In Brief.
Iron, Zinc, Dietary Beef, and Cognition

Does what we eat influence our cognition, or our perception, memory and reasoning? It is well known that protein-energy malnutrition, a multiple nutrient deficiency syndrome, compromises children's cognitive development and their ability to learn. Even short-term nutritional deficits such as hunger or skipping a meal such as breakfast can contribute to poor academic performance. Likewise in older adults, malnutrition resulting from insufficient food intake may contribute to cognitive deficits and impair their ability to live independently.

Findings from studies in experimental animals and humans indicate that deficiencies of iron and zinc can affect cognition. Experimental animal studies indicate that iron and zinc are essential components of the brain and are involved in brain development and central nervous system functions, including the production and catabolism of neurotransmitters.

In humans, iron deficiency contributes to cognitive impairments including lower neuropsychological performance in infants, preschool and school-age children, adolescents and adults. Some research findings indicate that early iron deficiency (e.g., in infancy) can cause poorly reversible neuropsychological consequences. However, iron repletion in preschool and older children appears to improve cognitive performance.

Compared to iron, few studies have examined zinc's role in human neuropsychological performance. A recently reported study found that zinc repletion improved some neuropsychological performance indices in young school-aged children when other limiting micronutrients were also repleted.

People consume food, not nutrients per se. Therefore, the effect of red meat, an excellent source of iron and zinc, on neuropsychological performance is of practical interest. Studies in animals indicate that repletion of iron and zinc status using beef corrects cognitive deficits. Similar studies have not been reported for humans.

Data from national food intake surveys indicate that many segments of the U.S. population have low intakes of iron and zinc. When one considers people's food choices and the availability of foods rich in bioavailable iron and zinc, deficiencies of these nutrients may be more common than recognized by most health professionals. Current recommendations that healthy Americans consume two to three servings per day of foods from the Meat Group may meet nutritional needs for iron and zinc if red meat is chosen. It is uncertain, however, if needs for these nutrients can be met if only white meats, poultry, fish and legumes are consumed.

Part I.
Nutrition and Cognitive Function

Many factors influence one's cognitive functioning or ability to perceive, think and remember. Nutrition is probably the most important factor affecting the expression of one's genetically determined cognition (1,2). Recognition of the positive association between nutrition and cognition, particularly school achievement, was one of the underlying motives for developing the U.S. government's child nutrition programs such as the school lunch program and the school breakfast program. For older adults, adequate nutrition may help reverse or delay age-related cognitive deficits. Impairments in cognitive functioning, evidenced by deficits in memory, problem solving, orientation or abstraction, may reduce older adults' ability to function independently (3).

Protein-energy malnutrition, a syndrome of multiple nutrient deficiencies, is associated with a variety of cognitive and behavioral deficits (1,4,5). Severe malnutrition reduces a child's interaction with the environment, which in turn can lead to problems of attention, short-term memory and poor school performance. Of particular interest is whether nutrition, especially at a critical period of brain growth or maturation, has long lasting effects on later cognitive functioning. In an effort to answer this question, a high energy supplement was fed to 334 Indonesian infants and toddlers who participated in a three month randomized trial in 1986 and 1987 (6). Eight years later memory function was measured in 231 children, 125 of the original supplemented children and 106 controls from the same community (6). The nutritional supplement had long-lasting beneficial effects on working memory, but only in the children who received the supplement early in life (i.e., before 18 months of age).

Despite a number of studies, much still remains to be learned about the impact of nutrition on adults' cognitive performance (1,4). Considering the increased numbers of older adults, understanding factors that contribute to the maintenance of cognitive performance is a high priority (7).

Data from national food intake surveys indicate that many segments of the U.S. population have low intakes of iron and zinc.

Even short-term nutritional deprivation or hunger is negatively associated with cognitive development (8-13). Hunger limits children's ability to learn, in part by reducing their ability to respond to the environment, to pay attention and to obtain information (14). Children from families reporting frequent experiences with food insufficiency and hunger were found to display behavioral, emotional and academic problems more often than children from similar low income families which did not experience hunger episodes (15).

Nutritional deficits in children resulting from skipping a meal such as breakfast have been associated with lower academic performance. In contrast, participating in the federal government's breakfast program has been reported to improve cognitive performance (8,10-12,16,17).

To understand how malnutrition, hunger and even skipping a meal can play a role on cognition, consideration of the quality of the diet and specific nutrients is important. There has been little research on the effects of animal products such as red meat on cognition (18). As reviewed below, the role of dietary iron intake in cognitive functioning has been studied in experimental animals and humans (5,19,20). Iron and zinc deficiencies may be involved in many of the same effects attributed to protein and energy malnutrition (19,21). Given that red meat such as beef is a major source of readily bioavailable iron and zinc, a logical assumption is that regular consumption of this food improves neuropsychological performance.

Part II.
Iron's Role in Cognitive Development and Functioning

a) Iron Deficiency is a Prevalent Nutritional Problem

Although iron deficiency has substantially declined in recent decades, it still remains the most prevalent nutritional disorder worldwide, affecting more than two billion people or more than one-third of the world's population (22). Infants, pubertal children and women of childbearing age are at greatest risk of iron deficiency (23,24). In the United States, iron deficiency occurs in 9% of children ages 12 to 35 months, less than 1% of children older than 3 years of age and 9 to 11% of adolescent girls and women aged 12 to 49 years (23,25). Iron deficiency anemia, the most severe form of iron deficiency, affects 3% of U.S. children ages 12 to 35 months and 3 to 5% of adolescent girls and women (23,25). Although the prevalence of iron deficiency anemia is relatively low in the U.S. compared to that in less developed countries, lack of iron stores and physiological consequences of iron deficiency are not uncommon in some groups such as premenopausal women (26).

What causes iron deficiency? Young children's rapid rate of growth, along with a low intake of dietary iron, particularly during the first two years of life, increases the risk of iron deficiency (23). Data from the USDA Continuing Survey of Food Intakes by Individuals (CSFII), 1994-96 (27) indicate that more than half of children 1 to 2 years of age fail to consume the Recommended Dietary Allowances (RDAs) (28) for iron through their diet **(Table 1)**. Beyond 2 years of age, the risk of iron deficiency in childhood decreases as a result of slower growth and a more diversified diet. For adolescent females and adult women, the risk of iron deficiency anemia is increased by: a diet low in iron, poor absorption of most dietary iron, the presence of other dietary factors that inhibit iron absorption, menstruation and medical conditions that affect iron status (22,23). When the nutrient intakes of young women 18 to 24 years of age who participated in the Second National Health and Nutrition Examination Survey (NHANES II) were examined, iron intake from foods (10.7 mg/day) was found to be well below the RDA of 18 mg iron/day (29).

b) How Does Iron Influence Cognition?

