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ABSTRACT

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Case Report: Here we report a severe case of Crohn’s disease where we successfully applied the paleolithic ketogenic diet. Dietary therapy resulted in resolution of symptoms, normalized laboratory parameters as well as gradual normalization of bowel inflammation as evidenced by imaging data and normalization of intestinal permeability as shown by the polyethylene glycol (PEG 400) challenge test. The patient was able to discontinue medication within two weeks. Currently, he is on the diet for 15 months and is free of symptoms as well as side effects.

Conclusion: We conclude that the paleolithic ketogenic diet was feasible, effective and safe in the present case.
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Keywords: Crohn’s disease, Dietary therapy, Inflammatory bowel disease, Ketogenic diet, Paleolithic diet

INTRODUCTION

Crohn’s disease, an inflammatory disease of the bowel, is regarded as having no cure [1]. Standard treatment which involves steroids, immunosuppressants and biological therapy is aimed at reducing symptoms [1]. Periods of flares and remissions typically alternate, however, the overall course of the disease is progressive. A set of ecological evidence, including a discrepancy between westernized and non-westernized countries in the occurrence of the disease, raises the possibility of lifestyle and/or dietary factors in the etiology of the disease [2]. There have been several attempts to use a dietary intervention in Crohn’s disease such as the specific carbohydrate diet [3] and the anti-inflammatory diet [4] as well as elimination-reintroduction diets [5]. Although clinical improvements and reduction of medicines have been reported being associated with these diets we are not aware of any diet inducing complete remission and long-term freedom of medicines at the same time.

The authors of the present report are using a diet referred to as the paleolithic ketogenic diet in the treatment of chronic conditions. So far we have published...
cases of successful treatment of diabetes type 1 [6, 7] and type 2 [8], epilepsy [9, 10] as well as other conditions [11].

CASE REPORT

Diagnosis

The 14-year-old boy presented with fatigue, low grade fever, iron deficiency anemia, lower abdominal tenderness and perianal dermatitis. He was of short stature for his age. On 30 September 2013 upper and lower endoscopy was performed. The latter showed ulcerative lesion in the terminal ileum. Biopsy was taken from multiple sites and histopathology showed severe inflammation of the terminal ileum and the Bauhin’s valve. Signs of mild-to-moderate degree aspecific inflammation were seen in the colon. On laboratory workup inflammatory marker C reactive protein (CRP) was elevated (58 mg/L). He was diagnosed with Crohn’s disease.

Standard treatment

At the time of diagnosis onset (on 07 October 2013) the patient was started on mesalazine, metronidazole and pantoprazole. Within ten days, ciprofloxacin and probiotics were added. Given that no improvement was seen immunosuppressant therapy was initiated on 13 November 2013 with azathioprine together with methylprednisolone, potassium citrate, calcium and vitamin D. Given that disease progressed, a year after diagnosis onset (on 25 September 2014), biological therapy was initiated: five cycles of adalimumab were given each two weeks apart. The condition of the patient further deteriorated and therefore on 07 November 2014 exclusive formula feeding was initiated. At this time mesalazine, multivitamin, vitamin D3 and calcium were discontinued. Pantoprazole was discontinued within two weeks. Formula-based nutrition resulted in the resolution of abdominal pain but other symptoms persisted (Table 1, Figures 1 and 2).

Laboratory data

As the disease progressed iron deficiency anemia of the patient worsened. Thromocyte number showed a decreasing tendency across the course of the standard treatment. Level of inflammatory markers CRP and erythrocyte sedimentation rate (ESR) dropped when initiating the immunosuppressant therapy and steroid but increased thereafter (Table 1, Figure 2).

Imaging

At the time of the diagnosis ultrasound examination performed on 07 October 2013 showed thickening of the terminal ileum and that of the small intestine at multiple sites. No thickening of the colon was seen. Three further follow-up ultrasound examinations were carried out during the next year. This showed progression of the disease as reflected by increasing diameter of the thickened bowel wall and an increasing intensity of hypervascularization. The last ultrasound out of the four (on 7 November 2014) already indicated the thickening of nearly all bowel segments including the colon ascendens and the colon transversum. Figure 3 shows as the largest diameter of the terminal ileum changed between 7 October 2013 and 7 November 2014.

