Exclusion of cereals from patients´ diets improves colon irritable, eczema and PMS. What are the mechanisms?

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1. Abstract:

It is well known that intolerance to certain foods may disturb the digestive system, cause skin problems and cause hormonal imbalance.
The aim of this study was to investigate the health effects of patients with colon irritable, eczema and PMS (premenstrual syndrome) after elimintion of cereals from the diet. A group of 20 patients with the diagnosis colon irritable, eczema and PMS eliminated meal from their diet. After some time follow up was done by telephone interview. 13 of the patients had the diagnosis colon irritable, 4 eczema and 2 had PMS. Almost all of the patients noticed a positive effect after the elimination of meal, some immediately, some after a couple of days and some after a couple of weeks.
The improvement after elimination of meal was rapid, more than half of the patients underwent an improvement after less then one week.
Patients with colon irritable showed an increased tendency of depression/beeing more stressed in general.
This study also show a significant sex distribution; 95% females and 5% males among the patients.

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2. Introduction:

Many people are suffering from different kinds of physical and psychical problems that are partly caused by intolerance to foods regularly consumed. This study reviews a group of patients that eliminate meal from their diet. The patient group is divided in three constitutions; colon irritable, eczema and PMS. The patients with colon irritable are belived to have irritable bowel syndrome (IBS) but candidiasis and coeliac disease are also possible diagnoses. Elimination of meal products is well known to improve these conditions.

2.1 Digestion: The primary function of the digestive tract is to extract nutrition from food. When the food particles are small enough they will be absorbed by passing through the tissue barrier into the body. The food that is not absorbed will pass through as feces. The internal canals of the body consist of specialized absorptive cells. Material from the outside environment is continuously entering the gut lumen and there might be a risk of absorption of disease-causing microorganisms, toxins and poisonous chemicals[(1)].
The food and materials are broken down into absorbable nutritients. Enzymes and secretions from organs are involved in this process. The important organs are salivary glands, pancreas, liver and gall bladder. The nutritients will bind to a transport protein and thereafter cross the epithelial cells that line the digestive tract[(2)].
Different foods are not digested at the same rate or efficiency. Therefore is it very important control is exerted by the digestive tract to ensure adequate mixing and digestion of each type of food at the various stages of its transport through the system. The first control in the small intestine is the ”duodenal break” which controls the passage of food from the stomach to the small intestine. If this system does not work the food material will pass out of the stomach too quickly and this results in the ”dumping syndrome”. The patient will develop upper abdominal pain, distention and early satiety. The dumping syndrome results in vasomotor effects. Some of these effects are thought to be caused by fluid beeing rapidly drawn into the jejunum from the surrounding tissues. This happens when the hypertonic gastric contents that has been dumped into the small intestine is diluted[(2)].

2.2 Cereals and the unwholesome content
Dry cereals contain in average 65-75% carbohydrate, mainly starch, 10-15% proteins and 2-8% lipids. The content of water of air-dry seeds is about 10-15%. There are four types of proteins present in cereals defined as albumins, globulins, prolamins and glutelins. 30-60% of the protein content consist of prolamin. The name prolamin refers to its high content of proline and glutamine. 50% of the protein in oat, barley and wheat consists of those aminoacids[(3)].
By eating carbohydrate the release of serotonin increases. Overeating of carbohydrates occur among patients who intend to make them feel better. This tendency to use certain food as drugs often causes obesity[(4)].
Cereals are among the most common food to induce hypersensitivity reaction. The most common antigen is wheat followed by barley and rye[(5)].

Several different foods can induce allergic reactions. Allergens that cross link the IgE on the mast cells along the gastrointestinal tract can induce symptoms as diarrhea and vasodilation. The degranulation of the mast cells along the gut can increase the permeability of mucous membranes, which enable the allergens to enter the blood stream[6].
Fragments of gliadin stimulate production of IL-8 and TNF-α. Gliadin also affects the production and a significantly increased INF-γ-induced cytokine secretion from T_H1-cells[7].