Iron deficiency, in particular iron deficiency anemia, can affect cognitive function directly and/or indirectly (30-32). Directly, iron deficiency leads to low brain levels of iron which in turn impairs myelination of nerve cells and neurotransmitters, particularly dopamine **(Figure 1)**. These changes could contribute to alterations in the maturation and function of a variety of aspects of the central nervous system. Indirectly, iron deficiency could impact cognitive behavior by reducing an individual's attentiveness and responsiveness to the environment. This in turn may lead to fewer learning experiences and less ability to acquire information.

c) Experimental Animal Studies Provide Insights into Iron's Role in Cognition

Findings from experimental animals provide support for an essential role for iron in cognitive development and reveal mechanisms by which iron impacts cognition. Rats fed an iron deficient diet beginning at birth have lower brain heme iron levels, are less responsive to environmental stimuli and exhibit deficits in learning compared to iron-replete animals (33-36). Further, the decrease in brain iron and deficits in learning persist despite increased iron intake (35). Animal models indicate that early iron deficiency decreases brain iron stores which impairs the activity of iron-dependent enzymes necessary for the synthesis, function and degradation of neurotransmitters such as dopamine (36). These findings from laboratory animals provide insights into the effects of iron deficiency

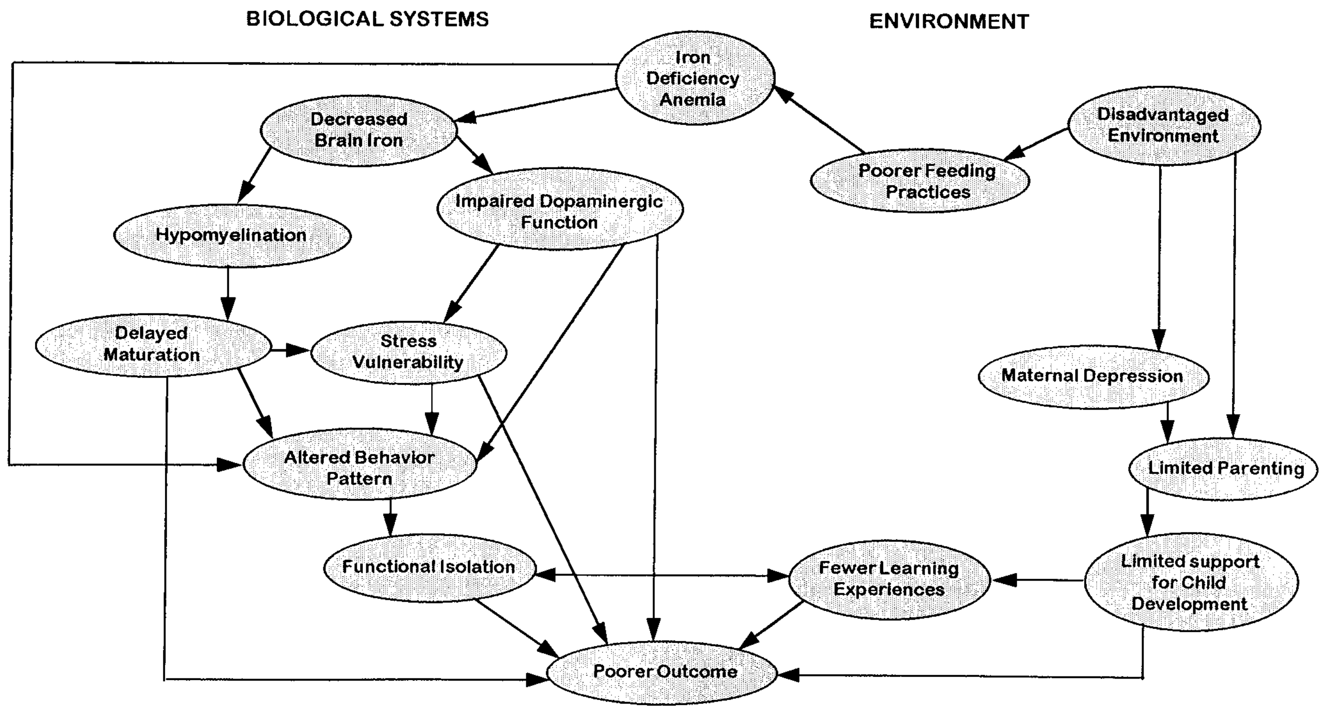
Table 1. Dietary Intakes of Iron and Zinc Based on Data from the USDA CSFII, 1994-1996

	Age/Sex Group									
	Infants* <12 months	Children 1-2 years	Girls 12-19 years	Boys 12-19 years	Women 20-29 years	Men 20-29 years	Women 60-69 years	Men 60-69 years	Women 70+ years	Men 70+ years
Proportion of Americans Meeting 100% of RDA for **Iron**	87.9	43.9	27.7	83.1	25.9	86.9	59.3	85.5	37.7	78.5
Proportion of Americans Meeting 100% of RDA for **Zinc**	73.0	15.2	23.9	34.7	19.6	36.6	13.3	24.4	17.4	14.5

*Excludes breast-fed infants.

Adapted from Ref. 27.

Figure 1. Conceptual Model for Developmental Effects of Early Iron Deficiency Anemia.*



*The right side of the model focuses on environmental influences on the child and the lift side begins with biologic influences. Both environmental and biologic mechanisms are shown to produce a poorer outcome.

From Ref. 32.

in human infants (32). Both the rat and human brains are vulnerable to nutritional and other environmental factors during neurological development and iron is distributed in similar brain regions in both species (32).

d) Human Studies Support An Essential Role for Iron in Cognition

Human studies provide evidence that adequate iron nutrition throughout life, from infancy through later adult years, is important to realize one's cognitive potential. By far, most human research on the cognitive effects of iron nutrition has focused on infants, preschoolers and school-age children (30). Considerably less information is available for adults.

- **Infants and Toddlers (less than 2 years of age)**

Because the most complex postnatal neural changes in the human brain occur during the first two years of life, an infant's cognitive development is considered to be particularly vulnerable to iron deficiency (30,32). Most studies of iron and cognition in infants and toddlers use the standardized test of infant development, the Bayley Scales of Infant Development. This test has three components, a mental developmental index, motor developmental index and an infant behavior record (30). Infants and toddlers with iron deficiency anemia generally perform poorly on tests of mental and motor development (30,31,37-42). Further, these infants and toddlers are described as being more withdrawn, cautious, hesitant and maintain closer physical proximity to their mothers than iron replete children (32,41). These types of behaviors could interfere with an infant's or toddler's ability to interact with the environment which in turn could compromise intellectual development.

Although iron deficiency is associated with impaired cognitive function in infants and children, a causal relationship has yet to be conclusively established. As reviewed by Abbott (31), both short-term and long-term iron intervention studies indicate little or an inconsistent improvement in infants' mental or cognitive function. These findings may be explained by differences in the duration and extent of iron deficiency, the design of the studies and the presence of confounding factors such as other nutrient deficiencies (43). Generally, lower scores of mental development have been observed in infants with iron deficiency anemia than in those with iron deficiency without anemia, indicating an effect of the severity of iron deficiency (39).