Magnetic Resonance Enterography

Magnetic resonance enterography performed five weeks after diagnosis onset (on 12 November 2013) indicated thickening of the small intestinal wall at multiple locations. A follow-up magnetic resonance enterography 13 months later, on 16 December 2014, showed an increase in the variability in the diameter of the bowel lumen and narrowing of the lumen (Figure 4). Due to the narrowing the patient was offered surgery in December 2014 which he refused.

Symptoms

Abdominal cramps as well as episodes of low grade fever lessened when initiating the immunosuppressant therapy together with steroid. However, within three months the patient developed bilateral knee pain as a new symptom. Later on his appetite deteriorated. At 12 months after diagnosis onset abdominal cramps increased and episodes of low grade fever returned. The patient reported fatigue along with a deterioration in his school performance. Following the onset of the biological therapy all symptoms persisted. Following the fourth cycle of adalimumab strong abdominal pain emerged abruptly which persisted for several hours. Given this experience and the overall ineffectiveness of the biological therapy the patient decided to stop it. He was put on exclusive enteral nutrition which resulted in a lessening of his abdominal cramps but other symptoms persisted.

Dietary advices while on the standard therapy

The patient was advised to follow a diet free of lactose and low in fat and fibers. Analysis of his diet-symptom diary did not show any consistent association between symptoms and food items.

Intervention with the paleolithic ketogenic diet

Given the ineffectiveness of standard therapies the parents of the child were seeking for alternative options. When we first met the patient he reported bilateral pain and swelling of the knee, frequent episodes of fever and night sweats as well as fatigue. He looked pale. We offered the paleolithic ketogenic diet along with close monitoring of the patient. The patient started the diet on 4 January 2015. The diet is consisting of animal fat, meat, offal and eggs with an approximate 2:1 fat : protein ratio.
RESULTS

Discontinuing medication
Within two weeks after diet onset the patient discontinued azathioprine, the only medicine he was taking at this time. Currently, he is without medicines for 15 months.

Symptoms
The frequent night sweats of the patient disappeared within three weeks after diet onset and thus his sleep improved significantly. The knee pains of the patient began to lessen at 4th week on the diet and completely disappeared by the third month. From this time onwards he regularly went to school by bike (20 km daily). He reported restored energy and increased physical and mental fitness. Although during the eight months before diet onset his weight was 41 kg and was 152 cm tall (BMI = 17.7). At 12 months after diet onset, his weight was 50 kg (BMI: 19.5). From this time on he did neither consume vegetables and fruits nor vegetable oil containing spices such as cumin and cinnamon.

We obtained written informed consent from the patient for the publication of his case.

Intestinal permeability test
Intestinal permeability was assessed using a polyethylene glycol (PEG 400) challenge test based on the method of Chadwick et al. [12]. PEG 400 contains a mixture of inert water soluble molecules of 11 different sizes that are absorbed independently of dose, but which display decreasing mucosal transport with increasing molecular size. PEG 400 is also nontoxic, not degraded by intestinal bacteria, not metabolized by tissues, and rapidly excreted in urine. After a 3.0-gram oral dose of PEG, the subject makes a six-hour urine collection. The PEG fractions are acetylated with acetic anhydride, using pyridine as a catalyst, and then quantitated by capillary gas-liquid chromatography. The percentage of each fraction of PEG excreted over 6 hours is calculated.