2.3 Cytokines
Cytokines are principally produced by T_H cells and macrophages[6], but can also be produced and activated by infections and trauma[8]. Cytokines are needed for the development of cellular and humoral responses, induction of the inflammatory response, regulation of the hematopoiesis, control of cellular proliferation and differentiation. There are two $CD4^+$ T_H cell subpopulations; T_H1 and T_H2[6](fig 2).
Antigens activate naive CD4+ T cells that produce IL-2 that has an autocrine effect, and then proliferate. The surroundings affect which subtype of T cells, that is going to be produced. If the proliferation occurs in an milieu rich of INF-γ, IL-12 and IL-18 a T_H1 subtype is formed, and if the milieu consists mostly of IL-4 a T_H2 subtype will be established[6].
The T_H1 subset forms pro-inflammatory cytokines. The main task for T_H1 subset is to mediate functions including the delayed-type hypersensitivity, T_C activation and promotion of excessive inflammation and tissue injury. The response profile to intracellular pathogens and viral infections is mainly built up by T_H1[6].
INF-γ activates macrophages and the level of class II MHC will be increased by upregulation, IL-12 will then induce differentiation of the proinflammatory T_H1 cells. INF-γ does also inhibit the expansion of the T_H2 subset[6].
IL-2 and interferones, proinflammatory cytokines, can induce enzymes that degrade tryptophan to kynurenine with the result decreased levels of tryptophan[9].
The T_H2 subset produces antiinflammatory cytokines, that stimulates eosinophil activation and differentiation, provides help to B cells and promotes production of IgM and IgE that induce allergic reactions. IL-4 and IL-5 activates the production of IgE that is significant for the hypersensitivity type I reaction[6].
These two subgroups can sometimes inhibit the developement and activity of the opposite subset, a process called cross-regulation[6].

2.4 Irritable bowel syndrome (IBS)
Irritable bowel syndrome consists of many symptoms, among the most common are; excessive abdominal pain, flatulence, bloating, change in bowel habits, constipation and diarrhea. It is well known that certain foods do increase the severity of symptoms. One estimation declares that 20-65% of the patients notice increased symptoms after eating a certain kind of food[1].
The underlying pathogenesis still remains unknown, but implicated for irritable bowel syndrome are disordered motility (small intestine, colon, oesophagus and stomach), disordered sensations (visceral hypersensitivity) and central nervous changes[10].
The symptoms vary between different patients, but the symptoms tend to get worse 20-90 minutes after a meal. Antigens from food and microbial origin which enter the gut lumen are free to interact with both the upper absorptive epithelial surface of small intestinal villi and the epithelium overlying Peyer`s patches and other organised lymphoid tissue[1].
Some IBS patients develop the IBS symptoms with the onset of gastroenteritis (postinfectious IBS; PI-IBS), while the majority do not. There are several risk factors of PI-IBS, including female gender and presence of psychological disturbances occuring around the time of infection. It is belived that gastero-enteritis may sensitize the bowel, but the developement of IBS depends on the coexistence with psycho-logical factors[11]. Patients with severe constipation (prolonged transit time) tend to have higher incidence of depression and patient with diarrhea (shortened transit time) higher incidence of anxiety[2].
2.5 Immunology: There is growing amount of evidence that inflammation and immune activation contribute to the onset of IBS. Findings of increased intraepithelial lymphocytes (IEL), CD3+ cells, natural killer cells and mastcells support this theory of inflammation in the colonic mucosa. It is belived that the inflammatory stimuli may induce a hyperalgesic state and alter motor function[10].
It has also been found that the levels of the proinflammatory cytokines IL-1 (interleukine-1) and TNF-α (tumour necrose factor-alfa) are increased in the intestinal mucosa in IBS. The level of antiinflammatory cytokines seems to be pretty low or being present in an insufficient amount, especially IL-4 and IL-10[12].
An IgE-mediated reaction to wheat can be suspected, since IgE against wheat flour proteins has been found in immunoblotting test of patients blood sera[13]. This hypersensitivity type I reaction starts when the meal proteins are recognized as antigens[1](fig. 1).
Studies have shown that there is an interaction between the immune system and the Entheric Nervous Systeme (ENS)[10].

2.6 Neurology: Numerous neurotransmittors are found in the brain and gut that regulate gastrointestinal activities, including 5-hydroxytryptamin (5-HT) and its 5-HT_3 and 5-HT_4 receptors. Neuropsychiatric drugs are the most common drugs that are used for treatment of IBS. It is not known whether the antidepressant drugs act on the associated psychological disorders, on bowel motility, on sensitivity or on all the mechanism together[1].
5-HT_3 receptor antagonists and selective muscarinergic type 3 receptor anticholinergics are indicated for patients with severe diarrhea. Patients with constipation are indicated 5-HT_4 agonists and patients in pain should take alfa$_2$-adrenergics[11].
An inflammatory process that involves the release of neuropeptides (substance P and VIP (vasoactive intestinal peptides)), in a response to psychological stress can be triggered. These peptides act on the mastcell in the GI (gastro intestinal) tract and cause degranulation and release of inflammatory mediators. Substance P is released from a sensory nerve ending and can also cause fluid to move into local tissue and cause swelling[1].