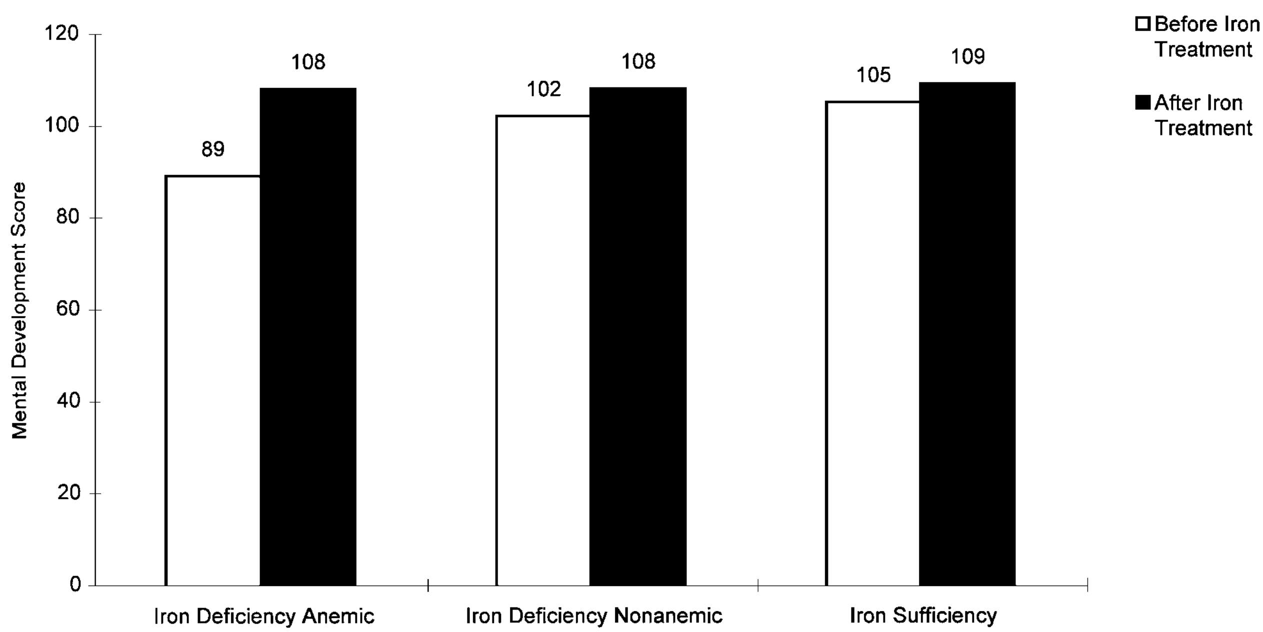
The strongest support for a causal link between iron deficiency and cognitive development in the early years comes from a double-blind, randomized controlled study of 126 toddlers between 12 and 18 months of age (37). The toddlers were grouped according to their iron status and within each group children were randomly assigned to receive either 3 mg ferrous sulfate/kg body weight a day or a placebo for four months. Before treatment, the mental development scores of toddlers with iron deficiency anemia were significantly lower than those of the nonanemic iron deficient and iron sufficient toddlers **(Figure 2)**. Iron supplementation significantly improved motor and mental development scores. Further, after 4 months of treatment, mental development scores of the iron supplemented toddlers were the same as those for iron sufficient toddlers and those with iron deficiency without anemia **(Figure 2)**. This study demonstrates that increasing the iron intake of iron deficient infants improves their performance on mental and motor development tests to a level of performance matching that of iron sufficient infants (37).

An important question relates to whether the adverse developmental and cognitive effects of early iron deficiency anemia persist. Some studies indicate that the mental developmental effects of iron deficiency anemia are reversible with appropriate iron treatment (37,44), whereas this finding is not supported by other studies (32,40,42). Infants with iron deficiency anemia who performed poorly on infant assessment tests have been found to have lower mental developmental scores at age 5 years and older than those who were not anemic (40). A recent follow-up study found that children who were iron deficient in infancy continued to test lower in reading, writing and arithmetic (i.e., basic learning skills), as well as overall motor skills 12 years later, despite normal iron status (42). These findings indicate that iron deficiency in infancy has a long term negative influence on cognition. However, questions remain regarding the effects of the timing, severity and/or chronicity of iron deficiency as well as the reversibility of iron deficiency on cognitive function (45,46).

- **Preschool Children (3 to 6 years)**

Iron deficiency anemia among preschool children is associated with poor performance on I.Q. tests, learning tests and school achievement measures which indicate specific cognitive processes such as short-term memory, attention, discrimination learning or tasks critical to solving visual problems (30). Compared to infants, the

Figure 2. Mean Mental Development Score Before and After Treatment with Ferrous Sulfate in 12 to 18 Month Infants



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cognitive benefits of iron treatment appear to be more apparent for preschool children, although the evidence is limited. A major influence of iron deficiency anemia on preschool children is thought to be on attention, arousal and motivation. Also, preschool children with iron deficiency anemia tend to be less happy and responsive to their environment than iron replete children.

• Primary School Children and Adolescents (6 years and older)

Similar to findings from infants and preschool children, iron deficiency anemia is associated with cognitive impairments in school age children and adolescents, as usually assessed by tests of cognition or school achievement (30). In a cross-sectional, case-control study in Northern Ireland involving school children aged 7 to 8 years, children who experienced learning difficulties were more likely to have iron deficiency anemia than controls (47). A study in Egypt involving 8 to 11 year old children also found that iron deficiency anemia adversely affects cognitive performance (20). The children with iron deficiency anemia made more errors and were less efficient in the "Matching Familiar Figure Test" than nonanemic children (20). This study demonstrated that anemic children treated with oral ferrous sulfate (50 mg or about 2 mg elemental iron) for 6 consecutive days/week for four months reduced their errors and improved their efficiency scores.

A major influence of iron deficiency anemia on preschool children is thought to be on attention, arousal and motivation.

Among adolescents, studies in different areas of the world including Indonesia (48,49), Thailand (50) and India (51), among other countries (20), have found that iron deficiency anemia is associated with poor academic performance and that iron supplementation (ferrous sulfate) improves test scores related to specific components of cognition. A recent study in the U.S. is perhaps one of the most important studies in recent years linking mild iron deficiency, which is common, with adverse effects on cognition (52). In this double-blind, placebo-controlled clinical trial, 73 non-anemic, iron deficient adolescent girls were randomly assigned to receive oral ferrous sulfate (650 mg twice daily or 260 mg elemental iron daily) or a placebo for eight weeks. Cognitive functioning was measured by four tests of attention and memory. Compared to the control group, the iron supplemented group displayed improved verbal learning and memory, both of which are important for academic performance (52). This study is unique in its finding that mild iron deficiency adversely affects cognitive function and that iron supplementation improves some aspects of cognition (52). The above findings with school-age and adolescent children are in contrast to those in infants for whom the benefits of iron treatment on mental development are less consistently observed.

