

Autoimmune and anti-inflammatory drugs

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In dealing with autoimmune illnesses, a common medical practice is the use of immunosuppressants¹ to address issues of inflammation. Often the drugs impact the tumor necrosis factor (TNF) which promotes the inflammation response. Diagnoses treated with this approach include rheumatoid arthritis, ankylosing spondylitis, crohn's disease, psoriasis, hidradenitis suppurativa and refractory asthma. Additional autoimmune conditions that are occasionally treated in this manner are sjogren's syndrome², fibromyalgia and chronic fatigue syndrome.

Conventional Approach

For illustration, for crohn's disease (CD), common prescription drugs used to suppress tumor necrosis factor (TNF) include:

- Abalimumab³
- Etanercept⁴
- Infliximab⁵

Included in side effects are increase risks of infection or re-occurrence of prior infections. Many autoimmune illnesses have been associated with certain infections and there is debate whether suppressing inflammation actually promotes the root cause of the autoimmune condition.

Some known risks⁶ include:

- serious and sometimes fatal blood disorders
- serious infections
- lymphoma and solid tissue cancers
- reports of serious liver injury
- reactivation of hepatitis B
- reactivation of tuberculosis
- lethal hepatosplenic T-cell
- drug-induced lupus
- demyelinating central nervous system disorders

The benefits of these drugs can be significant but often not sufficient for someone that is risk adverse. For example, 56-68% of patients with fistulae and crohn's responded to Infliximab⁷,

¹ <http://en.wikipedia.org/wiki/Immunosuppressant>

² <http://www.ncbi.nlm.nih.gov/pubmed/15593208>

³ <http://en.wikipedia.org/wiki/Adalimumab>

⁴ <http://en.wikipedia.org/wiki/Etanercept>

⁵ <http://en.wikipedia.org/wiki/Infliximab>

⁶ <http://en.wikipedia.org/wiki/Infliximab>

⁷ <http://www.nejm.org/doi/full/10.1056/NEJM199905063401804>

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what is often omitted is that 26% responded to a placebo. The difference in response rate (56% for the higher dosage (10mg/kg) versus 68% for the lower dosage (5mg/kg) is often ignored, and studies with dosages of 1mg/kg or lower have not been forthcoming. This same study found that 60% had adverse reactions.

In some cases, results from one condition may be used to infer an equivalent response for another condition. Subsequent studies do not find the expected response; to illustrate this, anti-TNF drugs worked with ulcerative colitis but they were statistically insignificant for crohn's disease⁸.

Many MDs would not present the above study as:

“You have a 50% chance of the fistula going into remission with this drug. Not taking any drugs, you have a 25% chance of going into remission. You have a 60% chance of having an adverse reaction taking this drug, and a significant risk of life-long complications”.

Many patients would decline the use of this drug because the risks exceed the benefits in their minds. In terms of economics, if the use of the drug includes 100% coverage of medical complications, lost earnings due to side-effects (and life insurance) for all of the known side-effects it is debatable if some of these drugs would have a net positive value for medical care costs.

Research Approach

Many current drugs are derived from analysis of traditional remedies. For example, for malaria, examining the traditional remedy of using Chinese wormwood resulted in the development of artemisinin which is now the WHO standard treatment. Several recent publications document alternatives to the standard prescription drugs cited above and their full text is available on line, for example:

A review of the efficacy of traditional Iranian medicine for inflammatory bowel disease.

Rahimi R, Shams-Ardekani MR, Abdollahi M. World J Gastroenterol. 2010 Sep 28;16(36):4504-14. PMID: 20857519⁹

Or the earlier:

Modulation of cytokine expression by traditional medicines: a review of herbal immunomodulators.

Spelman K, Burns J, Nichols D, Winters N, Ottersberg S, Tenborg M. Altern Med Rev. 2006 Jun;11(2):128-50.¹⁰

⁸ <http://www.ncbi.nlm.nih.gov/pubmed/17184965>

⁹ Full text: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2945480/?tool=pubmed>

¹⁰ Full text: <http://www.altmedrev.com/publications/11/2/128.pdf>

A summary table of traditional remedies with their documented medical vectors is shown below. For illustration, items impacting TNF- α (same mechanism as the above drugs) are the focus. These items are commonly available.