2.7 Candidiasis

Candida Albicans is the most common fungus of the Candida family. Detection is easy in human feces and it is hard for it to survive on dry surfaces. It causes mostly no harm to the host except if the fungus is in a favourable environment. C. Albicans does often take advantage of a host with an impaired immune system directly after a disease, when the immunesystem already is exhausted[1].
Drugs, medications and the diet (especially sugar, meal, milk-products and yeast) might be the reasons behind an overproduction of C.Albicans. Symptoms implicated are bloating, bad uptake of nutritients, digestion spasm, constipation, anxiety and depression. An imbalance in the relationship between fungi and the good colon bacteria will be the origin of the symptoms[8].
The inherent immunity represents the first line of defense against a microbial invasion of the host. The defenses against the fungal invasion also include the effective barrier function provided by the skin and the mucosal membranes and the composition of nutrition and binding sites by the normal bacterial bios[1412].
Neutrophiles and mononuclear phagocytes have very important properties for the defense against infections of C. albicans. It has been suggested that neutrophiles release IL-12 as a response of a C. Albicans infection[14].
The complement reaction is activated when mannose-binding-lectin (MBL) binds to mannose residues on carbohydrates and glycoproteins on the surface of C. albicans. After that MBL has bound to the surface of the pathogen, MBL-associated serine proteases bind to the MBL. The active complex will cause cleavage and activation of C4 and C2[6].
C. Albicans has metabolic pathways for the conversion of pyruvate to ethanol. The pyruvate decarboxylate to acetic aldehyde under anaerobic conditions and is thereafter reduced to ethanol. The ethanol will accumulate in the blood and cause feelings of intoxication, because the liver is not able to detoxify the metabolites of yeast fermentation[1].

2.8 Coeliac disease

Coeliac disease (CD) is an inflammation of the small intestine and is a response to ingested antigens (gluten, a complex mixture of gliadins and glutenins and related prolamins) in individuals with a genetic predisposition[7].
A 10-fold risk of developing CD has been observed in patients with a IgA deficiency[15].
Injury in the small intestine in the form of villus atrophy and increased amount of intraepithelial lymphocytes (IEL) caused by gluten is found. Gluten is broken down to gliadin, that in turn is broken down to polypeptides. All segments cause the same kind of harm as the complete gluten molecule. The symptoms that are associated with CD in the debut in children aged 1-2 years are primary diarrhea, swollen intestines, abdominal pain, vomiting, inhibition of growth and anemia[3].
35% of the gliadin is composed of glutamine that might have a central role in the toxicity of the proteins in the gliadin. Glutamine is deaminated to glutamate by the tissue transglutaminase (tTG) enzyme. The negative charge of glutamate results in peptides that bind to HLA-DQ with a high affinity. This process increase the stimulatory effect of tTG on gluten sensitive intestinal T lymphocytes[15].
Gliadin induces production of IL-8 and TNF-α and a significant increase of IFN-γ induce cytokine secretion by the T_H1 pathway[7].
Even the T_H2 pathway is activated and this will make gliadin to enhance IL-4 induced IgE production[8].
Diagnosis of CD is made through analysis of AntiGliadin-Antibody (AGA) and antiEndomucosa-Antibody (EmA) in sera by ELISA. EmA has been proven to have tTG as its main antigen and has when a very high specificity for CD. To establish the diagnose a biopsy is needed[15].

It is also necessary to measure the hemoglobulin, iron, folacin, zinc, albumin and sodium levels that might be decreased because of malabsorption due to villus atrophy[3].
High levels of serum antibodies to gliadin, endomucosa, jejunum and tTG have been found in CD patients exposed to gluten. When patients stop intake of gluten the level of antibodies decrease. Elimination of gluten may influence the disease in a favourable course and might prevent complications[15].
It is proposed that CD patients produce tTG antibodies since tTG can crosslink itself to gluten. This gluten-tTG complex will be taken up by B-cells that express tTG-specific immunoglobuline on the membrane. The complex will then be degraded intracellularly and the gluten peptides will bind to HLA-DQ and be expressed on the surface of the cell. Gluten specific T cells will recognize this HLA-DQ complex and start to produce antibodies[15].
tTG is also important for activation of transforming growth factor β (TGF-β). TGF-β is significant for the differentiation of the intestinal epithelium. An increase in T_H1 would take place and inflammatory cytokines establish if the formation of TGF-β should reduce[16].