• Adults

In a cross-sectional study of 69 healthy University students, iron deficiency was associated with abnormalities in electrophysiology (EEG) of the brain and abnormal cognition (53). Higher levels of serum ferritin were associated with greater activation of the left hemisphere of the brain than the right. Iron status was significantly related to cognitive performance on two of the cognitive tasks, and these relationships were consistent with EEG asymmetries. Higher serum ferritin predicted greater verbal fluency but poorer nonverbal auditory task performance. These findings indicate that body iron stores are relevant to specific neurophysiological processes supporting attention (53).

In adult women, dieting to lose weight may reduce iron status and the ability to sustain attention even with adequate dietary iron intake, according to a recent study (54). Following a 3 week baseline period, 14 obese women 25 to 42 years of age consumed a 50% energy restricted diet for 15 weeks and then a weight stabilization diet for 3 weeks. During the calorie restriction and weight stabilization periods, the women received a supplement providing 100% of the RDA (or estimated safe and adequate amount) of vitamins and minerals. Total dietary iron intake during the energy restricted and maintenance periods was at a level of twice the RDA for iron. Despite this relatively high intake of dietary iron, iron and hematological status declined during the study. Further, the decline in iron status (e.g., hemoglobin levels) was associated with a decreased ability to sustain attention (54). The researchers suggest that the inability to sustain attention may be an early sign of developing functional iron deficiency in the presence of normal iron status.

In older adults, maintenance of cognitive performance is particularly important for their functional independence (55). Few studies, however, have addressed the relationship of iron status and cognition in this growing segment of the population. In a study of 28 healthy adults over 60 years, three different indices of iron status (i.e., plasma iron, transferrin, and ferritin) were inconsistently associated with cognitive performance (55). However, iron deficiency was associated with subtle changes in an electroencephalogram indicative of neuropathologic changes in the aged brain (55). In another investigation in Spain involving 260 adults aged 65 to 90 years of age, dietary iron intake was positively associated with scores on two tests of cognitive function (3).

Adequate iron nutrition in infants and children is essentail for cognitive functioning and to provide a foundation for school and lifelong learning.

e) What Can Be Concluded About Iron and Cognition?

Adequate iron nutrition in infants and children is essential for cognitive functioning and to provide a foundation for school and lifelong learning. Considering that iron deficiency anemia in infancy may have long-lasting effects on mental and motor performance, prevention of iron deficiency in this age group should be a priority. Identifying iron deficiency in preschool, school-age children and adolescents is important given that improving their iron status has a positive effect on their cognitive performance and academic achievement. Although there are strong reasons to suspect that iron deficiency compromises cognitive functioning in adults, additional research on this population group is needed.

It is difficult to compare studies in different age groups because of the presence of confounding factors such as other dietary deficiencies which may influence brain function, socioeconomic factors which may affect tests of mental performance and measures used to test cognition (56). More information is needed on whether there is a critical time when individuals are particularly vulnerable to inadequate iron intake or when iron deficiency contributes to irreversible cognitive impairments (31). In addition, the effects of the duration and severity of iron deficiency on cognitive function remain to be established.

Part III. Zinc's Role in Cognitive Development and Functioning

a) Zinc Deficiency Is Not Uncommon

Severe zinc deficiency is relatively rare, but mild zinc deficiency affects a substantial segment of the world population, including the United States (57,58). Although mild zinc deficiency is difficult to identify clinically and dependent on a diet history, it may occur even in populations that appear adequately nourished (59).

What causes zinc deficiency? Physiological processes such as growth increase the need for zinc. Therefore, young children, adolescents and pregnant women may be at high risk of zinc deficiency (57). Low zinc intake and low bioavailability of zinc can compromise zinc status (58). Data collected from nationwide surveys, including the USDA CSFII, 1994-96, NHANES II and Phase I of NHANES III indicate low zinc intakes for many segments of the U.S. population (26,27,29,60, **Table 1**). The zinc intake of young women 18 to 24 years of age who participated in NHANES II was found to be well below (8.11 mg/day) the RDA of 15 mg zinc/day (29). Similarly, data from NHANES II indicate that many infants, children, young women and older adults consume less zinc than recommended (26,60). The bioavailability of zinc differs among foods (58). In general, zinc is more available from foods of animal than plant origin (60). For example, phytate in cereal bran and legumes limits the bioavailability of zinc (60). Individuals can be at risk of mild zinc deficiency as a result of poor food choices including a low intake of animal products such as red meat which contains a high amount of readily available zinc. For older adults, diseases or medications which decrease zinc bioavailability or increase its demand also place them at risk of marginal zinc deficiency. In addition, poverty and other socioeconomic factors can affect food choices and compromise zinc status (57).

b) How Does Zinc Influence Cognition?

Mechanisms linking zinc to cognitive development and function are unclear. However, zinc is essential for maturation of the brain and its function (57,61). Many zinc mediated mechanisms that affect brain function have been identified. Certain neurons of the hippocampus are rich in zinc (62), and about 8 to 10 % of zinc within neurons is transported in vesicles and can be exchanged with other neurons. Electrical stimulation of the hippocampal mossy fibers of zinc deficient rats has been demonstrated to cause an electrical signal that differs from that of normal rats (63). Zinc is released into interneuronal space during transmission where it may modulate responses of excitatory and inhibitory neurotransmitter receptors (64). Zinc plays a critical role in the development of the central nervous system during pre- and postnatal life (61). As reviewed by Caulfield et. al. (61), zinc-dependent enzymes play a role in cell replication processes necessary for brain growth, and zinc-dependent neurotransmitters influence memory. In addition, zinc is involved in metabolic processes outside the central nervous system such as transport of hormones and the production of neurotransmitter precursors which ultimately affect the central nervous system (61).

Although mild zinc deficiency is difficult to identify clinically and dependent on a diet history, it may occur even in populations that appear adequately nourished.

c) Experimental Animal Studies Link Zinc to Cognition

The essentiality of zinc for neuropsychological function was first demonstrated in studies of experimental animals, mostly rats and rhesus monkeys. These studies also indicated potential mechanisms by which zinc affects cognitive development. Zinc deficiency in animals is associated with structural malformations in the brain and changes in enzymes and proteins important for neurotransmission (65).

Behavioral problems such as reduced attention, memory and ability to learn have also been described in zinc deficient animals (21,65-70). In a series of studies in rhesus monkeys, zinc deficiency during prenatal, early postnatal and adolescent/puberty years altered cognitive behavior, evidenced by decreased motor activity and attention, abnormalities in short-term memory and difficulties solving problems (68-70). When monkeys were continually exposed to marginally low zinc intakes from the fetal period through puberty, motor activity and changes in behavior (e.g., vigilance as assessed by continuous performance tasks) decreased before reductions in growth and plasma zinc levels (70). These findings in non-human primates (68-70) have important implications for humans. Experimental animal studies indicate that zinc deficiency may interfere with cognitive performance by decreasing motor activity and increasing emotionality (21).

d) Human Studies Link Zinc and Cognition

Only a handful of studies have examined zinc's role in human cognition. Although the relationship is yet to be clearly established, emerging research supports a beneficial role for zinc in cognitive development and functioning.

