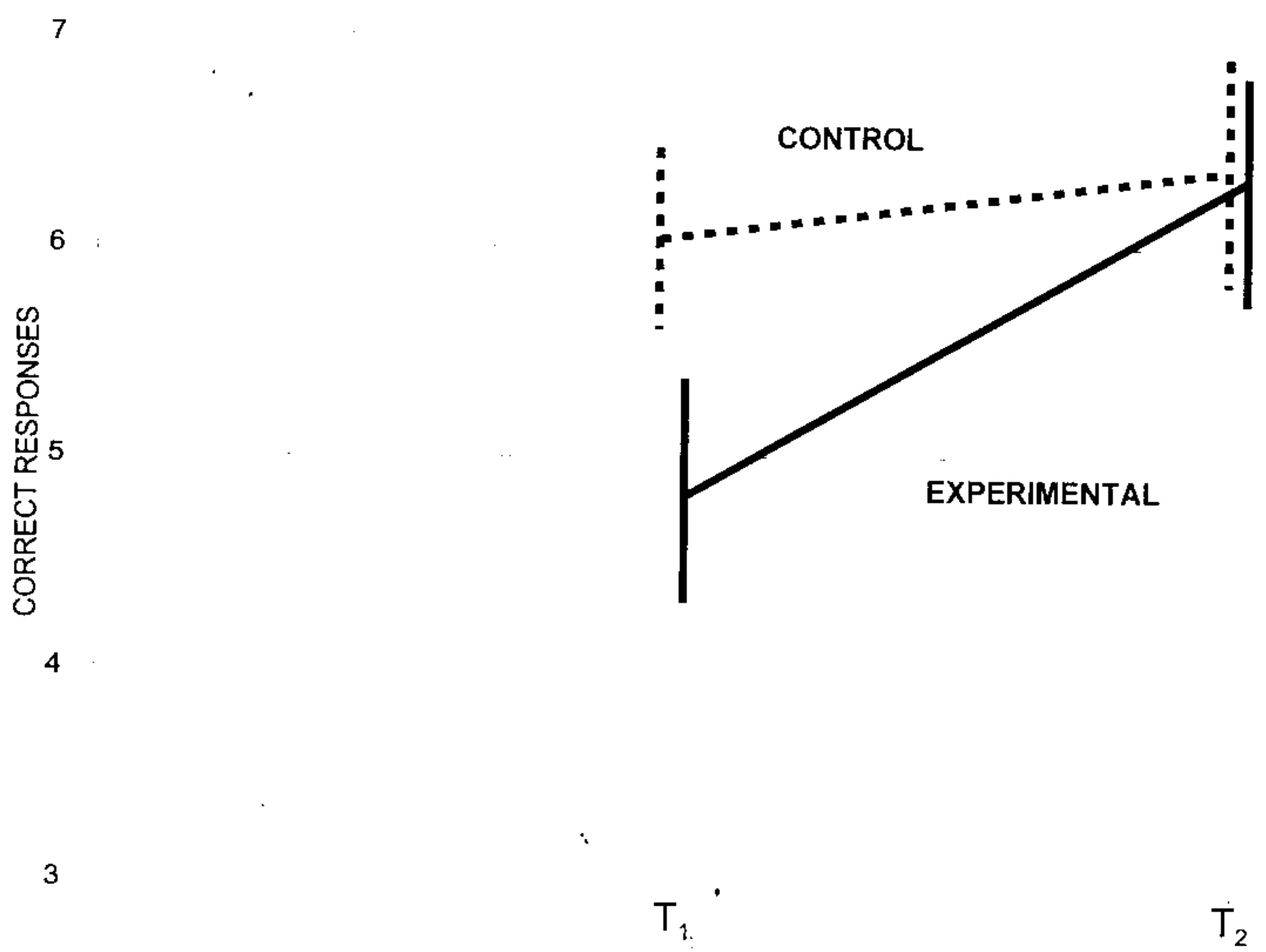
JCRIMSHAW - FIG. 3

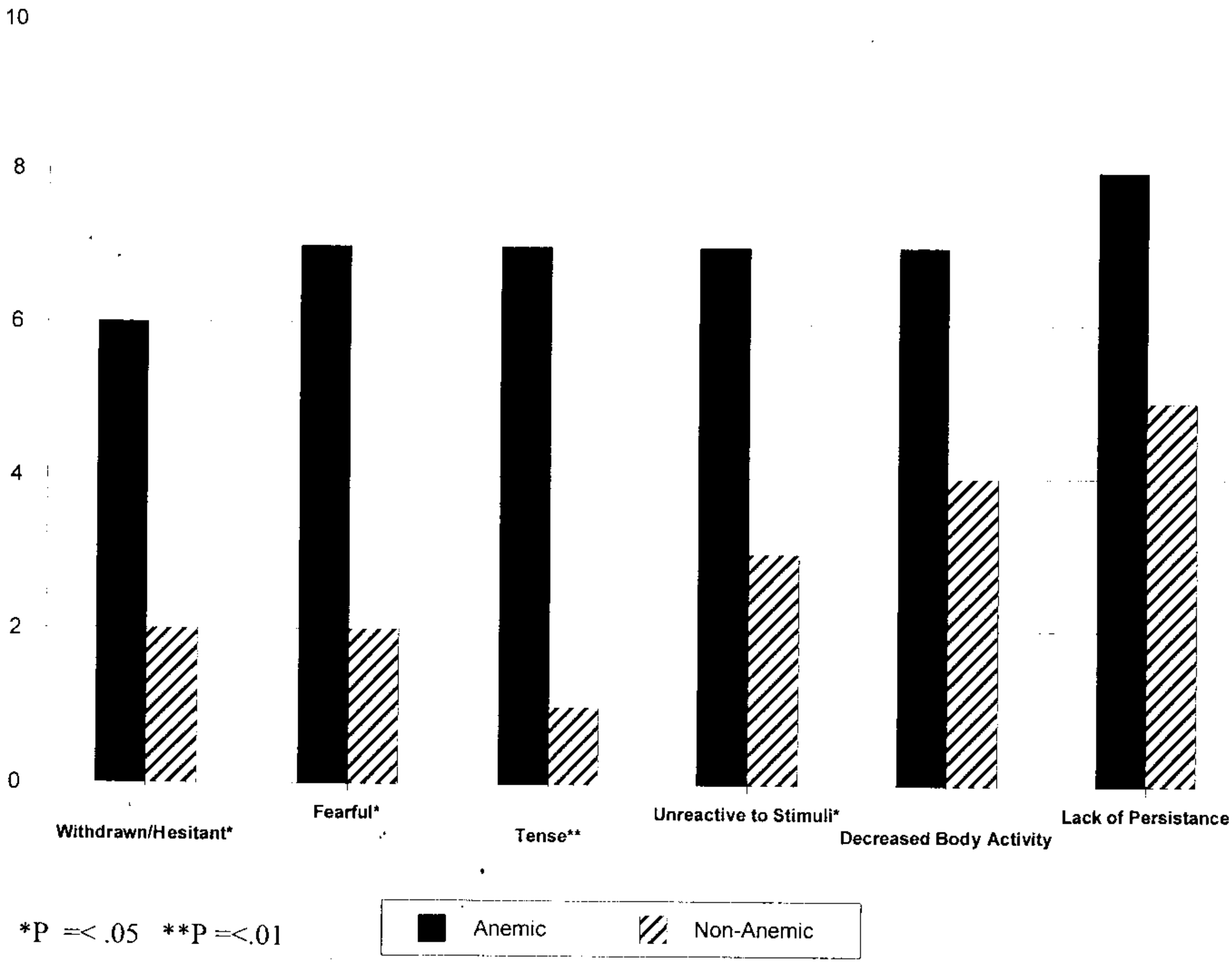
I.Q. By Age