2.9 Eczema

To get a proper diagnosis of atopic eczema, the anamnesis is of great importance. Atopic eczema can be divided into intrinsic and extrinsic forms, depending on if there is a reactivity against an allergen, or if the antibodies could be activated[17].
Eczema most often develops in childhood and often ”grows away”. Adults do not often develop atopic eczema, but they might have eczema in the childhood that returns in adulthood[18].
During the infantile phase the eczema is located mainly on the head, trunk and the extremities. During the childhood are the eczema mostly on the elbows, knees, wrists, ankles and neck, and during the adolescent mainly on the hands and sometimes also on the trunk, neck and the face[18].
The pathogenesis is not fully understood but it might involve genetic susceptibility, immune dysregulation and epidermal dysfunction[18].
Food allergy is a common problem in infants and small children and it has been shown that the elimination of cereals have decreased the symptoms of eczema and gastrointestinal problems such as vomiting, loose stools and diarrhea. Elevated IgE concentrations to wheat has also been reported*(fig* 1)[19].
It has been noticed that the T_H1 cytokine response is reduced and the T_H2 cytokine response is elevated in patients with atopic eczema and asthma, this is considered to be a principal mechanism in the onset of inflammation. The balance of cytokines is disturbed when the cytokine production does not work, which lead to decreased IFN-γ expression and increased expression of IL-4 and IL-5(*fig. 2)*[20].

2.10 PreMenstrualSymtoms (PMS)

During the late luteal phase of the menstrual cycle different symptoms of various degrees of severity occur in some women. The most common symptoms are somatic, appetitive and behavioral changes[21].
The concentration of progesterone is decreased during the late luteal phase and anxiolytic properties occur due to the action of progesterone metabolites at the $GABA_A$ receptors[22].
It has been detected that IL-8 mRNA is expressed in higher level during the time of menstruation in the endometrium (the lining of the uterus). The expression is decreasing after the menstruation and starts to rise again at the begining of the next. Progesterone seems to have a cooperating effect with IL-8 mRNA when IL-8 mRNA decreases increases progesterone and v.v.[23].
The intake of nutritients over the menstrual cycle has been investigated in women with and without premenstrual syndrome. Women with PMS have an increased energy intake during the premenstrual phase and eat more carbohydrate and fat. In one study the women got drugs that enhanced the serotonin neurotransmission and the PMS symptoms alleviated. Both animal and human studies support that low level of serotonin might play a role in PMS. The blood level of serotonin, which is belived to reflect the brain level, has been analysed during the last 10 days of menstrual cycle, and the level of serotonin was decreased in patients with PMS[21].
There is strong evidence that central nervous system serotonergic functioning is altered in CNS during the luteal phase in women with PMS. In the luteal phase lowered whole blood serotonin, decreased platelet uptake of serotonin and decreased platelet MAO (monoamino oxidase) activity is detected. It has also been noticed that ovarian sex steroids effect serotonin uptake, turnover, binding and transport. The most used treatment at the moment are drugs such as fluoxetine, but L-tryptophan is also used[22].

2.11 Why more women than men?

Autoimmune diseases are more common among female patients than male. Females are producing more antibodies than men and have a more vigorous immune response. The levels of CD4+ cells and serum IgM is also higher among females[6].

Psychological characteristics including depression, anxiety and a history of sexual abuse may also contribute to gender-related differences. Gender differences in the therapeutic benefit of serotonergic agents have been observed[24].

2.12 Other studies:

2.13 Bloodtype diet

According to: Dr. Peter J D`Adamo & Catherine Whitney

The four different blood types reflect the humans possibilities to suit different conditions. The first blood type that was developed was blood type 0. The cro-magnon ate mostly meat and no cereals products. Then the wild animals almost were obliterated, the humans needed to move to different surroundings to survive. They cultivated their own food and this change in living developed blood type A, the vegetarians. When the humans of blood type 0 and blood type A met and got mixed, blood type B was developed. A mixing of the humans in modern time developed blood type AB[25].

2.14 Lectines

A chemical reaction occur between the blood and our intaken food. Each blood type has its specific antigen and a specific chemical structure. Lectines are proteins that exist in the sustenance and if we are eating something that do not go well with our blood type a chemical reaction will occur. The lectines will begin agglutinating and the immune system will then react and try to destroy the agglutinated cells. The agglutination can affect diseases like colon irritable and liver cirrhosis[25].

2.15 Balance between signalsubstances

According to: Dr. Jay Lombard, Dr. Christian Renna

The signal substances play a big role in our health. Excitatory signal substances need to be in balance with the inhibitory. The two opposite signal substances must cooperate with the immune system and the endocrine system. If imbalance occurs disease developes. The balance that is right for you depends on your genotype, chemistry of the body, lifestyle, what your mother ate when she was pregnant, personality and the situation of life among other things. It does not exist a perfect balance, the excitatory and inhibitory signalsubstances influence each other[26].

Excitatory signalsubstances	Inhibitory signalsubstances
dopamine	GABA
norepinephrine	tryptophan
glutamate	
acetylcholine	

Dopamine: Dopamine is metabolized from the aminoacid tyrosine and controls the body movement and expression of mental mood. Fatigue is the distinguishing feature of deficiency of the excitatory signalsubstances. The interaction of all the excitatory signal substances help us to feel good, enjoy life, to get motivation, concentrate, create memories and to learn[26].

