How to perform a CAT?

The CAT (Critically Appraised Topic) is a structured one-page summary and critique of the best available evidence on a focused question. The CAT format requires the writer to:

1. Ask a clear, concise and focused question,
2. Conduct an efficient and effective search for the highest quality research evidence available,
3. Critically appraise the located evidence, and carefully consider the applicability/generalizability of the evidence,
4. Write the structured summary (see appendix 4) in 1-4 pages. This is the only document you need to send in.
5. Your document should have the name: 999cat.doc, where 999 should be substituted by your exam number you got from our office.
6. Make a powerpoint to help you to present your CAT at the exam. This powerpoint should not be sent in and must not contain more then 10 slides (4 slides could be sufficient).


Some important points

- A CAT is not presenting original research from yourself or your own institute, it is not a report of one study, it is diving in to literature and comparing a couple (at least three) independent papers dealing with the question you propose. Once you cannot find at least 3 appropriate papers you should reformulate your question or find another topic.
- Your CAT should be original work. We will scan your submission for plagiarism.
- Submit your CAT in word-format, preferentially in Calibri 11 points.
- Give your CAT a clear and informative title.
- Do not forget to write your name and exam number on the top of your document.
An Example

Step 1  Ask a clear, concise and focused question

What’s the evidence for the efficacy of Infliximab for generalized myositis without further comorbidity?

So studies on myositis with other concomitant diseases, studies not focusing on therapy and studies with focal myositis should be skipped. I did not make a differentiation between polymyositis and dermatomyositis. Inclusion body myositis will not be traced as this is not treated with Infliximab.

To keep the CAT limited, I confined myself to Infliximab and did not look at TNF-α blocking agents in general.

Step 2 Conduct an efficient and effective search.

Search Strategy:

www.pubmed.org  Key-Words Polymyositis AND Infliximab. No filters used.

www.thecochranelibrary.com  Polymyositis*, Infliximab* (ti, ab, kw)

Result: 46 Hits to be screened for relevance in Pubmed, 1 hit in Cochrane. See Appendix 1

Step 3 Critically appraise the located evidence

15 Papers remained and have been read. Some notes were made. See Appendix 2.

11 Papers appeared useful. These 11 have been read again to fill the table in Appendix 3.

The problem of this CAT is a very uncommon one. Therefore a couple of case reports have been studied. In more common problems, one can restrict oneself to some bigger studies. A table like in Appendix 3 is not always necessary, it was just my way of approach.
Step 4 Writing the Summary

This is the result of your CAT to be sent in to the exam-committee.

See appendix 4.

I decided to take the 3 multi-patient-Studies to describe and to give a global comment to the single patient cases. You may use another approach.

The only report we want you to send in is the summary following the structure

<table>
<thead>
<tr>
<th>Title</th>
<th>Short description of the CAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name Author</td>
<td>Your name and the date of the study</td>
</tr>
<tr>
<td>Question</td>
<td>Be sure the question is concise and focused!</td>
</tr>
<tr>
<td>Search Strategy</td>
<td>Pubmed and Cochrane are satisfactory</td>
</tr>
<tr>
<td>Search Outcome</td>
<td>Describe your selection strategy</td>
</tr>
<tr>
<td>Results</td>
<td>Make a table as depicted</td>
</tr>
<tr>
<td>Comments</td>
<td>Make a sophisticated narrative comment</td>
</tr>
<tr>
<td>Clinical Bottom Line</td>
<td>This is the final conclusion</td>
</tr>
<tr>
<td>References</td>
<td>Only mention the references studied</td>
</tr>
</tbody>
</table>

Within this frame-work many will be possible and accepted by the examiners.

Be prepared on questions concerning your CAT.

The scoring form as given in appendix 5 will be used.

Please do not hesitate to ask for further information: j.b.m.kuks@umcg.nl
Appendix 1

Results: 46

Successful treatment of calcinosis with infliximab in a patient with systemic sclerosis/myositis overlap syndrome.
Tosounidou S, MacDonald H, Situnayake D.
→ Skipped, because of further comorbidity

The vitamin D receptor agonist BXL-01-0029 as a potential new pharmacological tool for the treatment of inflammatory myopathies.
→ Skipped, because of not focusing to Infliximab

Bacterial endophthalmitis caused by an intraocular cilium in a patient under treatment with infliximab.
Jin XH, Namba K, Saito W, Iwata D, Ishida S.
→ Skipped, because of no focus on therapeutic effect of infliximab