Herb - Supplement	Decrease	Increase
Pistacia lentiscus ¹¹ (Mastic)	<ul style="list-style-type: none"> • iNOS and Cox-2 • TNF-α, • Plasma IL-6, • C-reactive protein • CD activity index 	<ul style="list-style-type: none"> • macrophage migration inhibitory factor • Total antioxidant potential
Boswellia ^{12 13 14} ¹⁵ (Frankincense)	<ul style="list-style-type: none"> • NO production • IL-1A, • IL-1B, • IL-2, • IL-6, • IFN-γ • TNF-α 	<ul style="list-style-type: none"> • antimicrobial activities • basal activities
Curcumin ^{16 17} (Turmeric)	<ul style="list-style-type: none"> • COX-1, • COX-2, • LOX, • TNF-α, • IFN-gamma, • NF-kappabeta • iNOS 	<ul style="list-style-type: none"> • anti-oxidant
Black pepper ¹⁸	<ul style="list-style-type: none"> • TNF-induced NF-kappabeta activation • LPO • COX • TNF-α, • (IL)-1β • IL-6 • MAPKs 	<ul style="list-style-type: none"> •
Commiphora mukul (Myrrh)	<ul style="list-style-type: none"> • IFN-γ, • IL-12, • TNF-α, • IL-1β • NO 	<ul style="list-style-type: none"> • antimicrobial activities

¹¹ http://en.wikipedia.org/wiki/Pistacia_lentiscus

¹² <http://www.ncbi.nlm.nih.gov/pubmed/17024588>

¹³ <http://www.ncbi.nlm.nih.gov/pubmed/21513768>

¹⁴ <http://www.ncbi.nlm.nih.gov/pubmed/21831620>

¹⁵ <http://www.ncbi.nlm.nih.gov/pubmed/20696559>

¹⁶ <http://www.ncbi.nlm.nih.gov/pubmed/19519446>

¹⁷ <http://www.ncbi.nlm.nih.gov/pubmed/16387689>

¹⁸ <http://www.ncbi.nlm.nih.gov/pubmed/20839630>, <http://www.ncbi.nlm.nih.gov/pubmed/21663734>

Herb - Supplement	Decrease	Increase
	<ul style="list-style-type: none"> • IL-2 • IL-4 	
Astragalus ¹⁹	<ul style="list-style-type: none"> • NO • TNF-α • IL-6 • NF-kappabeta activation 	<ul style="list-style-type: none"> •
Solanum nigrum ²⁰ (black nightshade)	<ul style="list-style-type: none"> • TNF-α • NF-kappaBp50 • iNOS • COX-2 • IL-6 	<ul style="list-style-type: none"> •
Uncaria tomentosa ^{21 22} (Cat Claw)	<ul style="list-style-type: none"> • TNF-α • IFN-alpha 	<ul style="list-style-type: none"> • IL-1beta
Urtica dioica ^{23 24} (stinging needle)	<ul style="list-style-type: none"> • IL-6 • hs-CRP • TNF-α • IL-1beta 	<ul style="list-style-type: none"> •
Ginger [Caution] ²⁵	<ul style="list-style-type: none"> • TNF-α 	<ul style="list-style-type: none"> •
Garlic ²⁶	<ul style="list-style-type: none"> • TNF-α • NO 	<ul style="list-style-type: none"> •
Cinnamon ²⁷	<ul style="list-style-type: none"> • ICOS-L), • MHCII • COX-2. • IL-1β, • IFN-γ • TNF-α 	<ul style="list-style-type: none"> • IL-10

Summary

In treatments there are several vectors that need to be considered such as cost (some herbs cited above are < \$100/year while recommended prescription drugs > \$10,000/year), side effects (herbs have much lower incidence with less severe consequences), and effectiveness of treatment. The value of selling patented drugs have resulted in many studies proving their benefit *against* placebos but studies comparing them to traditional remedies are rare. The few