PEG 400 challenge test performed at four months on the diet (on 18 May 2015) showed increased permeability to PEG between 242 and 418 molecular weight. A follow-up test performed at 10 months on the diet (on 26 November 2015) showed no abnormal intestinal permeability (Figure 6).
Table 1: Laboratory data while on a standard diet and corresponding medications, Dashes indicate that a given parameter was not measured

| Parameter          | 04 Oct 2013 | 17 Oct 2013 | 25 Nov 2013 | 17 Dec 2013 | 27 Mar 2014 | 04 Sep 2014 | 10 Nov 2014 | Normal value |
|--------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|--------------|
| WBC                | 9.6         | 7.5         | 23.2        | 13.8        | 6.3         | 7.6         | 7.7         | 4.5-11.5     |
| RBC                | 5.5         | 5.3         | 5.6         | 5.5         | 4.2         | 4.4         | 4.7         | 4.5-5.9     |
| Hgb                | 117         | 113         | 130         | 133         | 110         | 119         | 132         | 135-170     |
| Hct                | 0.38        | 0.36        | 0.41        | 0.41        | 0.33        | 0.35        | 0.39        | 0.41-0.51   |
| Thrombocyte        | 252         | 285         | 311         | 168         | 128         | 240         | 166         | 150-400     |
| CRP                | 23.1        | 21.1        | 2.6         | 2.4         | 12.3        | 46.7        | 19.6        | 0-5 mg/L    |
| ESR                | 12          | 8           | 1           | 1           | 14          | 25          | 15          | 0-15 mm/h   |
| T. protein         | 59          | 53.9        | 57.9        | 54.4        | 58.3        | 61.6        | 57.3        | 57-80 g/L   |
| Carbamide          | 0.8         | 1.7         | 4.2         | 5           | 3.5         | 2.7         | 2.8         | 2.8-7.2 mmol/L |
| Creatinine         | 49          | 47          | 44          | 58          | 41          | 45          | 56          | 53-100 µmol/L |
| Sodium             | 140         | 142         | 140         | 136         | -           | -           | 143         | 135-145 mmol/L |
| Potassium citrate  | 4.5         | 4.1         | 3.9         | 4.1         | -           | -           | 4.5         | 3.2-5.1 mmol/L |
| GOT                | 11          | 18          | 11          | 10          | 17          | 15          | 15          | 0-50 U/L    |
| GPT                | 6           | 11          | 12          | 8           | 7           | 7           | 7           | 0-50 U/L    |
| GGT                | 13          | 23          | 23          | 15          | 11          | 15          | 9           | 0-55 U/L    |
| Iron               | -           | -           | -           | -           | 6.9         | 3.6         | -           | 12.5-32 µmol/L |
| formula feeding    | x           |            |            |            |            |            |            |              |
| adalimumab         | x           |            |            |            |            |            |            |              |
| multivitamin       | x           | x           | x           |            |            |            |            |              |
| calcium            | x           | x           | x           | x           |            |            |            |              |
| vitamin D3         | x           | x           | x           | x           |            |            |            |              |
| potassium citrate  | x           | x           |            |            |            |            |            |              |
| methylprednisolone | x           | x           |            |            |            |            |            |              |
| azathioprine       | x           | x           | x           | x           | x           |            |            | x            |
| probiotics         | x           | x           |            |            |            |            |            |              |
| ciprofloxacin      | x           |            |            |            |            |            |            |              |
| pantoprazole       | x           | x           | x           | x           | x           | x           | x           |              |
| metronidazole      | x           |            |            |            |            |            |            |              |
| mesalazine         | x           | x           | x           | x           | x           |            |            |              |

Abbreviations: WBC: white blood cell count, RBC: red blood cell count, Hgb: hemoglobin, Hct: hematocrit, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, T. protein: total protein, GOT: glutamate-oxaloacetate transaminase, GPT: glutamate-pyruvate transaminase, GGT: gamma-glutamyl transferase
Figure 1: Timeline encompassing the medication of the patient, timing and the result of the MR enterography as well as that of the ultrasound examination. Abbreviations: ti: thickness of the terminal ileum, *: moderate hypervascularization, **: strong hypervascularization, IPT: intestinal permeability test.

