Iron and Immunity

Arzneimittelforschung. 2007;57(6A):417-25.

Effect of oral supplementation with iron(III)-hydroxide polymaltose complex on the immunological profile of adolescents with varying iron status.

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OBJECTIVE: To assess the effects of iron supplementation on immunological parameters of adolescents with varying iron status. METHOD: Adolescents of both sexes with varying iron status were allocated to four treatment groups by using inclusion criteria. Three of the four groups received iron(III)-hydroxide polymaltose complex (IPC, Maltofer) containing 100 mg of iron 6 days a week for 8 months. The fourth group was given a placebo. Immunological parameters were assessed at baseline and after 4 and 8 months of supplementation. RESULTS: Increases from baseline to 4 months and from 4 to 8 months of supplementation were observed for Bactericidal Capacity of Neutrophils (BCA), NitroBlue Tetrazolium Reduction Test (NBT), and phytohaemagglutinin (PHA) in all three supplemented groups. No increase was found in the control placebo group except for PHA. No side effects were noted in any participants. CONCLUSION: IPC supplementation for eight months led to significant improvements of immunological parameters in iron deficient adolescents with and without anemia.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 17691591 [PubMed - indexed for MEDLINE]

Biol Trace Elem Res. 2009 Feb;127(2):95-101. Epub 2008 Sep 30.

Early effects on T lymphocyte response to iron deficiency in mice. Short communication.

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Iron deficiency is a common nutritional disorder, affecting about 30% of the world population. Deficits in iron functional compartments have suppressive effects on the immune system. Environmental problems, age, and other nutrient deficiencies are some of the situations which make human studies difficult and warrant the use of animal models. This study aimed to investigate alterations in the immune system by inducing iron deficiency and promoting recuperation in a mouse model. Hemoglobin concentration, hematocrit, liver iron store, and flow cytometry analyses of cell-surface transferrin receptor (CD71) on peripheral blood and spleen CD4+ and CD8+ T lymphocyte were performed in the control (C) and the iron-deficient (ID) groups of animals at the beginning and end of the experiment. Hematological indices of C and ID mice were not different but the iron stores of ID mice were significantly reduced. Although T cell subsets were not altered, the percentage of T cells expressing CD71 was significantly increased by ID. The results suggest that iron deficiency induced by our experimental model would mimic the early events in the onset of anemia, where thymus atrophy is not enough to influence subset composition of T cells, which can still respond to iron deficiency by upregulating the expression of transferrin receptor.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 18825318 [PubMed - indexed for MEDLINE]

J Autoimmun. 2008 Feb-Mar;30(1-2):84-9.

New functions for an iron storage protein: the role of ferritin in immunity and autoimmunity.

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Ferritin is a ubiquitous and specialised protein involved in the intracellular storage of iron; it is also present in serum and other biological fluids, although its secretion processes are still unclear. We here review evidence supporting the hypothesis that macrophages play a role in the production and secretion of extracellular ferritin, as well as evidence supporting a novel function as a signalling molecule and immune regulator. In particular, H-ferritin, which inhibits the proliferation of lymphoid and myeloid cells, may be regarded as a negative regulator of human and murine hematopoiesis. The idea that it also acts as a signalling protein has been supported by the cloning and characterisation of the specific H-ferritin receptor TIM-2, a member of the TIM gene family. A number of studies of the mouse TIM gene family indicate that this protein plays an important role in immune-mediated diseases. This last finding, together with the fact that ferritin acts as an immuno-suppressor, has allowed us to formulate hypotheses regarding the possible role of alterations of H-ferritin/TIM-2 binding/signalling in the pathogenesis of autoimmune diseases.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 18191543 [PubMed - indexed for MEDLINE]

Br J Nutr. 2007 Oct;98 Suppl 1:S24-8.

Iron, copper and immunocompetence.