Supplemented & Unsupplemented Males and Females



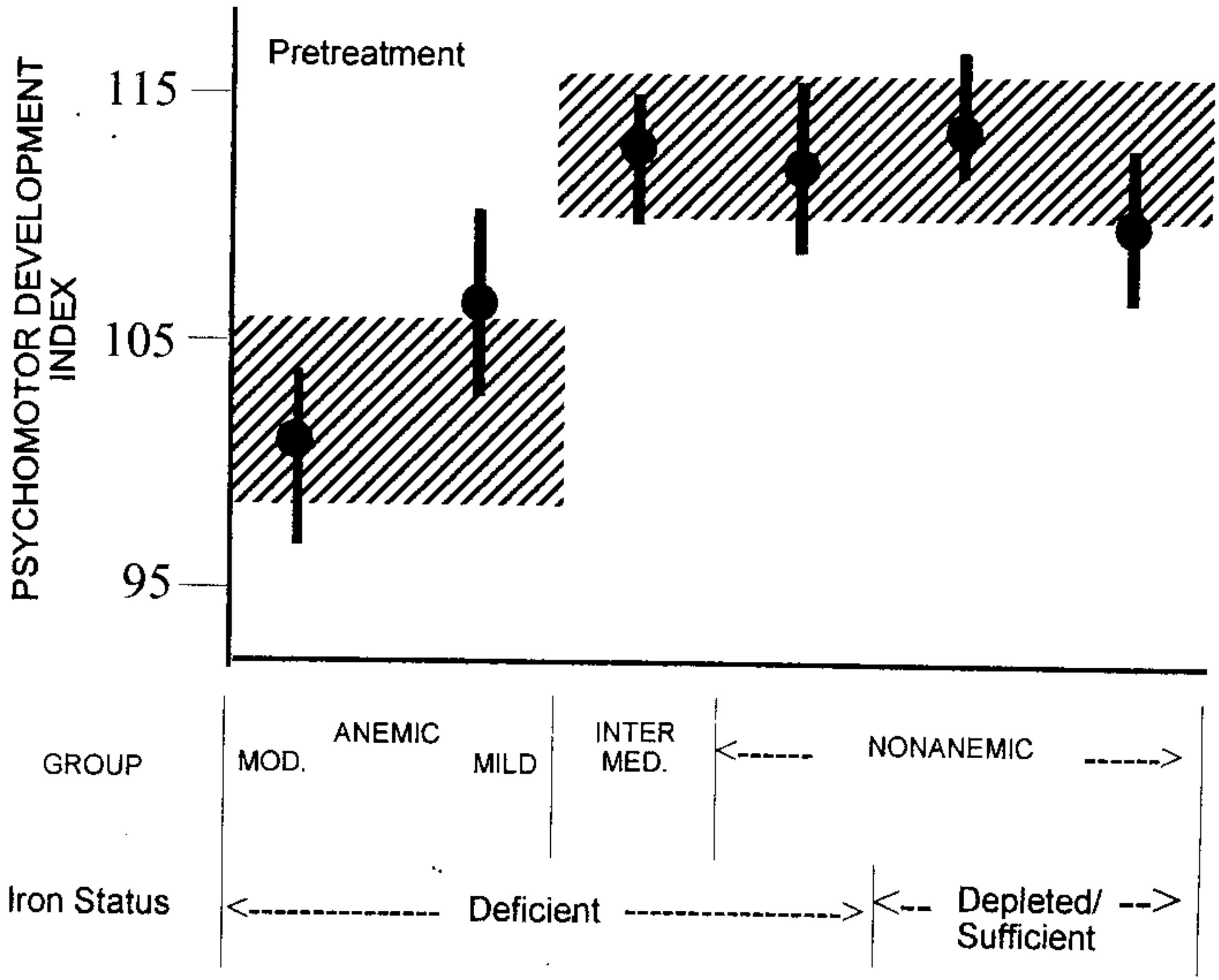
SCRIMSHAW - FIG. 4



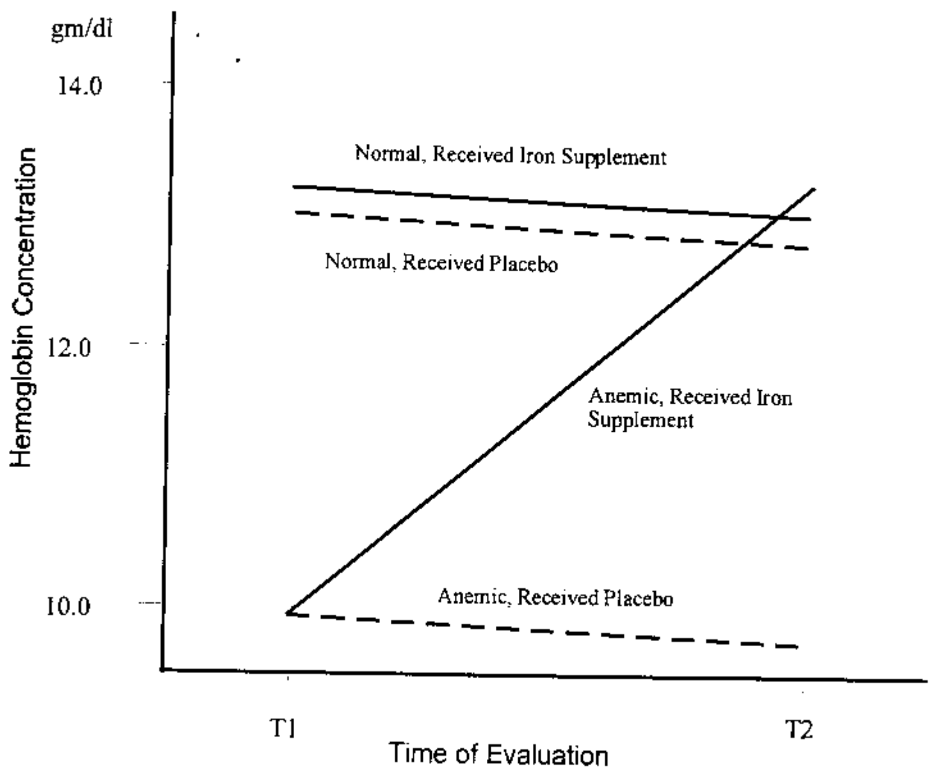