Figure 2: Timeline encompassing medication and the change in the inflammatory markers ESR (erythrocyte sedimentation rate) and CRP (C reactive protein).

Figure 3: Thickness of the terminal ileum (largest diameter is indicated) seen on ultrasound. Onset of the paleolithic ketogenic diet as well as the occurrence of a dietary failure is indicated with arrows. Note the improvement during the paleolithic ketogenic diet, the relapse following the single episode of dietary failure and the normal results on the last examination. * indicate mild degree hypervascularization while ** high degree hypervascularization.

**DISCUSSION**

Here we report a case where Crohn’s disease was reversed by the paleolithic ketogenic diet.

Disease symptoms began to improve a few weeks after diet onset. Within 10 months the patient achieved full remission from symptoms as well as normalization of intestinal inflammation as evidenced by imaging data, normalization of laboratory parameters and that of the

Figure 4: Magnetic resonance enterography on 16 December 2014 showed thickening of the terminal ileum (arrows).

Figure 5: Weight and height of the patient during the 14 months on the standard treatment and following the onset of the dietary therapy.

Figure 6: PEG 400 challenge test showing increased intestinal permeability to PEG from molecular weight 242 to molecular weight 418 at four months on the diet (A) while no abnormal at 10 months (B).
of the popular paleolithic diet including coconut oil, oil
Based on our experience this is due to the components
“paleo cakes”) resulted in a thickening of the bowel wall.
patient too where breaking the strict rules (eating the
result in lasting relapse. This was the case in the present
Crohn’s disease. In addition, our experience shows that
full fat-meat diet is needed in the most severe cases of
vegetables and fruits at all. Such a diet may first sound
diet was started in the strictest form thus containing no
monitoring of urinary ketones. Given the patient’s severe
intestinal permeability. Aside from a single dietary fault
the patient strictly adhered to the diet as assessed by
frequent patient feedback, laboratory data and home
in Crohn’s disease. In addition, our experience shows that
results when containing no plant components at all.
seeds and sugar alcohols which may trigger inflammation.
In contrast, honey, consumed in limited amounts is
tolerable and does not cause such symptoms. The
progressive worsening of symptoms. Standard therapies
may result in a temporary symptom relief but are
accompanied by significant side effects [1]. Surgical
resection is thought to be inevitable on the long-term [13].
Our patient also failed to respond to immunosuppressive
therapies, steroid, biological agents and exclusive formula
feeding. Within 14 months after diagnosis onset, he was
offered surgery due to the narrowing of the bowel. The
paleolithic ketogenic diet reversed the disease from this