Efficacy of infliximab in the treatment for dermatomyositis with acute interstitial pneumonia: a study of fourteen cases and literature review.
Chen D, Wang XB, Zhou Y, Zhu XC.
→ Skipped, because of further comorbidity

Verma S, Kroeker KI, Fedorak RN.
→ Skipped, because of no focus on therapeutic effect of infliximab

Raised circulating tenasin-C in rheumatoid arthritis.
Page TH, Charles PJ, Piccinini AM, Nicolaïdou V, Taylor PC, Midwood KS.
→ Skipped, because of no focus on therapeutic effect of infliximab

Therapeutic advances in myositis.
Aggarwal R, Oddis CV.
→ Not original! Screened for a new link not found in Pubmed

Immunosuppressant and immunomodulatory treatment for dermatomyositis and polymyositis.
Gordon PA, Winer JB, Hoogendijk JE, Choy EH
→ Not original! Screened for a new link not found in Pubmed

This study came up in both the Pubmed and the Cochrane search
Bilateral diffuse orbital myositis in a patient with relapsing ulcerative colitis.
Bennion J, Harris MA, Sivak-Callcott JA, Nguyen J.
→ Skipped, because of no focus on generalized myositis

Anti-tumor necrosis factor inhibitor therapy-induced dermatomyositis and fasciitis.
Riolo G, Towheed TE.
→ Skipped, because of no focus on therapeutic effect of infliximab

Inflammatory response in human skeletal muscle cells: CXCL10 as a potential therapeutic target.
→ Skipped, because of no focus on therapeutic effect of infliximab

Successful treatment for conventional treatment-resistant dermatomyositis-associated interstitial lung disease with adalimumab.
Park JK, Yoo HG, Ahn DS, Jeon HS, Yoo WH.
→ Skipped, because of comorbid therapy

Tubercular pyomyositis in a case of rheumatoid arthritis being treated with infliximab.
Khosla P, Aroaa N, Jain L.
→ Skipped, because of no focus on therapeutic effect of infliximab

Coexistent pyoderma gangrenosum and tibialis anterior myositis as presenting manifestations of Crohn's disease: case report and review of the literature.
→ Skipped, because of no focus on therapeutic effect of infliximab

Dysferlin deficiency treated like refractory polymyositis.
→ Skipped, because of no focus on myositis

Disseminated Histoplasma capsulatum infection presenting with panniculitis and focal myositis in rheumatoid arthritis treated with etanercept.
Bourré-Tessier J, Fortin C, Belisle A, Desmarais E, Choquette D, Senécal JL.
→ Skipped, because of comorbidity

mAbs in nonlupus autoimmune rheumatic disease.
Whelan BR, Isenberg DA.
→ Skipped, because of no focus on therapeutic effect of infliximab

A case of inclusion body myositis responsive to prednisolone therapy.
Kalla R, Soumakiyan M, Tuck S.
Recurrent posterior scleritis and orbital myositis as extra-intestinal manifestations of Crohn’s disease: Case report and systematic literature review.
Culver EL, Salmon JF, Frith P, Travis SP.

Inflammatory muscle diseases.
Mastaglia FL.
Neurol India. 2008 Jul-Sep;56(3):263-70. Review.
Not original, however screened to find a new reference

Successful treatment of idiopathic orbital inflammation with infliximab: an alternative to conventional steroid-sparing agents.

Treatment of idiopathic sclerosing inflammation of the orbit (myositis) with infliximab.
Sahlin S, Lignell B, Williams M, Dastmalchi M, Orrego A.

Effectiveness of infliximab in the treatment of refractory juvenile dermatomyositis with calcinosis.

Open-label trial of anti-TNF-alpha in dermato- and polymyositis treated concomitantly with methotrexate.

Autoimmune diseases induced by TNF-targeted therapies: analysis of 233 cases.

[Anti TNF-alpha treatment of a refractory polymyositis].
Polymyositis associated with infliximab treatment for rheumatoid arthritis.
Urata Y, Wakai Y, Kowatari K, Nitobe T, Mizushima Y.
→ Skipped, because of no focus on treatment of generalized myositis

Infectious myositis involving the piriformis in a patient with rheumatoid arthritis.
Oda S, Fujinaga H, Takahashi K.
→ Skipped, because of no focus on treatment of generalized myositis

Treatment of early and refractory dermatomyositis with infliximab: a report of two cases.
Dold S, Justiniano ME, Marquez J, Espinoza LR.
→ Included

Possible role for tumour necrosis factor inhibitors in the treatment of resistant dermatomyositis and polymyositis: a retrospective study of eight patients.
Efthimiou P, Schwartzman S, Kagen LJ.
→ Included