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Microminerals including copper and iron are essential to immunity and health in human beings. The development of powerful tools in analytical cell biology and molecular genetics has facilitated efforts to identify specific cellular and molecular functions of trace elements in the maturation, activation and functions of host defence mechanisms. Selected recent reports about the role of copper and iron nutrition on immune functions are critically analysed here. Effects of trace element supplementation on infectious morbidity are also reviewed. While micromineral deficiencies, in general, may have widespread effects on nearly all components of immune response, these effects can be reversed by supplementation. However, the conflicting effects of iron deficiency and iron supplementation in vitro on the defensive systems reveals the urgent need for further additional information on the in vivo situation. In the elderly, vaccination against respiratory infections is likely to protect only 30-70% of the population. However, it may be possible to modulate immune function and ultimately reduce the severity of infections through micronutrient supplementation. Thus, microminerals contribute to the maintenance of the balance between immunity and health in humans.

Publication Types:

- Research Support, Non-U.S. Gov't
- Review

PMID: 17922954 [PubMed - indexed for MEDLINE]

Free Radic Biol Med. 2008 Feb 1;44(3):483-92. Epub 2007 Oct 22.

Ceruloplasmin expression by human peripheral blood lymphocytes: a new link between immunity and iron metabolism.

Banha J, **Marques L**, **Oliveira R**, **Martins Mde F**, **Paixão E**, **Pereira D**, **Malhó R**, **Penque D**, **Costa L**.

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Ceruloplasmin (CP) is a multicopper oxidase involved in the acute phase reaction to stress. Although the physiological role of CP is uncertain, its role in iron (Fe) homeostasis and protection against free radical-initiated cell injury has been widely documented. Previous studies showed the existence of two molecular isoforms of CP: secreted CP (sCP) and a membrane glycosylphosphatidylinositol (GPI)-anchored form of CP (GPI-CP). sCP is produced mainly by the liver and is abundant in human serum whereas GPI-CP is expressed in mammalian astrocytes, rat leptomeningeal cells, and Sertolli cells. Herein, we show using RT-PCR that human peripheral blood lymphocytes (huPBL) constitutively express the transcripts for both CP molecular isoforms previously reported. Also, expression of CP in huPBL is demonstrated by immunofluorescence with confocal microscopy and flow cytometry analysis using cells isolated from healthy blood donors with normal Fe status. Importantly, the results obtained show that natural killer cells have a significantly higher CP expression compared to all other major lymphocyte subsets. In this context, the involvement of lymphocyte-derived CP on host defense processes via its anti/prooxidant properties is proposed, giving further support for a close functional interaction between the immune system and the Fe metabolism.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 17991445 [PubMed - indexed for MEDLINE]

Pediatr Res. 2007 May;61(5 Pt 1):520-4.

Maternal stress during pregnancy predisposes for iron deficiency in infant monkeys impacting innate immunity.

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The influence of maternal stress during pregnancy on the postpartum iron status and immune maturation of infants was investigated in a nonhuman primate model. Forty infant rhesus monkeys were generated from two types of disturbed pregnancies, early or late gestation stress, and compared with 24 undisturbed controls. Prenatal stress increased the prevalence and magnitude of iron deficiency (ID) as the infants' growth-related demands for iron exceeded dietary intake from breast milk. At 4-6 mo of age, the emergence of ID significantly accentuated an effect of prenatal stress on natural killer cell activity, an important component of innate immunity. These findings indicate that maternal stress, especially early in pregnancy, should be added to the list of risk factors that warrant closer scrutiny of hematological profiles in fast-growing babies.

Publication Types:

- Research Support, N.I.H., Extramural

PMID: 17413860 [PubMed - indexed for MEDLINE]

Indian J Med Res. 2006 Dec;124(6):647-54.

Impact of iron deficiency anaemia on T lymphocytes & their subsets in children.