Glutamate: Glutamate is metabolized from glutamine, but also taken up from what we are eating. A big part of the amount of glutamate helps to regulate the nutritional metabolism. Glutamate is one of the most important excitatory signal substances in the brain but a surplus of glutamate might overstimulate the cells and conditions as stroke, epilepsi, manodepressitivity, dementia, chronic ache, migraine and ALS[26].

GABA: GABA has an important role in the nervous system to modulate the communication between cells. If GABA did not have this effect the nerve cell should not be able to moderate the action potentials and the nerve cell synapsis would get overheated. GABA is helping serotonin to regulate the central nervous system[26].

Tryptophan: Tryptophan is a precursor to serotonin which is built up in the brain. The most important receptor for serotonin is hypothalamus, the part that the urge to eat, fight and reproduce. Deficency in serotonin causes anxiety and bad self esteem[26].

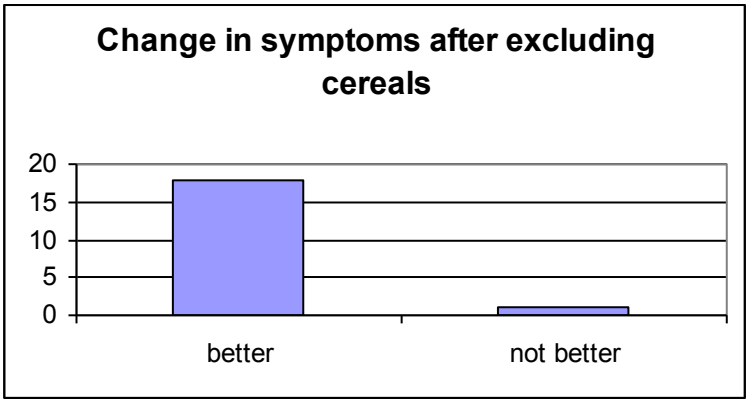
In stress the hypothalamus releases a hormone called corticotrophin releasing factor (CRF) that coordinates the stress response and prepares the body for the dangerous situation. The blood pressure and pulse will increase. The nutritional metabolism is upgraded and more glucose is used. CRF will affect the immune system and increase secretion of inflammatory cytokines. The cytokines will tell the immunesystem to prepare for problems. GABA and tryptophan are now trying to cool down the stress reaction. If GABA and tryptophan do not manage to reduce the stress reaction it might lead to high blood pressure, muscle tonus and stomach trouble[26].

3. Mateal/Methods:

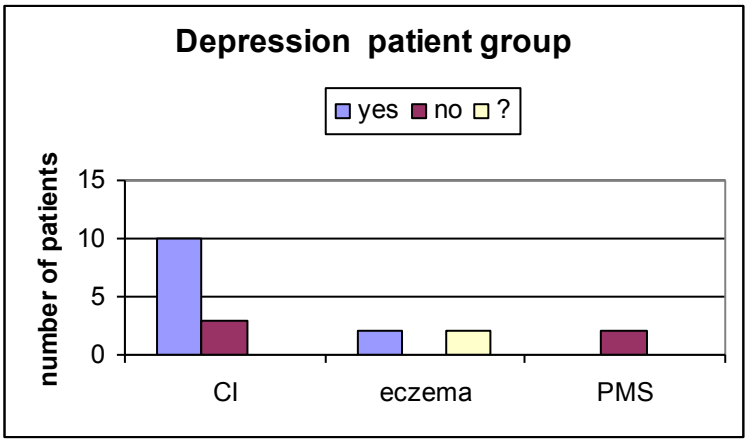
Patients that had stomach troubles (colon irritable), PMS and eczema got written diet change program excluding cereals from their diet by M.D. Jenny Stejskal. A questionaire was developed by Dr. Stejskal and Linda Särkimukka. Dr. Stejskal made telephone interviews and Särkimukka did literature search, analysis of the inteviews and a summary.
The questions that patients were asked are the following:

1. When did you change your diet?
2. How long time did it take before you noticed an improvement?
3. What was improved?
   bowel/skin/PMS/something else?
4. Have you continued with the new diet?
   Yes-still good effect
   No-problems returned
5. Do you feel stressed or depressed daily/often?
6. What is your bloodtype?