Fatal Mycobacterium peregrinum pneumonia in refractory polymyositis treated with infliximab.
Marie I, Heliot P, Roussel F, Hervé F, Muir JF, Levesque H.
→ Included

Connective tissue disease in children.
Buka RL, Cunningham BB.
→ Skipped, because of no focus on treatment of generalized myositis

Advanced refractory polymyositis responding to infliximab.
Anandacoomarasamy A, Howe G, Manolios N.
→ Included

Treatment of recalcitrant idiopathic orbital inflammation (chronic orbital myositis) with infliximab.
Garry TA, Coleman AW, Matteson EL, Eggenberger ER, Waitzman DM.
→ Skipped, because of no focus on generalized myositis

Refractory polymyositis responding to infliximab.
Uthman I, El-Sayad J.
→ Included

Refractory adult dermatomyositis with pneumatosis cystoides intestinalis treated with infliximab.
Treatment of dermatomyositis and polymyositis with anti-tumor necrosis factor-alpha: long-term follow-up.
Hengstman GJ, van den Hoogen FH, van Engelen BG.

Fatal myositis due to the microsporidian Brachiola algerae, a mosquito pathogen.

Successful treatment of alveolar hypoventilation due to dermatomyositis with anti-tumour necrosis factor-alpha.
Korkmaz C, Temiz G, Cetinbas F, Büyükkidan B.

Refractory polymyositis responding to infliximab: extended follow-up.

Polyarthritis associated with infliximab treatment for rheumatoid arthritis.
Musiał J, Undas A, Celińska-Lowenhoff M.

Kane D, Balint PV, Wood F, Sturrock RD.

Successful treatment of dermatomyositis and polymyositis with anti-tumor-necrosis-factor-alpha: preliminary observations.
Hengstman GJ, van den Hoogen FH, Barrera P, Netea MG, Pieterse A, van de Putte LB, van Engelen BG.

Non-Hodgkin's lymphoma in a patient with refractory dermatomyositis which had been treated with infliximab.
Roddy E, Courtney PA, Morris A.
Appendix 2

**Inflammatory muscle diseases.**
Mastaglia FL.
Neurol India. 2008 Jul-Sep;56(3):263-70. Review.

**Not Useful**

(1)
_A high incidence of disease flares in an open pilot study of infliximab in patients with refractory inflammatory myopathies._

*Open label trial*

13 patients with treatment resistant myositis. 3 drop outs because of side effects, 1 because of a tumor. No effect of infliximab in the remaining patients.

**Useful**

(2)
_Immunosuppressant and immunomodulatory treatment for dermatomyositis and polymyositis._
Gordon PA, Winer JB, Hoogendijk JE, Choy EH.


*Randomized Controlled Trial*

11 patients therapy resistant. Unblinding to an open label study after 16 weeks. No statistical significant effect.

**Useful**

(3)
_Open-label trial of anti-TNF-alpha in dermato- and polymyositis treated concomitantly with methotrexate._
Eur Neurol. 2008;59(3-4):159-63.

*Open label trial*

6 patients 18-70 years old, drug naive! 4 drop-outs, three because of disease progression, 1 because of a possible infusion reaction. Only 2 had a follow-up of ½ jaar, these patients did respond.

**Useful**
Case report

30 years old female with Infliximab with moderate success and relapses. After discontinuation an unexpected improvement occurred. Methotrexate was given as well.

Useful

Treatment of early and refractory dermatomyositis with infliximab: a report of two cases.
Dold S, Justiniano ME, Marquez J, Espinoza LR.

Female 40 years, resistant to other therapies, good response, afterward steroids and MTX. Self-discontinuation of therapies after 11 months led to death.
Female 29 years, no satisfactory response to steroids. Infliximab for led to improvement. Follow-up 6 months (?)

Possible role for tumour necrosis factor inhibitors in the treatment of resistant dermatomyositis and polymyositis: a retrospective study of eight patients.
Efthimiou P, Schwartzman S, Kagen LJ.

Case study

Eight patients with dermatomyositis or polymyositis refractory to corticosteroids and immunosuppressives who were treated with TNF inhibitors between 1998 and 2004. Only one was treated with infliximab. This 73-year old male did not respond to Infliximab.

Useful

Fatal Mycobacterium peregrinum pneumonia in refractory polymyositis treated with infliximab.
Marie I, Heliot P, Roussel F, Hervé F, Muir JF, Levesque H.