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BACKGROUND & OBJECTIVES: While there is evidence of an altered immune profile in iron deficiency, the precise immunoregulatory role of iron is not known. Information particular in children who are vulnerable to iron deficiency and infection, is lacking. We undertook this study with the aim of documenting the changes in T cell subsets in children in the age group of 1 to 5 yr with iron deficiency. METHODS: The levels of T lymphocytes, their CD4+ and CD8+ subsets and the CD4 : CD8 ratio were evaluated in 40 iron deficient and 30 healthy children. The impact of oral iron supplementation for three months on the same parameters was also noted in 30 children. RESULTS: Significantly lower levels of T lymphocytes as well as CD4+ cells was observed in the iron deficient children ($P<0.01$ and 0.002 respectively). The CD4 : CD8 ratio was also significantly lower in this group ($P<0.05$). Iron supplementation improved the CD4 counts significantly. INTERPRETATION & CONCLUSION: Our study demonstrated quantitatively altered T cell subsets in iron deficiency in children, and a relationship between the severity of haematological and immunological compromise. The clinical and epidemiological implications of this relationship have topical relevance since ID is the most common micronutrient deficiency worldwide.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 17287552 [PubMed - indexed for MEDLINE]

Immunobiology. 2006;211(4):295-314. Epub 2006 Apr 17.

Iron-withholding strategy in innate immunity.

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The knowledge of how organisms fight infections has largely been built upon the ability of host innate immune molecules to recognize microbial determinants. Although of overwhelming importance, pathogen recognition is but only one of the facets of innate immunity. A primitive yet effective antimicrobial mechanism which operates by depriving microbial organisms of their nutrients has been brought into the forefront of innate immunity once again. Such a tactic is commonly referred to as the iron-withholding strategy of innate immunity. In this review, we introduce various vertebrate iron-binding proteins and their invertebrate homologues, so as to impress upon readers an obscured arm of innate immune defense. An excellent comprehension of the mechanics of innate immunity paves the way for the possibility that novel antimicrobial therapeutics may emerge one day to overcome the prevalent antibiotic resistance in bacteria.

Publication Types:

- Research Support, Non-U.S. Gov't
- Review

PMID: 16697921 [PubMed - indexed for MEDLINE]

Wei Sheng Yan Jiu. 2006 Jan;35(1):79-81.

[Effects of iron deficiency anemia on immunity and infectious disease in pregnant women]

[Article in Chinese]

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OBJECTIVE: To review the changes in immune function and incidence of infectious diseases in pregnant women with iron deficiency anemia (IDA), especially marginalde-ficiency of iron. METHODS: T lymphocyte subsets level (CD3+, CD4+ and CD8+), nature kill cells activity (CD16), interleukin-2 (IL-2) and serum IgA, IgG, IgM and complement C3 were determined in 3 different wormen groups, including 69 IDA pregnant women who were diagnosed by Hemoglobin, concentrations of free erythocyte porphrin and serum ferritin from 280 pregnant women during 30-38weeka of gestation, 52 random sampling normal pregnant women and 50 no pregnant women examined before marriage. RESULTS: The prevalenoe of IDA for pregnant women is 24.6%. The average concentration of Hb for pregnant women of IDA is 102.00(6.00 g/L The level of CD3+ and CD4+ cells, the ratio of CD4+/CD8+ cells, serum IL-2 as well as IgG levels in the pregnant women were significantly lower than that of those normal pregnant women ($P < 0.01$, $P < 0.05$, $P < 0.05$, $P < 0.01$). With the decreasing extent of Hb, these significant immunological indices of pregnant women will degrease. The incidence of infectious diseases in IDA pregnant women was significantly higher than that in normal pregnant women ($P < 0.05$). CONCLUSION: There are significantly effects of IDA on cellular immune function and infectious disease during pregnancy. The study on effects of IDA during pregnancy on nature kill cells activity (CD16) and incidence of infectious diseases during puerperium should be continued by increasing sample's number.

Publication Types:

- English Abstract

PMID: 16598942 [PubMed - in process]

Exp Mol Med. 2005 Aug 31;37(4):297-310.

Iron chelator induces MIP-alpha/CCL20 in human intestinal epithelial cells: implication for triggering mucosal adaptive immunity.