10
8
6
4
2
0
Withdrawn/Hesitant*
Fearful*
Tense**
Unreactive to Stimuli*
Decreased Body Activity
Lack of Persistance
Anemic
Non-Anemic

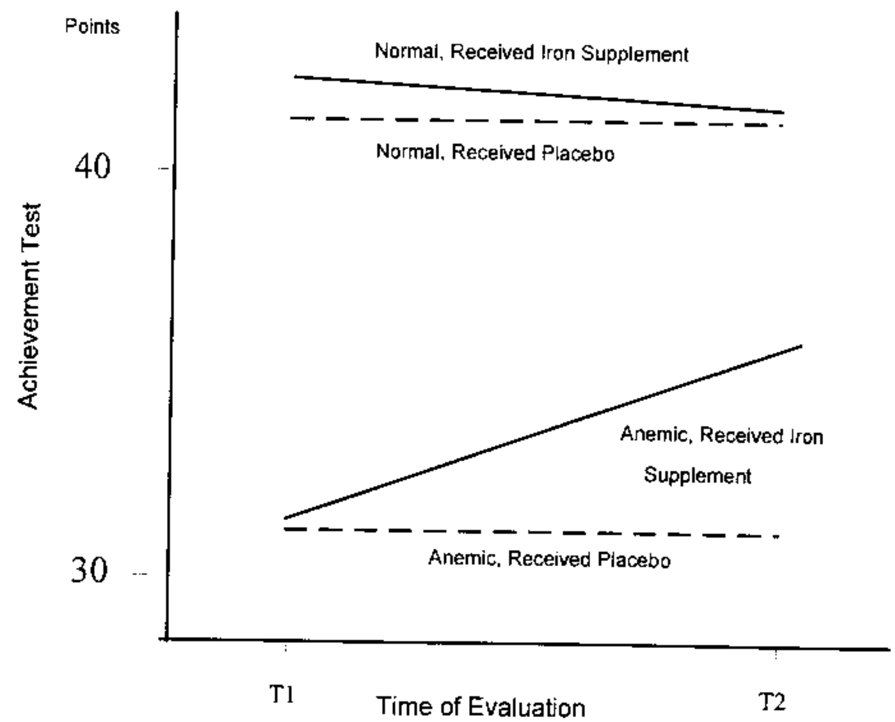
*P =< .05 **P =<.01

SCRIMSHAW - FIG 6



Scrimshaw Fig 1a, 1b





SCRIMSHAW - FIG. F