|                | 02 Feb 2015 | 09 Apr 2015 | 29 Apr 2015 | 19 Jun 2015 | 17 Sep 2015 | 10 Nov 2015 | 14 Dec 2015 | normal value |
|----------------|------------|------------|------------|------------|------------|------------|------------|--------------|
| WBC            | 7.1        | 8.5        | 5.7        | 7.1        | 7.1        | 7.8        | 8          | 4.5–11.5 G/L |
| RBC            | 5          | 4.8        | 4.8        | 5.2        | 4.8        | 5.3        | 5.4        | 4.5–5.9 T/L  |
| Hgb            | 145        | 135        | 137        | 147        | 135        | 146        | 151        | 135–170 g/L  |
| Hct            | 0.42       | 0.39       | 0.4        | 0.42       | 0.39       | 0.43       | 0.44       | 0.41–0.51 L/L |
| Thrombocyte    | 71         | 75         | 68         | 82         | 95         | 65         | 100        | 150–400 G/L  |
| CRP            | 3.75       | 9.9        | 9.3        | 9.3        | 14.3       | 4.4        | 7.1        | 0–5 mg/L     |
| ESR            | 3          | 8          | 8          | 5          | 10         | 6          | 5          | 0–15 mm/h    |
| Total protein  | 60         | 62         | -          | -          | 63         | 65         | 66         | 57–80 g/L    |
| Carbohydrate   | 5.3        | 6.2        | -          | -          | 5.8        | 6.3        | 6.9        | 2.8–7.2 mmol/L |
| Creatinine     | 53         | 63         | -          | -          | 48         | 66         | 7.3        | 53–100 μmol/L |
| Sodium         | 141        | 138        | -          | -          | 139        | 140        | 139        | 135–145 mmol/L |
| Potassium      | 4.3        | 3.9        | -          | -          | 4.1        | 4.1        | 4.2        | 3.2–5.1 mmol/L |
| GOT            | 18         | 20         | -          | -          | 21         | 24         | 24         | 0–50 U/L     |
| GPT            | 12         | 14         | -          | -          | 18         | 18         | 18         | 0–50 U/L     |
| GGT            | 12         | 13         | -          | -          | 13         | 13         | 12         | 0–55 U/L     |
| Iron           | 12.1       | 10.3       | -          | -          | 10.6       | 11         | 13.7       | 12.5–32 μmol/L |
| Uric acid      | 258        | 264        | -          | -          | 332        | 329        | 329        | 208–428 μmol/L |
| Glucose        | 5          | 5          | -          | -          | 5.3        | 5.2        | 5.4        | 3.5–6.1 mmol/L |
| Magnesium      | 0.76       | 0.86       | -          | -          | 0.81       | 0.87       | 0.89       | 0.73–1.06 mmol/L |
| Cholesterol    | 4.6        | 4.9        | 4.7        | 4.8        | 4.3        | 4.1        | 4.3        | <5.2 mmol/L  |
| Triglyceride   | 0.9        | 1.46       | -          | -          | 0.56       | 0.93       | 1.34       | <1.7 mmol/L  |
| Fibrinogen     | -          | -          | 2.5        | 2.3        | -          | -          | -          | 2–4 g/L      |
| Urinary ketones| ++         | +++        | +++        | +++        | +++        | +          |           |              |

Abbreviations: WBC: white blood cell count, RBC: red blood cell count, Hgb: hemoglobin, Hct: hematocrit, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, T. protein: total protein, GOT: glutamate-oxaloacetate transaminase, GPT: glutamate-pyruvate transaminase, GGT: gamma-glutamyl transferase.
very advanced stage. Although Crohn’s disease is known to be characterized by an alternation of better and worse periods, a complete remission from a very advanced stage is highly unlikely to be the part of the normal course of the disease.

While on the biological therapy thrombocyte number dropped and continued to decrease while on the diet. Our previous experience does not indicate thrombocytopenia on the paleolithic ketogenic diet. However, low thrombocyte number is a well-known side effect of the use of adalimumab in Crohn’s disease [14, 15]. It is also noteworthy that a return to the strictest form of the paleolithic ketogenic diet resulted in an increase in thrombocyte number.

Crohn’s disease is regarded as an autoimmune disease. Autoimmune diseases and Crohn’s disease specifically have been linked to increased intestinal permeability [16]. Yet currently there is no known means to reverse pathological intestinal permeability [17]. A previous study with the paleolithic diet found no change in intestinal permeability as assessed by the lactulose-mannitol test [18]. As far as we know this is the first documented case where pathological intestinal permeability was reversed as assessed by a diagnostic test.

Experts in the field of evolutionary medicine has long been suggesting that chronic diseases of civilization emerge from a mismatch between our ancient genome and current lifestyles [19, 20]. In recent years an increasing number of studies showed that the metabolic syndrome and associated conditions can be reversed or improved by applying a diet denoted as “paleolithic” (for a review see: [21]). In the paleolithic diet, as described in the implied papers, macronutrient ratios are undefined or variable, as well as that of the ratio of animal/plant foods including the ratio of animal/plant fats. Our clinical experience, however, indicate that the most severe chronic conditions, including the Crohn’s disease, can only be reversed by the paleolithic ketogenic diet based on animal fat, meat and offal. A same conclusion was drawn in our previous case study showing that the paleolithic ketogenic diet was more effective than the popular form of the paleolithic diet in the case of Gilbert’s syndrome [11]. The paleolithic ketogenic diet we use in the treatment of chronic diseases is close to the evolutionary diet originally proposed by gastroenterologist Voegtlin [22]. With regard to the main principals, background, sustainability and further issues such as vitamin supply while on a meat-fat based diet we refer to the excellent book of Voegtlin [22].