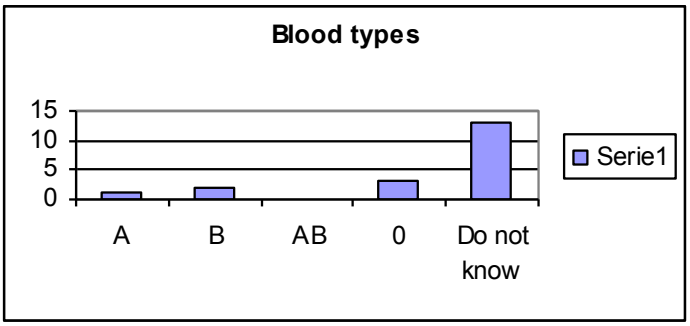
4. Results:



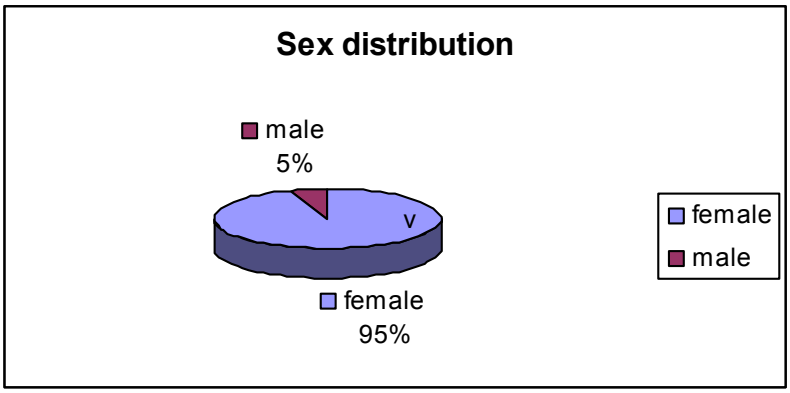
Everybody without one patient showed improvement after excluding cereals from the diet. The patient that did not show improvement did not completely exclude cereals from the diet.



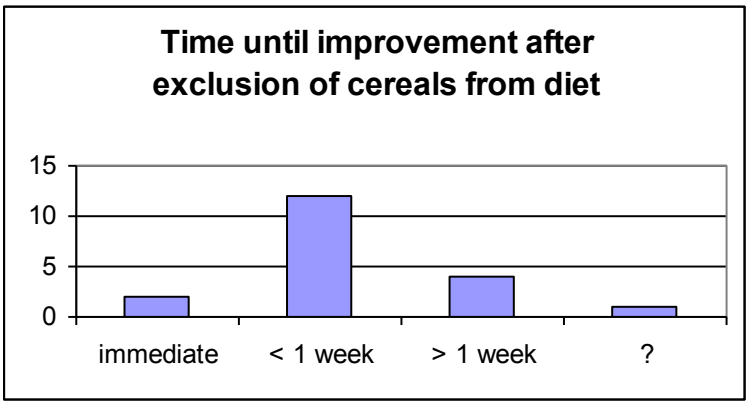
Patients with IBS seemed to have a tendency to be depressed/feeling stressed.



Only a few patients´ knew their blood group



There was a predominance of females in the group of patients with colon irritable and eczema. PMS patients excluded.



After eliminating meal from the diet most patients´improved within a week

5. Discussion:

IBS might be induced by a variety of reasons. It is important to diagnose a possible celiac disease or candida infection in these patients. Ceveral patients in the IBS-group feel stressed or depressed daily or often, which might induce production of the proinflammatory cytokines IL-1 and TNF-α and the antiinflammatory cytokines IL-4 and IL-10.
It seems like only proinflammatory cytokines are involved in the pathogenesis of IBS, but insufficient levels of antiinflammatory cytokines has also been detected. IL-4 induce a hypersensitivity type 1 reaction which in turn produces more cytokines, vasoactive amines and pharmacologically active mediators. Patients with IBS are treated with tryptophan and SSRI drugs successfully with regard to depression among other symptoms. More research is needed about the neuronal:gastrointestinal interaction in IBS.
In the eczema group there seems to be an imbalance of the T_H1- and T_H2-cytokine response. The T_H1 response is reduced and the T_H2 response is elevated that trigger the establishment of IL-4 and IL-5. Perhaps cereals may be identified as allergensby the immune system and hence increase the production of IL-4 and IL-5. These cytokines will induce a hypersensitivity reaction.
Imbalance in the levels of neurotransmittors seem to be one reason behind PMS, since it has been noticed that women during the last 10 days of menstrual cycle have decreased blood levels of serotonin. At the same time the women also increase their intake of carbohydrate and fat. IL-8 increases during the menstrual phase, maybe as an response on the depression or the increased carbohydrate intake.
The proinflammatory interferons that are stimulated by gliadin in cereals can induce enzymes that degrade tryptophan. The level of tryptophan will then decrease and less serotonin will be produced. This might be one reason behind the depression among many of the patients.