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A previous report by this laboratory demonstrated that bacterial iron chelator (siderophore) triggers inflammatory signals, including the production of CXC chemokine IL-8, in human intestinal epithelial cells (IECs). Microarray-based gene expression profiling revealed that iron chelator also induces macrophage inflammatory protein 3 alpha (MIP-3alpha)/CC chemokine-ligand 20 (CCL20). As CCL20 is chemotactic for the cells involved in host adaptive immunity, this suggests that iron chelator may stimulate IECs to have the capacity to link mucosal innate and adaptive immunity. The basal medium from iron chelator deferoxamine (DFO)-treated HT-29 monolayers was as chemotactic as recombinant human CCL20 at equivalent concentrations to attract CCR6(+) cells. The increase of CCL20 protein secretion appeared to correspond to that of CCL20 mRNA levels, as determined by real-time quantitative RT-PCR. The efficacy of DFO at inducing CCL20 mRNA was also observed in human PBMCs and in THP-1 cells, but not in human umbilical vein endothelial cells. Interestingly, unlike other proinflammatory cytokines, such as TNF-alpha and IL-1beta, a time-dependent experiment revealed that DFO slowly induces CCL20, suggesting a novel mechanism of action. A pharmacologic study also revealed that multiple signaling pathways are differentially involved in CCL20 production by DFO, while some of those pathways are not involved in TNF-alpha-induced CCL20 production. Collectively, these results demonstrate that, in addition to some bacterial products known to induce host adaptive immune responses, direct chelation of host iron by infected bacteria may also contribute to the initiation of host adaptive immunity in the intestinal mucosa.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 16155407 [PubMed - indexed for MEDLINE]

Int J Biochem Cell Biol. 2005 Sep;37(9):1768-73. Epub 2005 Mar 16.

Hepcidin: a direct link between iron metabolism and immunity.

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Hepcidin, originally discovered in urine as a bactericidal peptide synthesized by hepatocytes was later proved to be a key regulator of iron metabolism at the whole body level, namely, in conditions of altered iron demand such as the increased or decreased total amount of body iron, inflammation, hypoxia and anemia. The major mechanism of hepcidin function seems to be the regulation of transmembrane iron transport. Hepcidin binds to its receptor, protein ferroportin, which serves as a transmembrane iron channel enabling iron efflux from cells. The hepcidin-ferroportin complex is then degraded in lysosomes and iron is locked inside the cells (mainly enterocytes, hepatocytes and macrophages). This leads to lowering of iron absorption in the intestine and to a decrease in serum iron concentration. Utilizing this mechanism, hepcidin regulates serum iron levels during inflammation, infection and possibly also in cancer. Under these conditions iron is shifted from circulation into cellular stores in hepatocytes and macrophages, making it less available for invading microorganisms and tumor cells. In anemia and hypoxia, hepcidin regulates the availability of iron for erythropoiesis. Hepcidin or hepcidin-related therapeutics could find a place in the treatment of various diseases such as hemochromatosis and anemia of chronic disease.

Publication Types:

- Research Support, Non-U.S. Gov't
- Review

PMID: 16009323 [PubMed - indexed for MEDLINE]

Biomed Pharmacother. 2005 Jul;59(6):307-11.

Phagocytic capacity and apoptosis of peripheral blood cells from patients with iron deficiency anemia.

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Following clinical observations that patients with iron deficiency anemia (IDA) are more susceptible to infections than non-anemic individuals, the phagocytic capacity and number of apoptotic peripheral white blood cells (PWBC) from patients with IDA were examined. PWBC from 15 patients with IDA and from 18 healthy donors were incubated with various doses of iron. Phagocytosis was examined using latex particles and apoptosis was evaluated by a flow cytometric assay using propidium iodide staining. The percentage of phagocyting polymorphonuclear cells was lower in IDA patients compared to that of the controls. However, there was no difference in the percentage of phagocyting monocytes from individuals of both groups. The number of latex beads engulfed by each polymorphonuclear or monocyte was lower in IDA patients. Incubation with 100 microg% of iron did not affect the phagocytic ability of both cell types in IDA patients, but increased that of control cells. Incubation with 300 microg% of iron caused an increase in the phagocytic capacity of patients' cells and a decrease in that function in cells from controls. Higher dose (500 microg%) induced suppression of phagocytosis in cells from both groups. There was no difference in the number of apoptotic cells from individuals of both groups. Apoptosis of polymorphonuclears, but not mononuclear cells from both controls and IDA patients showed a linear dependency on the iron concentration in the medium. It is possible that the impaired phagocytic capacity of the PBWC found in patients with IDA contribute to the increased susceptibility to infections observed in these individuals.