Case report

68-years old male patient with several immunosuppressive drug failures. Concomitant infection, no information on effect infliximab.

Not useful

Advanced refractory polymyositis responding to infliximab.
Anandacoomarasamy A, Howe G, Manolios N.
Case Study

66 year old female with a 15 years history, unsatisfactory responses to steroids, azathioprine, IVIG, mycophenolate. Follow-up of 22 Months but still on an 4-8 weeks schedule.

Useful

(8) Refractory polymyositis responding to infliximab.
Uthman I, El-Sayad J.

Case Study

33 year old female with a 5 years history, non responding to steroids, azathioprine, methotrexate. Remission with 1 year follow up.

Useful

(9) Treatment of dermatomyositis and polymyositis with anti-tumor necrosis factor-alpha: long-term follow-up.
Hengstman GJ, van den Hoogen FH, van Engelen BG.

Case Study

2 Patients demonstrated a marked and sustained subjective and objective improvement without the occurrence of any side effects at a first treatment. There was a relapse after 3-4 months with a second successful treatment period, however 1 patients got an anaphylaxis. Concomitant treatment with Methotrexate is advised.

Useful

(10) Successful treatment of alveolar hypoventilation due to dermatomyositis with anti-tumour necrosis factor-alpha.
Korkmaz C, Temiz G, Cetinbas F, Büyükkidan B.

19-years old girl with hypoventilation due to myositis. No response to other therapies. Improved.

Useful

(11) Refractory polymyositis responding to infliximab: extended follow-up.
Case Study

One 63-years old female with polymyositis refractory to steroids, intravenous immunoglobulins, methotrexate, azathioprine. Rapid sustained improvement. Follow-up of two years. Probably additional effect of azathioprine!

Useful

Successful treatment of dermatomyositis and polymyositis with anti-tumor-necrosis-factor-alpha: preliminary observations.
Hengstman GJ, van den Hoogen FH, Barrera P, Netea MG, Pieterse A, van de Putte LB, van Engelen BG.

Case Study

2 Patients demonstrated a marked and sustained subjective and objective improvement without the occurrence of any side effects. Further details are not known.

Not useful

Recent advances in the management of adult myositis.
Fam AG.

Not useful
<table>
<thead>
<tr>
<th>Year</th>
<th>#</th>
<th>Side Effects</th>
<th>Concom Immune Suppression?</th>
<th>Infliximab Dose and Frequency</th>
<th>Follow-Up</th>
<th>Other</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2008</td>
<td>13pp ankle flare</td>
<td>Yes</td>
<td>5 mg/kg 4*/14 wk</td>
<td>4 mo</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2008</td>
<td>12pp ??</td>
<td>-</td>
<td>5 mg/kg 0, 2, 6, 14, 22, 30, 38, and 46 wk</td>
<td>16 wk</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2008</td>
<td>6 pp Infusion Reaction</td>
<td>No</td>
<td>MTX 10mg/kg 0, 2, 6, 14, 22, 30, 38, and 46 wk</td>
<td>26 wk</td>
<td>3+/3 -</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2007</td>
<td>F40</td>
<td>Yes</td>
<td>6*5mg/kg/6 wk</td>
<td>2 yrs</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2007</td>
<td>F40 F29</td>
<td>Yes</td>
<td>3*5 mg/kg/2 wk</td>
<td>11mo 6 mo</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>2006</td>
<td>M73</td>
<td>Yes</td>
<td>3 mg/kg/8 wk</td>
<td>4 mo</td>
<td>Contin. Therapy</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>2005</td>
<td>F66 Peptic Ulcer?</td>
<td>Yes</td>
<td>??</td>
<td>5 mg/kg/4 wk</td>
<td>22 wk</td>
<td>Contin. Therapy</td>
</tr>
<tr>
<td>8</td>
<td>2004</td>
<td>F33</td>
<td>Yes</td>
<td>5x 300 mg/6 wk</td>
<td>1 year</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>2004</td>
<td>2 pp Anaphylaxis</td>
<td>No</td>
<td>10 mg/kg 0,2,4 wk</td>
<td>20 wk</td>
<td>Relapse after 20 wk</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>2004</td>
<td>F19 - Steroids</td>
<td>Yes</td>
<td>8 mg/kg 0, 2, 6 wk</td>
<td>?</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>2004</td>
<td>F63</td>
<td>Yes</td>
<td>10 mg/kg 5x each 2 weeks</td>
<td>2 yr</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 4  Summary (this is the only document to send in)

Infliximab to treat myositis.