This study is pretty limited since the patient group studied is small.The patients also live in the same area. Another study based on a larger patient group with differing background and living conditions is needed to be done.
It would also have been intresting to analyze the patients diet, especially for carbohydrate content then many patients seems to be depressed and cereals will increase the release of serotonin.
More research is important.

6. Conclusion:

Depression seems to be one of the most common symptoms for IBS and PMS patients and the conditions are treated with psychopharmaca. Even patients with eczema might have an increased tendency for depression. Cereals might be a substitue for the neuropsychiatric drugs since it supports the release of serotonin. However increased intake of meal products, that contain gliadin, might stimulate production of IL-8 and TNF-α which can give an inflammatory response. This might be the reason for the improvement of the patients´ health after eliminating cereals from the diet.
On the contrary might it be the depression that triggers the inflammation since it could release proinflammatory cytokines.
An other possibility is that an increased intake of carbohydrate perhaps induce overgrowth of C. Albicans thereby disrupting the balance in the intestinal flora.

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28. Fig 2: http://www.biosource.com/content/techCornerContent/pathway2002/pdfs/imunology/3Th1 Th2Diffpathway.pdf

8. Acknowledgements:

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9. Tables:

Gender	Diagnose	Start diet-change	Improvement of health	Time for improvement	Continued change of diet?	Stressed or depressed daily or often?	Bloodtype
f	CI	2004-10-29	yes	< 1 week	yes	yes	A
f	CI	2004-11-16	yes	< 1 week	no	yes	?
f	CI	2004-12-23	yes	< 1 week	yes	no	O
f	CI	2004-07-26	yes	> 1 week	yes	yes	B
f	CI	2004-12-14	yes	> 1 week	yes	yes	?
m	CI	2004-09-08	yes	< 1 week	no	yes	O
f	CI	2004-08-26	yes	<1 week	no	yes	?
m	CI	2004-11-22	yes	immediate	yes	no	O
f	CI	2004-11-01	yes	< 1 week	no	yes	?
f	CI	2005-02-14	yes	<1 week	no	yes	0
f	CI	2005-02-23	yes	< 1 week	yes	yes	?
f	CI	2005-02-16	yes	< 1 week	yes	yes	B
f	CI	2005-03-22	yes	< 1 week	not completely	no	?
f	Eczema	2005-02-16	no	still eating mealproducts		yes	?
f	Eczema	2004-11-08	yes	< 1 week	no	yes	?
f	Eczema		yes	immediate			?
f	Eczema	2004-04-02	yes	not done the change completely			?
f	PMS	2004-07-28	yes	> 1 week	no	no	?
f	PMS	2004-09-03	yes	> 1 week	no	no	?

10. Figures:

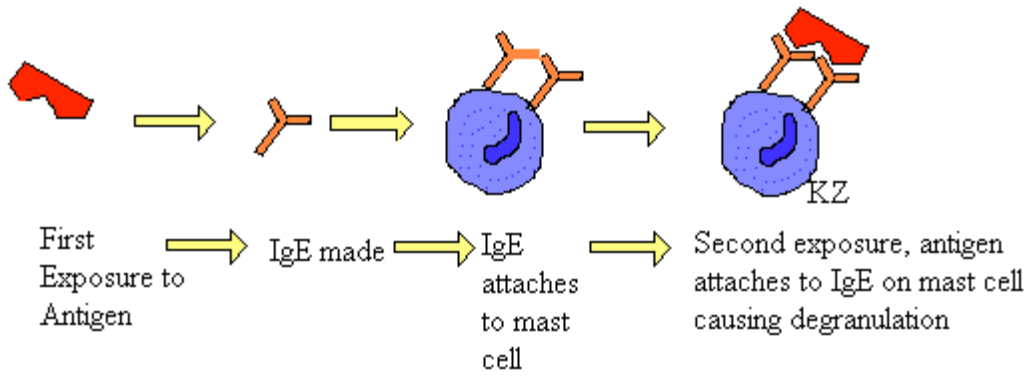

fig. 1: http://www.pathoplus.com/_borders/IgE.gif

Hypersensitivity type 1: Since the antigen is exposed to the B-cell, the B-cell will start to produce IgE secreting plasma cells. The IgE molecules will bind to IgE-specific Fc receptors on mast cells. When a second exposure of antigen occur it will lead to crosslinking of the bound IgE and trigger a release of pharmacologically active mediators and vasoactive amines from mast cells and basophils. Degranulation of mast cells and basophils are when commenced. The mast cells might also secrete a large variety of cytokines[3].