PMID: 15996848 [PubMed - indexed for MEDLINE]

Hematol J. 2005;5(7):579-83.

The effect of iron deficiency anemia on the function of the immune system.

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We aimed to study the effect of iron deficiency anemia (IDA) on immunity. In 32 children with IDA and 29 normal children, the percentage of T-lymphocyte subgroups, the level of serum interleukin-6 (IL-6); and the phagocytic activity, the oxidative burst activity of neutrophils and monocytes and the levels of immunoglobulins were compared. There was no difference in the distribution of T-lymphocyte subgroups. The mean IL-6 levels was 5.6+/-3.9 pg/ml in children with IDA and 10.3+/-5.3 pg/ml in the control group (P<0.001). The percentage of neutrophils with oxidative burst activity when stimulated with pma was 53.4+/-32.7% in children with IDA and 81.7+/-14.3% in the control group (P=0.005). The percentage of monocytes with oxidative burst activity was 13.8+/-11.7% in children with IDA and 35+/-20.0% in the control group (P<0.001) when stimulated with pma. and 4.3+/-3.1 versus 9.7+/-6.0% (P=0.008) when stimulated with fMLP. The ratio of neutrophils with phagocytic activity was 58.6+/-23.3% in the anemic group; and 74.2+/-17.7% in the control group (P=0.057). The ratio of monocytes with phagocytic activity was 24.3+/-12.0% in the anemic group; and 42.9+/-13.4% in the control group (P=0.001). IgG4 level was 16.7+/-16.6 mg/dl in children with IDA and 51.8+/-40.7 mg/dl in healthy children (P<0.05). These results suggest that humoral, cell-mediated and nonspecific immunity and the activity of cytokines which have an important role in various steps of immunogenic mechanisms are influenced by iron deficiency anemia.

Publication Types:

- Comparative Study
- Research Support, Non-U.S. Gov't

PMID: 15692603 [PubMed - indexed for MEDLINE]

Zhonghua Xue Ye Xue Za Zhi. 1997 Nov;18(11):566-7.

[Cellular immunity in childhood iron deficiency anemia with recurrent respiratory infections]

[Article in Chinese]

Liu W, **Jiang A**, **Guo C**.

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OBJECTIVE: To examine interleukin-2 (IL-2) activity,serum soluble IL-2 receptor (sIL-2R) level and T lymphocyte subsets in peripheral blood from 63 childhood iron deficiency anemia (IDA) patients with recurrent respiratory infections(RRI). METHODS: IL-2 activity, sIL-2R level and T lymphocyte subsets were assayed by MTT, ELISA and APAAP, respectively. RESULTS: IL-2 activity, percentages of CD3+ and CD4+ cells as well as the ratio of CD4+/ CD8+ cells in the patients were significantly lower ($P < 0.01$),while sIL-2R levels were higher than that in normal controls ($P < 0.01$). No significant change was found in the percentage of CD8+ cells. CONCLUSION: Cellular immunity was impaired in childhood IDA with RRI.

Publication Types:

- English Abstract

PMID: 15625892 [PubMed - in process]

Nat Rev Microbiol. 2004 Dec;2(12):946-53.

Iron and microbial infection.

Schaible UE, **Kaufmann SH**.

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The use of iron as a cofactor in basic metabolic pathways is essential to both pathogenic microorganisms and their hosts. It is also a pivotal component of the innate immune response through its role in the generation of toxic oxygen and nitrogen intermediates. During evolution, the shared requirement of micro- and macroorganisms for this important nutrient has shaped the pathogen-host relationship. Here, we discuss how pathogens compete with the host for iron, and also how the host uses iron to counteract this threat.

Publication Types:

- Research Support, Non-U.S. Gov't
- Review

PMID: 15550940 [PubMed - indexed for MEDLINE]

Nature. 2004 Dec 16;432(7019):917-21. Epub 2004 Nov 7.

Lipocalin 2 mediates an innate immune response to bacterial infection by sequestrating iron.