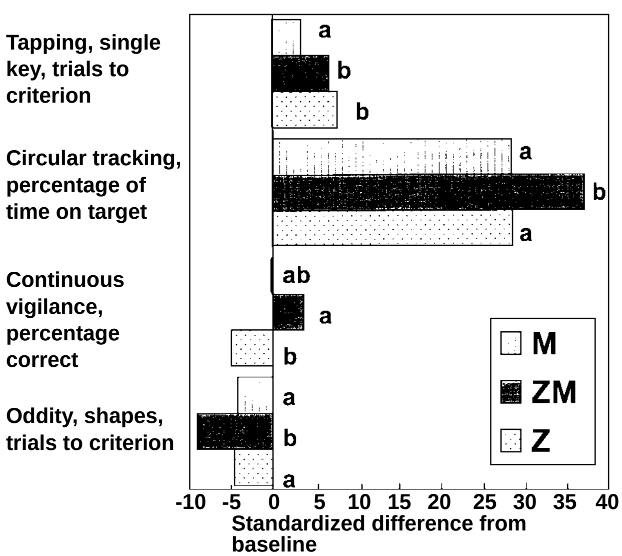
- **Children**

As reviewed by Black (21), studies of infants and children through the preschool years indicate that zinc may be important to children's cognitive development. In children born with acrodermatitis enteropathica, a rare genetic disorder of severe zinc deficiency, deficits in behavioral and cognitive performance have been reported (4). Increasing the zinc intake of infants with low birth weights and those living in countries such as India and Guatemala has been associated with improved motor development and functional activity (71,72).

A recent study involving 6 to 9 year old first grade children from low-income families in China demonstrated that zinc improves cognitive performance once other micronutrient deficiencies are corrected (73). In this double-blind, controlled trial, 740 Chinese children received 20 mg zinc alone, 20 mg zinc with a supplement of vitamins, minerals and trace elements, or the micronutrient supplement alone six times/week for 10 weeks (73). Neuropsychologic performance, including fine and gross motor skills and eye-hand coordination, attention, visual perception, short-term memory, concept formation and abstract reasoning were assessed by a variety of tests. Improved performance was observed after treatment with zinc and the micronutrient supplement than with the supplement or zinc alone **(Figure 3)**. The change in neuropsychologic performance was similar for the mineral supplement and the zinc treated groups (73).

Other studies in children have failed to find a positive association between zinc and cognition (74,75). Cognitive functioning and attention were unchanged in school-age Ontario boys who received a zinc supplement of 10 mg/day for one year (74). Likewise, measures of attention were unchanged in stunted 6 to 7 year old children in Guatemala who received a zinc supplement (10 mg/day) for about three months (75). The failure of these zinc supplement studies to improve children's cognition (74,75) may be explained by deficiencies of other micronutrients which limit the response to zinc or by insensitivity of the tests used. Also, children's zinc status may influence their cognitive development by affecting their emotionality, response to environmental stress, and motor activity (21).

Figure 3. Effect of Zinc (Z) and Micronutrients (M) on Neuropsychologic Performance in 6 to 9 Year Old Chinese Children*



*An increase in score indicates a positive response for all but the number of trials needed for correct recognition of odd shapes, for which a decrease is a positive response.

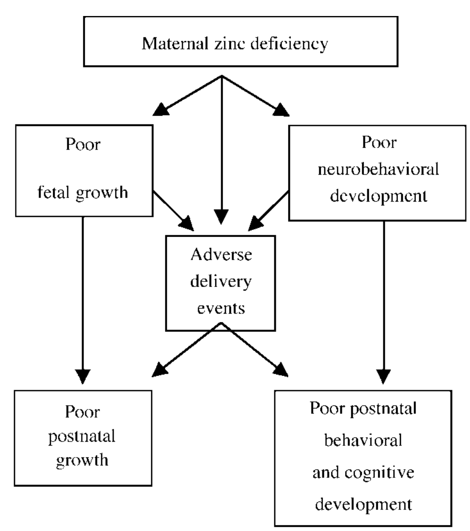
From Ref. 73.

- **Adults**

Few studies have examined the effect of zinc status on adults' cognitive functioning. However, two pilot studies in humans found that mild zinc deficiency impaired performance on neuropsychological tasks such as short term visual memory (76,77). Based on experimental animal data, mild to moderate maternal zinc deficiency could be expected to adversely affect both human mother's cognitive functioning and the cognitive development of her infant (61, **Figure 4**). A positive association has been reported between maternal zinc status during pregnancy and infants' developmental status (78,79). The association was particularly strong between mothers' zinc intake and status during the second trimester of pregnancy and neonatal measures of attention and processing of information, both of which reflect cognitive ability (79). These findings, along with data from non-human primates, indicate that maternal zinc status during midpregnancy may be especially important for the development of infants' central nervous system and later cognitive functioning.

Little information is available regarding the role of zinc in cognitive functioning in older adults. However, a positive association between dietary zinc intake and cognitive function in adults aged 65

Figure 4. Interrelations Between Maternal Zinc Deficiency and Pre- and Postnatal Growth and Development



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to 90 years in Spain was recently reported (3). In the early 1980s, Burnet (80) hypothesized that zinc deficiency could be associated with senile dementia of Alzheimer's type because several zinc-dependent enzymes are involved in neuronal metabolism. Other researchers related plasma zinc levels one year prior to death to plaque intensity in the brain at death (81). Impaired zinc metabolism, specifically low plasma levels of zinc and thymulin (a zinc carrier peptide), has been found in patients with senile dementia of Alzheimer's type (82). The finding of reduced levels of zinc in the blood and brain tissues of patients with Alzheimer's disease has led to the suggestion that zinc may play a role in the processing of memory (83). A preliminary study involving six patients with this disease found that 15 mg oral zinc in the form of zinc chelated with methionine twice daily for one year corrected platelet membrane microviscosity in the six patients and modestly improved cognition in four patients as measured by psychometric testing (83). These findings, albeit suggestive, support the need for more research on zinc and Alzheimer's disease.