JBM Kuks MD PhD 15th November 2014

**Question**  What’s the evidence for the efficacy of Infliximab for generalized myositis without further comorbidity?

**Search Strategy**  Pubmed [myositis] AND [infliximab]

Result: 46 papers, 11 containing direct information relevant for the question: 8 case studies, 2 open label trials, 1 randomized controlled trial. The Cochrane review was included.

Cochrane  myositis*, infliximab* (ti, ab, kw)

Result: 1 review

**Search Outcome**

From the 46 papers, 11 were studied in depth, out of these 3 were selected for this CAT

**Results**

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Patient Group &amp; Intervention</th>
<th>Study Type</th>
<th>Outcome</th>
<th>Key Results</th>
<th>Study Weakness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dastmalchi</td>
<td>13 patients 5mg/kg Infliximab</td>
<td>Open label</td>
<td>Improvement of weakness</td>
<td>Negative</td>
<td>Concomitant immunosuppressives.</td>
</tr>
<tr>
<td>Coyle</td>
<td>12 patients 5mg/kg Infliximab against placebo</td>
<td>RCT</td>
<td>Improvement of weakness</td>
<td>Not significant</td>
<td></td>
</tr>
<tr>
<td>Hengstman</td>
<td>6 patients 10mg/kg Infliximab</td>
<td>Open label</td>
<td>Improvement of weakness</td>
<td>Doubtful, not really predictable</td>
<td>Concomitant immunosuppressives Low number of patients</td>
</tr>
</tbody>
</table>

**Comments**

The subject is not really topical anymore, as most relevant studies have been written between 2004-2008.

Most studies on Infliximab for Myositis are case reports of patients refractory to other medication and all these case studies report a positive result, so that publication bias is likely. On the other hand the quoted studies with 6-13 patients report negative or at most doubtful effects of Infliximab. Except for in the randomized all patients have been treated with concomitant other immunosuppressive medication, making it difficult to assess the pure effect of Infliximab. This was
clearly negative in the RCT-study without concomitant medication, however, the medication dose was relatively low. Finally the effect of Infliximab has been tested in a selected population: nearly all patients have failed in other regimes with immunosuppression. Only one study describes the effect in patients without previous immunomodulation (but with concomitant immunosuppressive medication). The results were equivocal.

**Clinical Bottom Line**

There is no statistical evidence for the effect of Infliximab in patients with otherwise refractory myositis. Case studies suggest that in individual cases Infliximab may be helpful, but it is not possible to predict this effect. A randomized controlled study with patients using Infliximab without concomitant immunosuppressive medication and without previous immunosuppression would be needed to really assess the effect of Infliximab.

**References**

*A high incidence of disease flares in an open pilot study of infliximab in patients with refractory inflammatory myopathies.*

*A randomized, double-blind, placebo-controlled trial of infliximab in patients with polymyositis and dermatomyositis.*

*Open-label trial of anti-TNF-alpha in dermato- and polymyositis treated concomitantly with methotrexate.*

**Further Case Reports**

[Anti TNF-alpha treatment of a refractory polymyositis].

*Treatment of early and refractory dermatomyositis with infliximab: a report of two cases.*

Possible role for tumour necrosis factor inhibitors in the treatment of resistant dermatomyositis and polymyositis: a retrospective study of eight patients.

*Advanced refractory polymyositis responding to infliximab.*

*Refractory polymyositis responding to infliximab.*
Uthman I, El-Sayad J.
**Treatment of dermatomyositis and polymyositis with anti-tumor necrosis factor-alpha: long-term follow-up.**  
Hengstman GJ, van den Hoogen FH, van Engelen BG.  
**Successful treatment of alveolar hypoventilation due to dermatomyositis with anti-tumour necrosis factor-alpha.**  
Korkmaz C, Temiz G, Cetinbas F, Büyükkidan B.  
**Refractory polymyositis responding to infliximab: extended follow-up.**  
## Appendix 5

### Scoring form for CAT

<table>
<thead>
<tr>
<th>Item</th>
<th>Maximal Score</th>
<th>Actual score*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. There is a clear, concise and focused question</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2. The question is original and relevant for clinical practice</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3. The search strategy is adequate</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>4. The research outcome is adequate</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>5. The table with results is correct</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>6. The comments described are adequate</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>7. The final conclusion is sound</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>8. The references are really the current key-references for this problem</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>9. The answers to the questions are adequate</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>10. Handling ignorance is adequate</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>15</strong></td>
<td></td>
</tr>
</tbody>
</table>

*There will be a conversion of the score to a mark between 0 and 10