Flo TH, **Smith KD**, **Sato S**, **Rodriguez DJ**, **Holmes MA**, **Strong RK**, **Akira S**, **Aderem A**.

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Although iron is required to sustain life, its free concentration and metabolism have to be tightly regulated. This is achieved through a variety of iron-binding proteins including transferrin and ferritin. During infection, bacteria acquire much of their iron from the host by synthesizing siderophores that scavenge iron and transport it into the pathogen. We recently demonstrated that enterochelin, a bacterial catecholate siderophore, binds to the host protein lipocalin 2 (ref. 5). Here, we show that this event is pivotal in the innate immune response to bacterial infection. Upon encountering invading bacteria the Toll-like receptors on immune cells stimulate the transcription, translation and secretion of lipocalin 2; secreted lipocalin 2 then limits bacterial growth by sequestrating the iron-laden siderophore. Our finding represents a new component of the innate immune system and the acute phase response to infection.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 15531878 [PubMed - indexed for MEDLINE]

J Vet Med B Infect Dis Vet Public Health. 2004 Jun;51(5):231-7.

Impairment of the peripheral lymphoid compartment in iron-deficient piglets.

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The aim of this study was to investigate the effect of neonatal iron deficiency on immune functions in young piglets. While control piglets were not given any iron preparation until the age of 21 days, another group of piglets was given 200 mg of Fe(3+)-dextran i.m. on day 3. Red blood cell parameters in the former, iron-deficient group were characteristic of hypochromic anaemia. In addition, the total leucocyte count ($P < 0.01$), relative and absolute neutrophil count ($P < 0.01$) and absolute lymphocyte count ($P < 0.05$) in peripheral blood were found significantly lower in iron-deficient piglets than in their iron-supplemented counterparts. Lymphocyte activity as measured by in vitro lymphocyte transformation test was impaired in iron-deficient piglets. A statistically significant decrease in circulating B-lymphocyte numbers was found in non-supplemented animals. Iron deficiency apparently negatively influenced the immunocompetence in piglets.

Publication Types:

- Clinical Trial
- Controlled Clinical Trial
- Research Support, Non-U.S. Gov't

PMID: 15330983 [PubMed - indexed for MEDLINE]

Cytokine. 2004 Apr 21;26(2):73-81.

Differential effects of iron deficiency and underfeeding on serum levels of interleukin-10, interleukin-12p40, and interferon-gamma in mice.

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BACKGROUND: Over-production of interferon-gamma (IFN-gamma) and under-production of interleukin-10 (IL-10) are associated with autoimmunity, whereas the opposite is associated with overwhelming infections. The influence of iron deficiency, a public health problem for children on in vivo secretion of these cytokines has not been previously investigated. OBJECTIVE: To determine whether iron deficiency alters serum levels of IFN-gamma, IL-10, and IL-12 in mice. DESIGN AND METHODS: Cytokine levels were measured by enzyme immunoassay in iron-deficient (ID), control (C), pair-fed (PF), and iron replete C57BL/6 mice for 3 (R3) and 14 (R14) days (n = 24-28, 12 R14). RESULTS: Iron deficiency was associated with > or = 50% reduction in hemoglobin, hematocrit, liver iron stores, and thymus weight ($p < 0.05$). Iron repletion improved these measurements. While iron deficiency significantly reduced IL-12p40 (64%) and IFN-gamma (66%) levels, underfeeding reduced those of IL-10 (48%) ($p < 0.05$). Iron repletion improved cytokine concentrations to PF levels. Thymus atrophy observed in 16 ID and 19 R3 mice, had no effect on IL-12p40 and IFN-gamma, whereas it further decreased IL-10 levels by 72% ($p < 0.05$). Cytokine levels positively correlated with indicators of iron status, body and thymus weights ($r < or = 0.688$, $p < 0.05$). CONCLUSION: Data suggest that iron deficiency alters the balance between pro- and anti-inflammatory cytokines, a change that may affect innate and cell-mediated immunity, and risk of autoimmune disorders.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 15050607 [PubMed - indexed for MEDLINE]

Am J Clin Nutr. 2004 Mar;79(3):516-21.