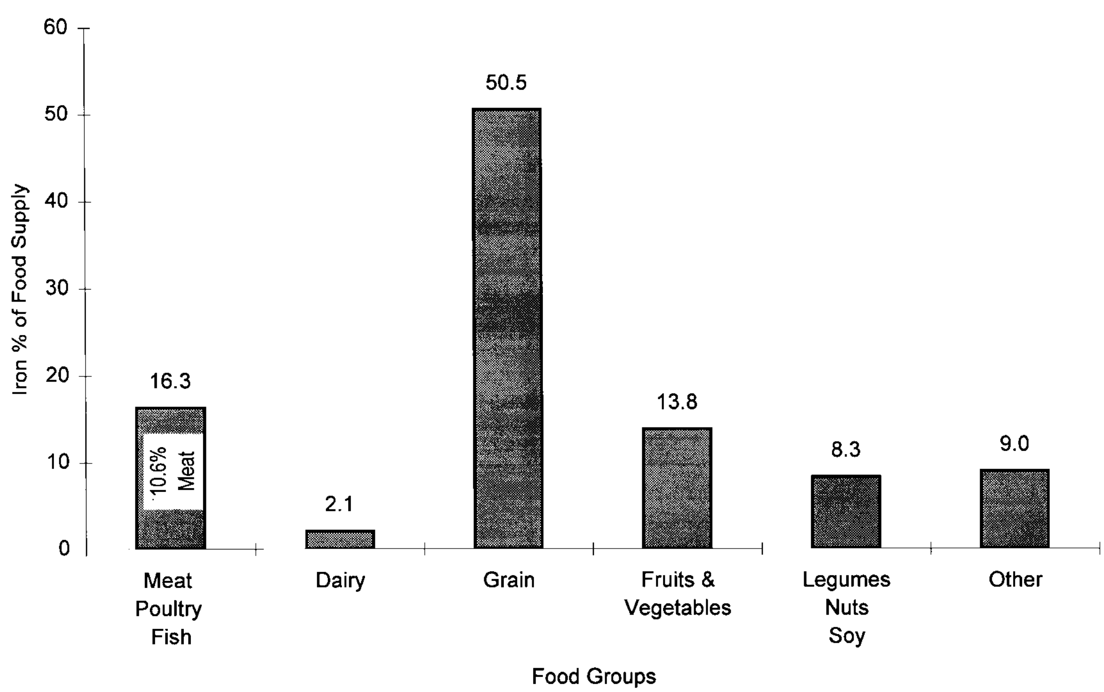
e) What Can Be Concluded About Zinc and Cognition?

Experimental animal studies indicate a biological role for zinc in central nervous system development and cognitive function. Also, behavioral effects have been demonstrated in zinc deficient animals. In humans, a recent study involving young school-age children in China found that correction of other micronutrient deficiencies was necessary before a beneficial effect of zinc on cognitive performance was observed (73). Zinc deficiency in humans, as in experimental animals, reduces motor activity which may impede cognitive development by interfering with the ability to acquire new or more complex skills. Well-controlled, randomized trials are needed to conclusively demonstrate the importance of zinc in human cognition and to determine whether infants and children are more vulnerable to the cognitive effects of zinc than adults.

Part IV. Can Beef Intake Improve Cognitive Performance?

As discussed below, red meat is a major source of bioavailable iron and zinc in the diet. Considering the potentially beneficial role of these nutrients in cognitive development and functioning, intake of red meat such as beef can be expected to improve cognition, particularly in individuals with or at risk of iron and/or zinc

Figure 5. Sources of Iron Available in the U.S. Food Supply, 1994.



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deficiency. Preliminary studies in adolescent rhesus monkeys have found that dietary beef protein not only corrects the hematological effects of an iron-zinc deficient diet, but it also alleviates some of the behavioral deficits associated with this diet (84,85). Increasing iron and zinc in the form of beef protein offset deficits in the animals' functioning of the central nervous system and significantly improved the percentage of correct scores on a sustained attention task (85). Nearly all research on the role of iron and zinc in cognition uses supplements rather than food sources of these nutrients. Considerably more research needs to be conducted using food sources of these nutrients such as meat, and beef in particular, to determine how these foods benefit cognition.

Part V. Meeting Iron and Zinc Needs

Meat Group foods (particularly red meat) are a major source of bioavailable iron and zinc in the diet (86). According to the latest data (1994), foods in the Meat Group contributed 16.3% of the iron and 41.5% of the zinc available in the nation's food supply (86, **Figures 5,6**). Meat alone contributed 10.6% of the iron and 30.4% of the zinc available for consumption.

In terms of actual intake, a nationwide survey of over 4,700 individuals found that the Meat Group provided 3.4 mg iron/day and 5.3 mg zinc/day (87, **Figure 7**). Due to its high content of iron and zinc, along with frequent consumption, beef provided nearly 58% of the iron and 68% of the zinc from all meats (87, **Figure 7**). Beef is a major source of iron and zinc for U.S. children ages 2 to 18 years and for adults, according to a recent analysis of major food sources of nutrients and dietary constituents (88,89). For both children and adults, beef was the third source of iron and the number one source of zinc in their diets (88,89). Nearly 8% of the iron intake of children 2 to 18 years of age, 6% of the iron intake of children 2 to 5 years of age, and 9.4% of adults' iron intake was provided by beef (88,89). Beef provided 22 % of total zinc consumed by children 2 to 18 years of age, 17% of the zinc intake of children 2 to 5 years of age, and 25.7% of adults' zinc intake (88,89). Other foods in the Meat Group such as poultry and dried beans made a considerably smaller contribution to iron and zinc intakes than did beef (88,89).

Red meat such as beef is a source of readily available iron and zinc. Due to fortification or enrichment with iron, foods in the Grain or Bread Group contribute more iron than foods in the Meat Group (**Figures 5,7**). However, foods from the Meat