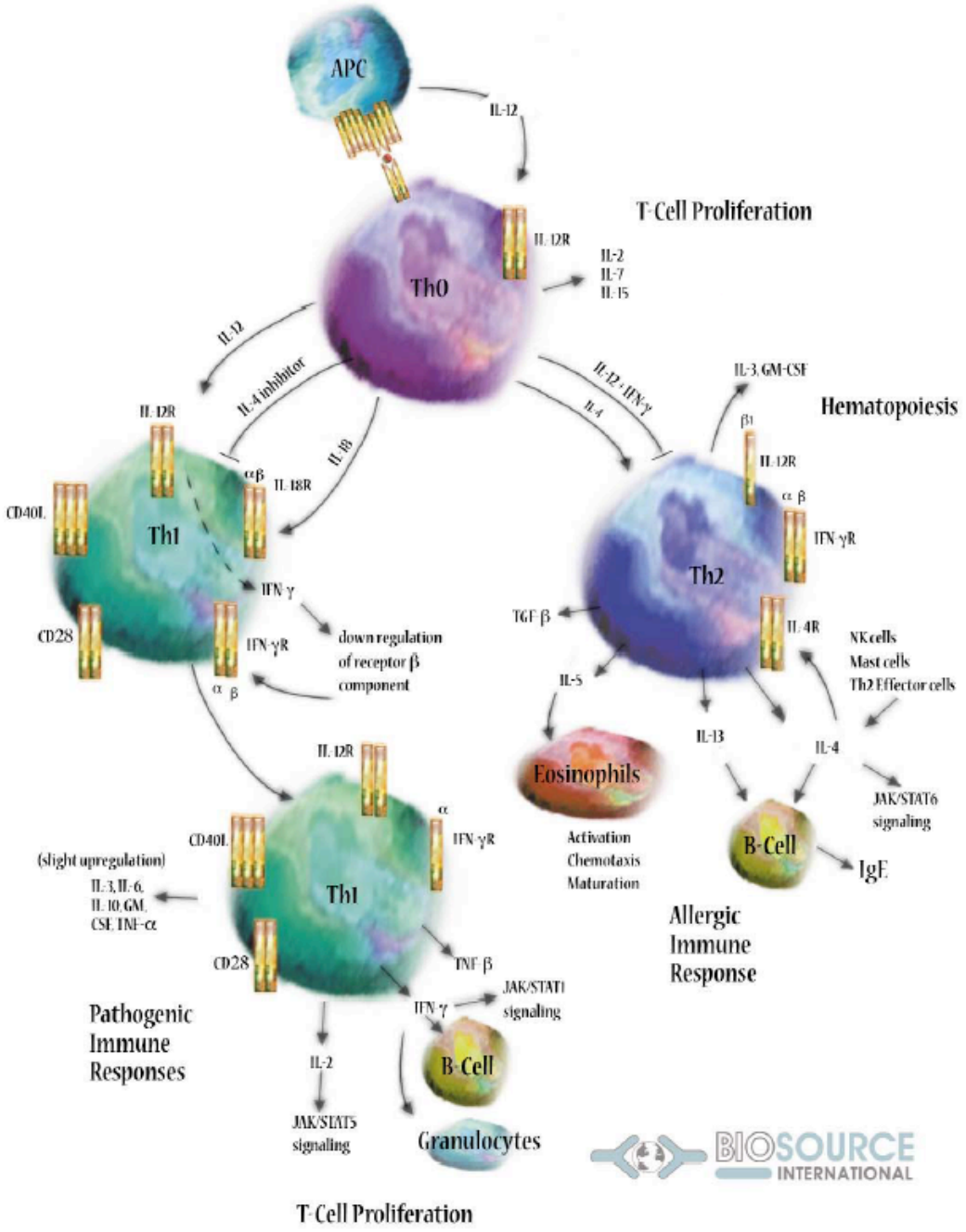

fig. 2:
http://www.biosource.com/content/techCornerContent/pathway2002/pdfs/imunology/3Th1Th2Diffpathway.pdf

Cytokine-mediated generation and cross regulation of T_H subsets: The T_H-cell produce two subpopulation with different capabilities to secrete cytokines. They both got the capability to secrete IL-3 but differ in the other cytokines they produce[3].
If the antigen-activated naive CD4+ T cell proliferate in an IL-12 dominated environment it generates a population of T_H1 cells. The T_H1 cell will secrete IFN-γ, IL-2 and TNF-β. A positive feedback-loop is established when IFN-γ is secreted and more IL-12 is produced. The T_H2 cell will get activated if IL-4 is dominating the environment and secrete specific cytokines like IL-4, IL-5, IL-10 and IL-13[3].
T_H1 subset is good suited to respond to viral infections and intracellular pathogens. Secretion of IL-4 and IL-5 by cells of T_H2 subset induces the IgE production[3].