¹⁹ <http://www.ncbi.nlm.nih.gov/pubmed/21937031>

²⁰ <http://www.ncbi.nlm.nih.gov/pubmed/19184365>

²¹ <http://www.ncbi.nlm.nih.gov/pubmed/19995599>

²² <http://www.ncbi.nlm.nih.gov/pubmed/18279801>

²³ <http://www.ncbi.nlm.nih.gov/pubmed/22303583>

²⁴ <http://www.ncbi.nlm.nih.gov/pubmed/15338166>

²⁵ <http://www.ncbi.nlm.nih.gov/pubmed?term=20144628> Positive and negative responses reported.

²⁶ <http://www.ncbi.nlm.nih.gov/pubmed/22260639>

²⁷ <http://www.ncbi.nlm.nih.gov/pubmed/21451725>

studies that have been done have occasionally found superior efficiency against existing drugs²⁸.

“Clinical studies, so far with pilot character, suggest efficacy [of Boswellia] in some autoimmune diseases including rheumatoid arthritis, Crohn's disease, ulcerative colitis and bronchial asthma. Side effects are not severe when compared to modern drugs used for the treatment of these diseases.”²⁹

“ All parameters tested improved after treatment with Boswellia serrata gum resin, the results being similar compared to controls: 82% out of treated patients went into remission; in case of sulfasalazine remission rate was 75%.”³⁰

Items to be avoided

It should be noted that some traditional remedies are counter-indicated, for example elderberry increases immune response. With the availability of pubmed it is relatively easy to determine if a supplement increases or decrease specific responses.

Herb - Supplement	Decrease	Increase
Sambucus ³¹ (elderberry)	•	<ul style="list-style-type: none">• IL-1 beta,• TNF-alpha,• IL-6,• IL-8• TNF-α

Conclusions

The choice between a traditional remedy and a modern prescriptive drug should always be the patient's -- based on accurate information on the benefit, risks and costs of each option. Many MDs do not have accurate quantitative information available because their education on new drugs is often the result of education by pharmaceutical agents-sales persons who have a vested interest.

Many MDs are not able to advise a patient with chronic colitis as follows:

I could prescribe sulfasalazine (3 gm/day), which may be covered by your medical plan, and which has a 40-75% % remission rate in some studies, or I could suggest taking 0.9 gms of boswellia daily which has a 70-82% remission rate in the same studies. You can buy this at most supplement shops. Sulfasalazine had a known risk of liver disease and abnormality and hepatic necrosis; boswellia does not have this known risk.

This raises a medical ethics question on whether a patient has been sufficiently informed to

²⁸ <http://www.ncbi.nlm.nih.gov/pubmed/11488449>

²⁹ <http://www.ncbi.nlm.nih.gov/pubmed/17024588>

³⁰ <http://www.ncbi.nlm.nih.gov/pubmed/9049593>

³¹ <http://www.ncbi.nlm.nih.gov/pubmed/11399518>, full text: <http://www.jle.com/medline.md?issn=1148-5493&vol=12&iss=2&page=290>

really have informed consent. Failing to present information on viable alternatives becomes an ethical question.

Pub Med Bibliography

The following articles were also reviewed in the preparation of this document.

- <http://www.ncbi.nlm.nih.gov/pubmed/21910171>
- <http://www.ncbi.nlm.nih.gov/pubmed/21912766>
- <http://www.ncbi.nlm.nih.gov/pubmed/8951512>
- <http://www.ncbi.nlm.nih.gov/pubmed/15942912>
- <http://www.ncbi.nlm.nih.gov/pubmed/22043203> (Full text available)
- <http://www.ncbi.nlm.nih.gov/pubmed/20838436> (Full text available)
- <http://www.ncbi.nlm.nih.gov/pubmed/20857519> (Full text available)
- <http://www.ncbi.nlm.nih.gov/pubmed/9049593>
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