Figure 6. Sources of Zinc Available in the U.S. Food Supply, 1994

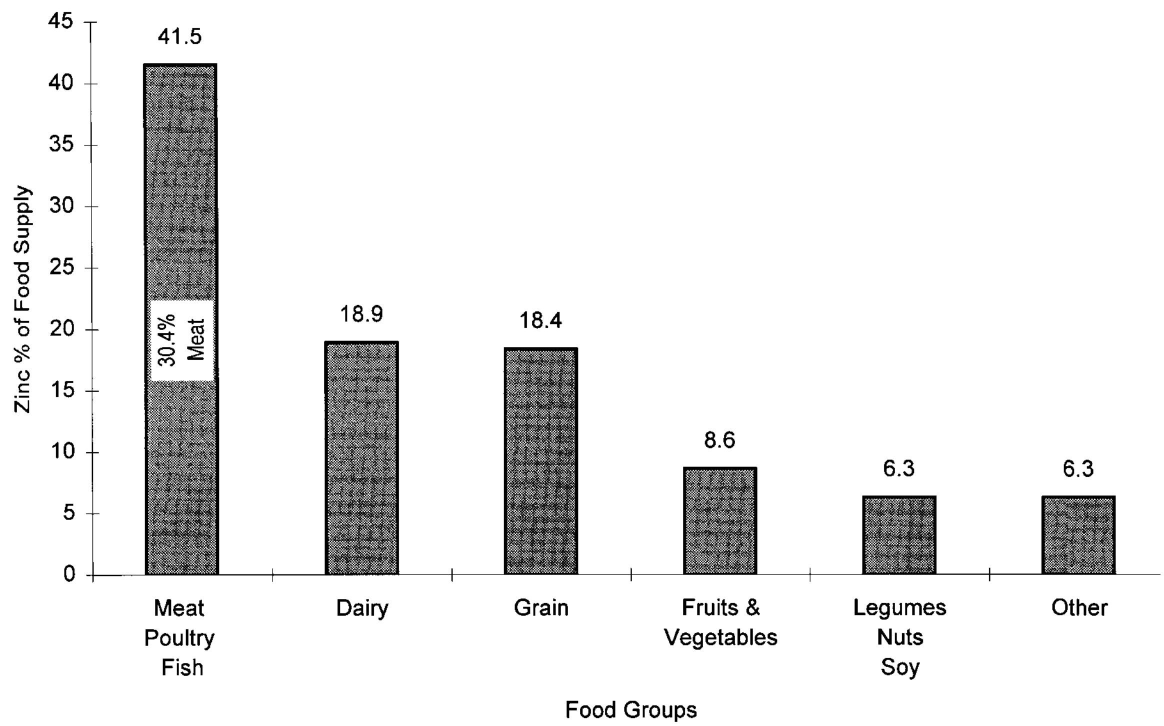

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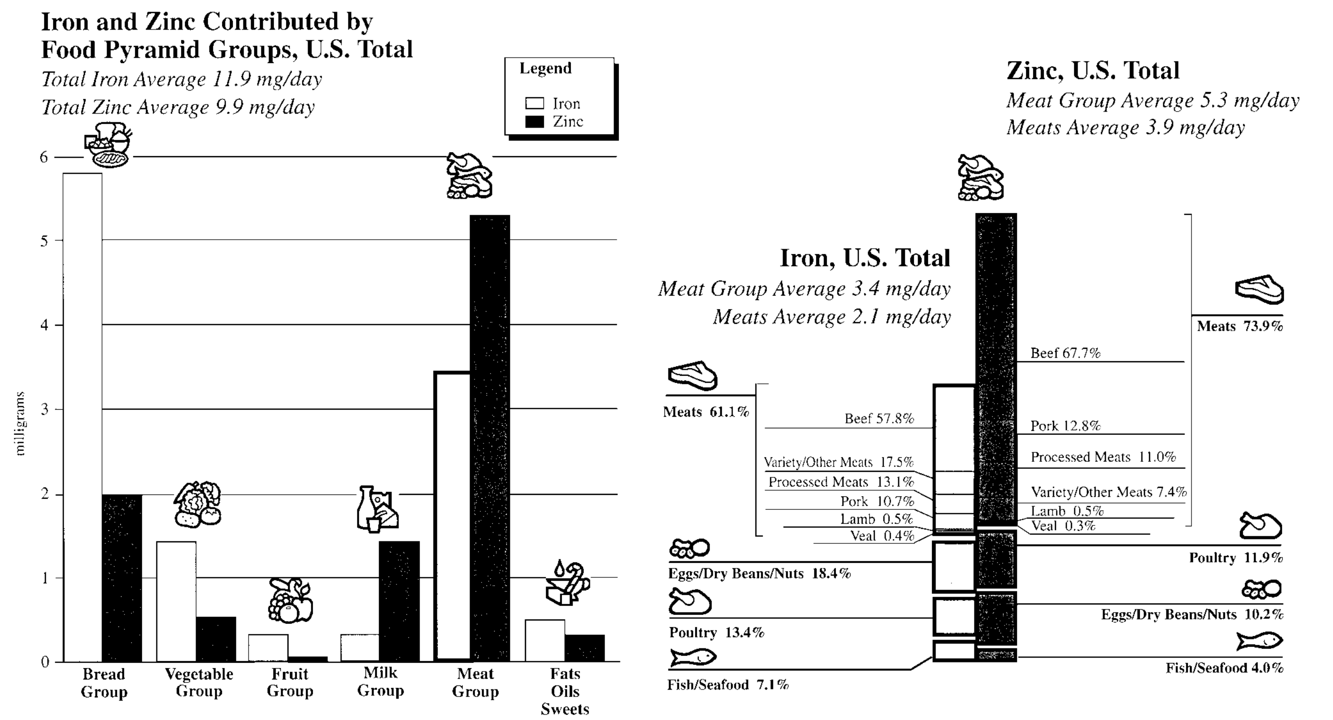
Figure 7. Iron and Zinc Contributed by Food Pyramid Groups, U.S. Total

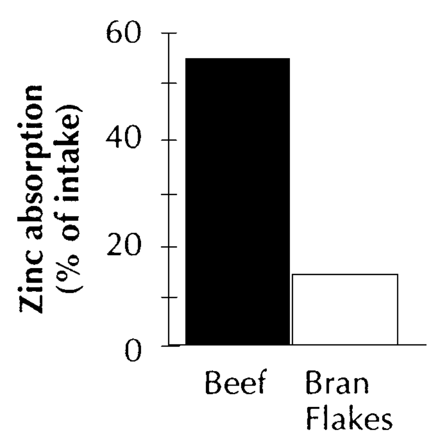


From Ref. 87.

Group contain heme iron which is more readily absorbed than non-heme iron found in grains, fruits, vegetables, eggs and dairy products. Heme iron is about two to three times more absorbable than non-heme iron (23). The bioavailability of non-heme iron is strongly affected by other foods consumed at the same meal (23,90). Absorption of non-heme iron in meat is facilitated by meat factor which also facilitates non-heme absorption from non-meat sources. Vitamin C enhances non-heme iron absorption, whereas polyphenols in tea and coffee, and phytates in the bran fraction of whole grain cereals and legumes inhibit iron absorption.

Zinc is also readily available from red meats such as beef (91,92). The bioavailability of zinc from beef was found to be about four times greater than that from a high-fiber breakfast cereal when consumed by healthy adults (93, **Figure 8**). Similarly, a recent study in infants found that the fractional absorption of zinc was higher from beef than from cereal (94). Typical infant weaning foods in the U.S. are poor sources of iron and zinc. Introducing meat as an early infant food benefits growth and provides adequate bioavailable iron and zinc to meet infants' needs for these nutrients, according to a recent one-year longitudinal study (95). This study compared growth in 19 breastfed infants who were fed either beef or iron-fortified rice cereal as initial weaning foods. Adequate intake of dietary iron and zinc is particularly important during the weaning period when infants' liver stores of these nutrients often are depleted and intake of cereals, from which these nutrients are poorly available, is increased. In the study noted (95), there was high acceptability of beef, as an initial weaning food, by both the infants and mothers. This contrasted with existing "dogma" that cereal should always be introduced first.

Figure 8. Comparison of Zinc Absorption from Beef and Cereal



Adapted from Ref. 93.