Immune function is impaired in iron-deficient, homebound, older women.

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BACKGROUND: Aging is often associated with a dysregulation of immune function. Iron deficiency may further impair immunity in older adults. Published reports on iron deficiency and immune response in humans are inconsistent. Most studies are focused on young children in developing countries and are often confounded by comorbid conditions, infections, and nutrient deficiencies. OBJECTIVE: Our objective was to determine the relation of iron status with immune function in homebound older women, who often have impairments in both iron status and immune response. The subjects were selected according to rigorous exclusion criteria for disease, infection, and deficiencies in key nutrients known to affect immunocompetence. DESIGN: Seventy-two homebound elderly women provided blood for comprehensive evaluation of iron status and cell-mediated and innate immunity. Women were classified as iron-deficient or iron-sufficient on the basis of multiple abnormal iron status test results. Groups were compared with respect to lymphocyte subsets, phagocytosis, oxidative burst capacity, and T cell proliferation upon stimulation with mitogens. RESULTS: In iron-deficient women, T cell proliferation upon stimulation with concanavalin A and phytohemagglutinin A was only 40-50% of that in iron-sufficient women. Phagocytosis did not differ significantly between the 2 groups, but respiratory burst was significantly less (by 28%) in iron-deficient women than in iron-sufficient women. CONCLUSIONS: Iron deficiency is associated with impairments in cell-mediated and innate immunity and may render older adults more vulnerable to infections. Further prospective studies using similar exclusion criteria for disease, infection, and concomitant nutrient deficiencies are needed for simultaneous examination of the effects of iron deficiency on immune response and morbidity.

Publication Types:

- Research Support, Non-U.S. Gov't
- Research Support, U.S. Gov't, Non-P.H.S.

PMID: 14985230 [PubMed - indexed for MEDLINE]

J Cell Biochem. 2003 Oct 1;90(2):278-86.

Effects of iron deficiency on the secretion of interleukin-10 by mitogen-activated and non-activated murine spleen cells.

Kuvibidila S, **Yu L**, **Ode D**, **Velez M**, **Gardner R**, **Warrier RP**.

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Interleukin (IL)-10 plays crucial regulatory roles in immune responses by inhibiting the secretion of several cytokines (IL-2, IL-12, interferon-gamma (IFN-gamma)) and lymphocyte proliferation. Iron deficiency, a public health problem for children, alters these immune responses. To determine whether these changes are related to altered IL-10 secretion, we measured IL-10 in 24 and 48 h supernatant of spleen cell cultures from iron deficient (ID), control (C), pairfed (PF), and ID mice fed the control diet (iron repletion) for 3 (R3) and 14 (R14) days (d, n = 12/group). Mean levels of hemoglobin, hematocrit, and liver iron stores varied as follows: C approximately equal PF approximately equal R14 > R3 > ID ($P < 0.01$). Mean baseline IL-10 levels of ID mice tended to be higher than those of other groups ($P > 0.05$, ANOVA). Mean IL-10 levels secreted by concanavalin A (Con A) and antibody raised against cluster of differentiation molecule 3 (anti-CD3)-treated cells (+/-background) were lower in ID than in C (48 h) and iron replete mice ($P < 0.05$). Underfeeding also reduced IL-10 secretion by anti-CD3-treated cells (48 h, $P < 0.05$). Lymphocyte proliferative responses to anti-CD3 +/- anti-CD28 antibodies were lower in ID than in C and PF mice, and they were corrected by iron repletion ($P < 0.05$). IL-10 levels negatively correlated with indicators of iron status (r <or= -0.285) and lymphocyte proliferation (r <or= -0.379 [r <or= -0.743 for ID mice]), but positively correlated with IFN-gamma levels (r <or= 0.47; $P < 0.05$). Data suggest that iron deficiency has a generalized deleterious effect on cells that secrete both cytokines. Reduced IL-10 secretion by activated cells does not overcome the inhibition of lymphocyte proliferation due to other factors of T cell activation that are regulated by iron.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 14505344 [PubMed - indexed for MEDLINE]