As regards the underlying mechanism, we put forward that normalizing pathological intestinal permeability is crucial in tackling autoimmune diseases, including Crohn’s disease. Accordingly, increased intestinal permeability has been shown to predict relapses in Crohn’s disease [23]. It is known that under physiological conditions, dietary macromolecules are not transported paracellularly from the intestinal lumen to the blood or the lymph. It has been suggested that certain components of the Western-type diet are able to destroy cell junctions and thereby compromise the intestinal barrier function [24, 25]. As a result, large molecules including protein fragments and glycoproteins, possessing antigenic properties, may appear in the circulation and promote chronic inflammation [26]. Given their specific structure, these macromolecules may bind to and form complexes with the surface molecules of certain cell types. Such a complex is then destroyed by the immune system through apoptosis [27, 28]. We assume that a continued exposition to these macromolecules may maintain the autoimmune destruction of tissues. We put forward that the animal fat-meat based diet, the only diet humans are evolutionary adapted to, is lacking substances that are destroying the intestinal barrier. A shift toward the paleolithic ketogenic diet may normalize intestinal permeability (as also seen in our patient) and thereby may halt the autoimmune destruction of the affected tissues, in our case the intestine. With the attenuation of the autoimmune process the intestine may regenerate.

CONCLUSION

We conclude that the paleolithic ketogenic diet was effective while producing no side effects in this case of Crohn’s disease. In contrast to standard therapeutic approaches which are aimed to control certain components of the disease only, the paleolithic ketogenic diet was able to reverse the cluster of symptoms and abnormalities associated with the disease. Assuming a long term dietary compliance, we believe that the patient would remain disease-free in the future.

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Author Contributions

Csaba Tóth – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Andrea Dabóczi – Acquisition of data, Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
Mark Howard – Acquisition of data, Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
Nicholas J. Miller – Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Zsófia Clemens – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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REFERENCES