The RDAs for iron and zinc for various age groups are presented in **Table 2** (28). Good sources of these nutrients include foods in the Meat Group, especially meat such as beef (96, **Table 3**). In many cases, meats rich in zinc are also rich in iron. With the exception of iron supplements for pregnant women, foods are considered the best source of nutrients such as iron and zinc (97). The U.S. Department of Agriculture's Food Guide Pyramid (**Figure 9**) recommends that all healthy Americans consume two to three servings/day of foods from the Meat Group (98). Following the Food Guide Pyramid may provide adequate intakes of bioavailable zinc and iron (99). This is especially true if red meat is consumed. However, if poultry, fish and beans are eaten instead of red meat and if the diet is rich in foods containing substances that interfere with the absorption of zinc and iron, needs for these nutrients may not be met by following the Food Guide Pyramid (60,99)

Part VI. The Bottom Line

Accumulating evidence from experiments in animals and humans indicates that iron and zinc have important roles in cognition. Adequate intakes of these nutrients during the early years of life are important for brain development and subsequent function. Though limited, data from adults indicate that iron and zinc are also important for adult cognition.

Most research examining the effect of iron and zinc on cognition has used supplements to demon-

Table 2. Recommended Dietary Allowances for Iron and Zinc, 1989

	Age (yrs)	Iron (mg)	Zinc (mg)
Infants	0 - 0.5	6	5
	0.5 - 1	10	5
Children	1 - 10	10	10
Males	11 - 18	12	15
	19 - 51+	10	15
Females	11 - 50	15	12
	51+	10	12
Pregnant		30	15
Lactating -			
1st 6 months		15	19
2nd 6 months		15	16

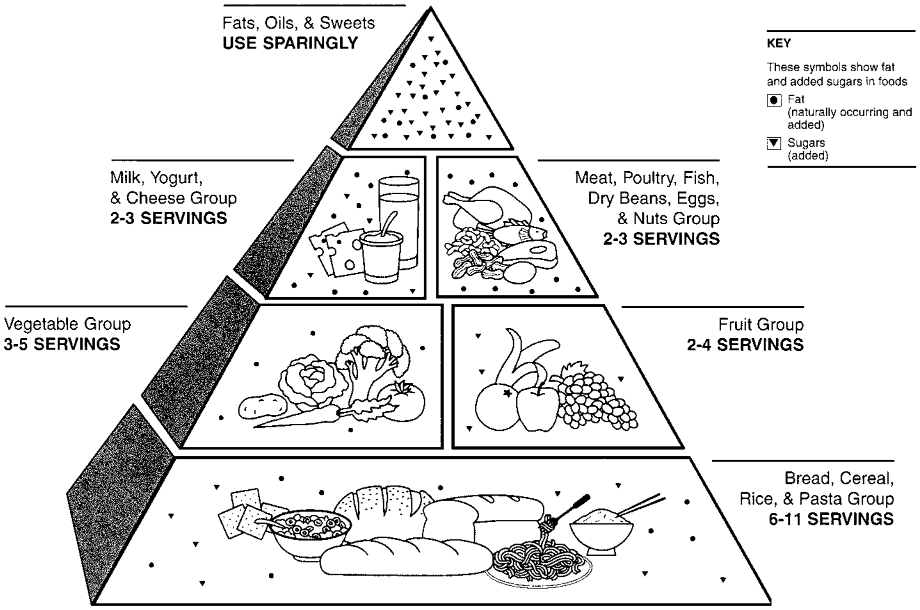
From Ref. 28.

Table 3. Iron and Zinc Content of Selected Foods

Food	Iron (mg)	Zinc (mg)
Meat/Poultry/Fish (3 ounces, cooked, lean only)		
Beef Chuck, Arm Pot Roast, Braised	3.2	7.4
Beef Round Tip, Roasted	2.5	6.0
Beef Sirloin, Broiled	2.9	5.5
Beef Top Round, Broiled	2.4	4.7
Beef Tenderloin, Roasted	3.1	4.1
Beef, Ground, Extra Lean, Broiled, Well-done	2.4	5.5
Ham, Boneless, 5-11% fat	1.2	2.4
Pork Tenderloin, Roasted	1.2	2.2
Lamb Loin, Roasted	2.1	3.5
Veal Cutlet, Pan Fried	0.7	2.4
Chicken Leg, Roasted	1.1	2.4
Chicken Breast, Roasted	0.9	1.0
Turkey Leg, Roasted	2.2	3.8
Turkey Breast, Roasted	1.3	1.7
Tuna, Light Meat, Canned	1.3	0.7
Salmon, Sockeye, Dry Heat	0.5	0.4
Oysters, 6 Medium Raw	4.8	49.8
Shrimp, Moist Heat	2.6	1.3
Dairy Products		
Yogurt, Lowfat, Plain, 1 Cup	0.2	2.2
Milk, Lowfat, 1 Cup	0.1	1.0
Cheese, Cheddar, 1 ounce	0.2	0.9
Cereals/Grains		
Raisin Bran Cereal, Dry, 1 Cup	5.0	3.0
Shredded Wheat, Dry, 1Cup	1.2	1.0
Oatmeal, Instant, 1/2 Cup	4.2	0.6
Bran Muffin, 1 Medium	2.4	0.6
Bagel, 1-3 1/2 inch	1.2	0.6
Whole Wheat Bread, 1 Slice	0.9	0.5
White Rice (enriched), Cooked, 1/2 Cup	1.0	0.4
White Bread (enriched), 1 Slice	0.8	0.2
Fruits/Vegetables		
Banana, 1 Medium	0.4	0.2
Apricots, Dried, 7 Halves	1.2	0.2
Prunes, Dried, 3 Medium	0.6	0.1
Apple, 1 Medium	0.2	0.1
Peas, Green, Cooked, 1/2 Cup	1.3	0.9
Potato, Baked with Skin, 1 Medium	2.8	0.6
Broccoli, Raw, 1/2 Cup	0.6	0.2
Carrots, Raw, 1 Medium	0.3	0.1
Beans/Legumes/Other		
Baked Beans, Canned, Plain, 1/2 Cup	0.4	1.8
Kidney Beans, Boiled, 1/2 Cup	2.6	0.9
Peanut Butter, 2 Tablespoons	0.6	0.9

From Ref. 96.

Figure 9. USDA's Food Guide Pyramid



From Ref. 98.

strate the essentiality of these nutrients. These data have been translated into intakes of food sources of these nutrients. Unfortunately, the effects of bioavailability have sometimes been ignored. Red meat is the best source of iron and zinc in the diet. The bioavailability of these nutrients from red meat such as beef is greater than that from plant sources such as many grain products, fruits and vegetables. Consuming at least 5 to 7 ounces (i.e., 2 to 3 servings)/day of lean cooked meat, including red meat, as part of a nutritionally balanced diet containing a variety of foods is important to help meet iron and zinc needs, achieve overall good health and potentially benefit cognitive development and functioning.

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