1. Akobeng AK. Crohn's disease: current treatment options. Arch Dis Child 2008 Sep;93(9):787–92.
2. Barreiro-de Acosta M, Alvarez Castro A, Souto R, Iglesias M, Lorenzo A, Domínguez-Muñoz JE. Emigration to western industrialized countries: A risk factor for developing inflammatory bowel disease. J Crohns Colitis 2011 Dec;5(6):566–9.
3. Cohen SA, Gold BD, Oliva S, et al. Clinical and mucosal improvement with specific carbohydrate diet in pediatric Crohn disease. J Pediatr Gastroenterol Nutr 2014 Oct;59(4):516–21.
4. Olendzki BC, Silverstein TD, Persuitte GM, Ma Y, Baldwin KR, Cave D. An anti-inflammatory diet as treatment for inflammatory bowel disease: a case series report. Nutr J 2014 Jan 16;13:5.
5. Donnellan CF, Yann LH, Lal S. Nutritional management of Crohn's disease. Therap Adv Gastroenterol 2013 May;6(3):231–42.
6. Tóth C, Clemens Z. Type 1 diabetes mellitus successfully managed with the paleolithic ketogenic diet. Int J Case Rep Images 2014;5:599–703.
7. Tóth C, Clemens Z. A child with type 1 diabetes mellitus (T1DM) successfully treated with the Paleolithic ketogenic diet: A 19-month insulin freedom. Int J Case Rep Images 2015;6:752–7.
8. Tóth C, Clemens Z. Successful treatment of a patient with obesity, type 2 diabetes and hypertension with the paleolithic ketogenic diet. Int J Case Rep Images 2015;6:161–7.
9. Clemens Z, Kelemen A, Fogarasi A, Tóth C. Childhood absence epilepsy successfully treated with the paleolithic ketogenic diet. Neurol Ther 2013 Sep 21;2(1-2):71–6.
10. Clemens Z, Kelemen A, Tóth C. NREM-sleep Associated Epileptiform Discharges Disappeared Following a Shift toward the Paleolithic Ketogenic Diet in a Child with Extensive Cortical Malformation. Am J Med Case Rep 2015;3:212–5.
11. Tóth C, Clemens Z. Gilbert's Syndrome Successfully Treated with the Paleolithic Ketogenic Diet. Am J Med Case Rep 2015;3:117–20.
12. Chadwick VS, Phillips SF, Hofmann AF. Measurements of intestinal permeability using low molecular weight polyethylene glycols (PEG 400). I. Chemical analysis and biological properties of PEG 400. Gastroenterology 1977 Aug;73(2):241–6.
13. Baumgart DC, Sandborn WJ. Crohn's disease. Lancet 2012 Nov 3;380(9853):1590–605.
14. Salar A, Bessa X, Muñiz E, Monfort D, Besses C, Andreu M. Infliximab and adalimumab-induced thrombocytopenia in a woman with colonic Crohn's disease. Gut 2007 Aug;56(8):1169–70.
15. Casanova MJ, Chaparro M, Martínez S, Vicuña I, Gisbert JP. Severe adalimumab-induced thrombocytopenia in a patient with Crohn’s disease. J Crohns Colitis 2012 Dec;6(10):1034–7.
16. Hollander D. Crohn’s disease—a permeability disorder of the tight junction? Gut 1988 Dec;29(12):1621–4.
17. Odenwald MA, Turner JR. Intestinal permeability defects: is it time to treat? Clin Gastroenterol Hepatol 2013 Sep;11(9):1075–83.
18. Boers I, Muskiet FA, Berkelaar E, et al. Favourable effects of consuming a Palaeolithic-type diet on characteristics of the metabolic syndrome: a randomized controlled pilot-study. Lipids Health Dis 2014 Oct 11;13:160.
19. Cordain L. The Paleo Diet: Lose Weight and Get Healthy by Eating the Foods You Were Designed to Eat. New York: John Wiley; 2002.
20. Lindeberg S. Food and western disease: health and nutrition from an evolutionary perspective. Chichester: Wiley-Blackwell; 2009.
21. Manheimer EW, van Zauren EJ, Fedorowicz Z, Pijl H. Paleolithic nutrition for metabolic syndrome: systematic review and meta-analysis. Am J Clin Nutr 2015 Oct;102(4):922–32.
22. Vogeilin WL. The stone age diet: based on in-depth studies of human ecology and the diet of man. New York: Vantage Press; 1975.
23. Wyatt J, Vogelsang H, Höbl W, Waldhör T, Lochs H. Intestinal permeability and the prediction of relapse in Crohn's disease. Lancet 1993 Jun 5;341(8858):1437–9.
24. de Punder K, Pruimboom L. The dietary intake of wheat and other cereal grains and their role in inflammation. Nutrients 2013 Mar 12;5(3):771–87.
25. Lerner A, Matthias T. Changes in intestinal tight junction permeability associated with industrial food additives explain the rising incidence of autoimmune disease. Autoimmun Rev 2015 Jun;14(6):479–89.
26. Ménard S, Cerf-Bensussan N, Heyman M. Multiple facets of intestinal permeability and epithelial handling of dietary antigens. Mucosal Immunol 2010 May;3(3):247–59.
27. Cordain L, Toohey L, Smith MJ, Hickey MS. Modulation of immune function by dietary lectins in rheumatoid arthritis. Br J Nutr 2000 Mar;83(3):207–17.
28. Mavrogiannis E, Kim K, Shimoda M, et al. Glycans in the immune system and The Altered Glycan Theory of Autoimmunity: a critical review. J Autoimmun 2015 Feb;57:1–13.