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continued peer review
case presentation of disseminated herpes zoster (Mayo Clin Proc 2004 Aug)
topical application of povidone-iodine associated with rapid crusting and pain resolution in case report (Lancet 2004 Aug 7)

Click the blue triangles to expand sections.

- ▶ **Description (including ICD-9 Codes)**
- ▶ **Causes and Risk Factors**
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▼ **Diagnosis**

Making the diagnosis:

- usually diagnosed clinically
 - in large series using expert opinion and clinical course as gold standard, 38 (7%) of 505 cases diagnosed clinically by general practitioners in Iceland were incorrect, most incorrect diagnoses were likely due to herpes simplex infections (Eur J Gen Pract 1996 Mar;2:12 in [Journal Club on the Web 1996 May 9](#))
- Tzanck smear showing multinucleated giant cells can be done, but laboratory expertise is limited and this test has a low sensitivity and specificity
- viral culture would provide definitive diagnosis, but results are delayed
- DNA specific testing available in some centers

Rule out:

- when pain occurs before (or without) lesions, many other causes of pain must be considered, such as cholecystitis, pleuritis, cardiac ischemia, diabetic painful neuropathy
- for vesicular or papular lesions - contact dermatitis, herpes simplex (typically not dermatomal), coxsackievirus infection, bullous impetigo, spider or insect bite or sting

Tests to order:

- testing should be reserved for rare cases when diagnostic certainty is clearly important, as clinical diagnosis almost always made easily (only 7% error rate in Iceland)

Recommended Testing from UPCMD.com:



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Recommended Testing from UPCMD.com:

Initial Testing
Direct Fluorescent Antibody Test (DFA)
Polymerase Chain Reaction (PCR)

Confirmatory Testing
Viral Shell Vial Culture/Viral Tissue Culture

Monitoring Testing
No tests recommended

further details from UPCMD.com

- Copyrighted material used by permission of the University Pathology Consortium, LLC 2002. The data herein have been compiled by a collaboration of six University Medical School Departments of Pathology and Laboratory Medicine in 2000-2001 and has not been actively updated.

Blood tests:

- serology not useful during acute symptoms, but can provide retrospective diagnosis

Other diagnostic testing:

- Tzanck smear, from scrapings of base of vesicle, may show multinucleated giant cells, but does not differentiate zoster from herpes simplex



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Recommended Testing from UPCMD.com:

Initial Testing

- Direct Fluorescent Antibody Test (DFA)
- Polymerase Chain Reaction (PCR)

Confirmatory Testing

- Viral Shell Vial Culture/Viral Tissue Culture

Monitoring Testing

No tests recommended

▼ further details from UPCMD.com

Direct Fluorescent Antibody Test (DFA) [CPT-87206]

Source: Fresh vesicle/lesions, epithelial cells from the base of the vesicles; minimum 2-3 fresh vesicles.

Handling: Unroof vesicles and vigorously swab the base of the lesion to collect a large amount of epithelial cells. Place on 2 (preferably 3) double ringed slides.

Special handling: For transport delay, air dry and fix the slides by flooding with acetone for 1-2 minutes. Drain, air dry, and send to the laboratory in a protective cardboard slide container.

Polymerase Chain Reaction (PCR) [CPT-87532]



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▼ Treatment

Treatment Overview:

- zoster is self-limited and usually resolves without complications; treatment goals are to reduce symptoms, speed rash resolution and prevent complications
- treatments that may reduce acute pain
 - corticosteroids may reduce acute zoster pain and improve quality of life at 1 month (**level 2 [mid-level] evidence**), but have no benefit for postherpetic neuralgia
 - other treatments that may reduce acute pain (**level 3 [lacking direct] evidence**) include cool compresses, calamine lotion, analgesics, tricyclic antidepressants
- limited evidence that any treatments prevent postherpetic neuralgia, but famciclovir, valacyclovir or amitriptyline may be considered
- antiviral treatment
 - antiviral treatments achieve modest reduction in time to full healing of rash if started within 3 days of initial rash (e.g. full crusting may occur in 10 days without antiviral agent and 8 days with antiviral agent)
 - antiviral agents should be strongly considered in ophthalmic zoster, disseminated zoster, and ill severely immunocompromised patients
 - antiviral treatment options
 - valacyclovir (Valtrex) 1 g PO tid for 7 days \$118.69
 - famciclovir (Famvir) 500 mg PO tid for 7 days \$154.91
 - acyclovir (Zovirax) 800 mg PO 5x/day for 7-10 days \$184.82, generic \$42.56
 - Reference - [The Medical Letter 2002](#) Feb 4;44(1123):9
 - parenteral antiviral agents indicated for some cases of ophthalmic zoster, immunocompromised hosts, and disseminated zoster
 - in immunocompromised host, acyclovir (Zovirax) 10 mg/kg (500 mg/m² in children) IV q8h

Medications:

- analgesics or [tricyclic antidepressants](#) for acute pain
- antiviral treatment
 - useful for hastening of healing of acute zoster (modest benefit)
 - valacyclovir and famciclovir also have been shown to reduce duration of postherpetic neuralgia in randomized trials, but most patients (especially those aged < 50) do not develop postherpetic neuralgia
 - ophthalmic zoster should be treated with oral antiviral agents in consultation with ophthalmology consultants
 - **famciclovir 500 mg PO tid and acyclovir 800 mg PO 5 times daily for 7 days had equivalent efficacy in randomized trial** of 454 patients with ophthalmic zoster of trigeminal nerve, 58% of both groups had one or more ocular manifestations over 6 months ([Br J Ophthalmol 2001 May;85\(5\):576](#))
 - **valacyclovir 1,000 mg PO bid and acyclovir 800 mg PO 5 times daily for 7 days had equivalent efficacy in randomized trial** of 110 immunocompetent patients with herpes zoster ophthalmicus diagnosed within 72 hours of skin eruption ([Ophthalmology 2000 Aug;107\(8\):1507](#))
 - **oral antiviral therapy associated with lower complication rate in patients with acute herpes zoster ophthalmicus**; retrospective study comparing 202 such patients treated with oral antivirals vs. 121 who were not, 0 vs. 3.3% had neurotrophic keratitis (p = 0.02, NNT 30), 2.1% vs. 8.9% had adverse outcome (visual acuity 20/200 or worse, trichiasis, or surgery for eyelid malposition) at 5-10 years (p = 0.009, NNT 15) ([Arch Ophthalmol 2003 Mar;121\(3\):386](#) in [Global Family Doctor 2003 Mar 13](#))
 - for localized zoster in immunocompetent adults (start within 48-72 hours of onset of rash)
 - valacyclovir (Valtrex) 1 g PO tid for 7 days

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Tricyclic antidepressants (TCAs)

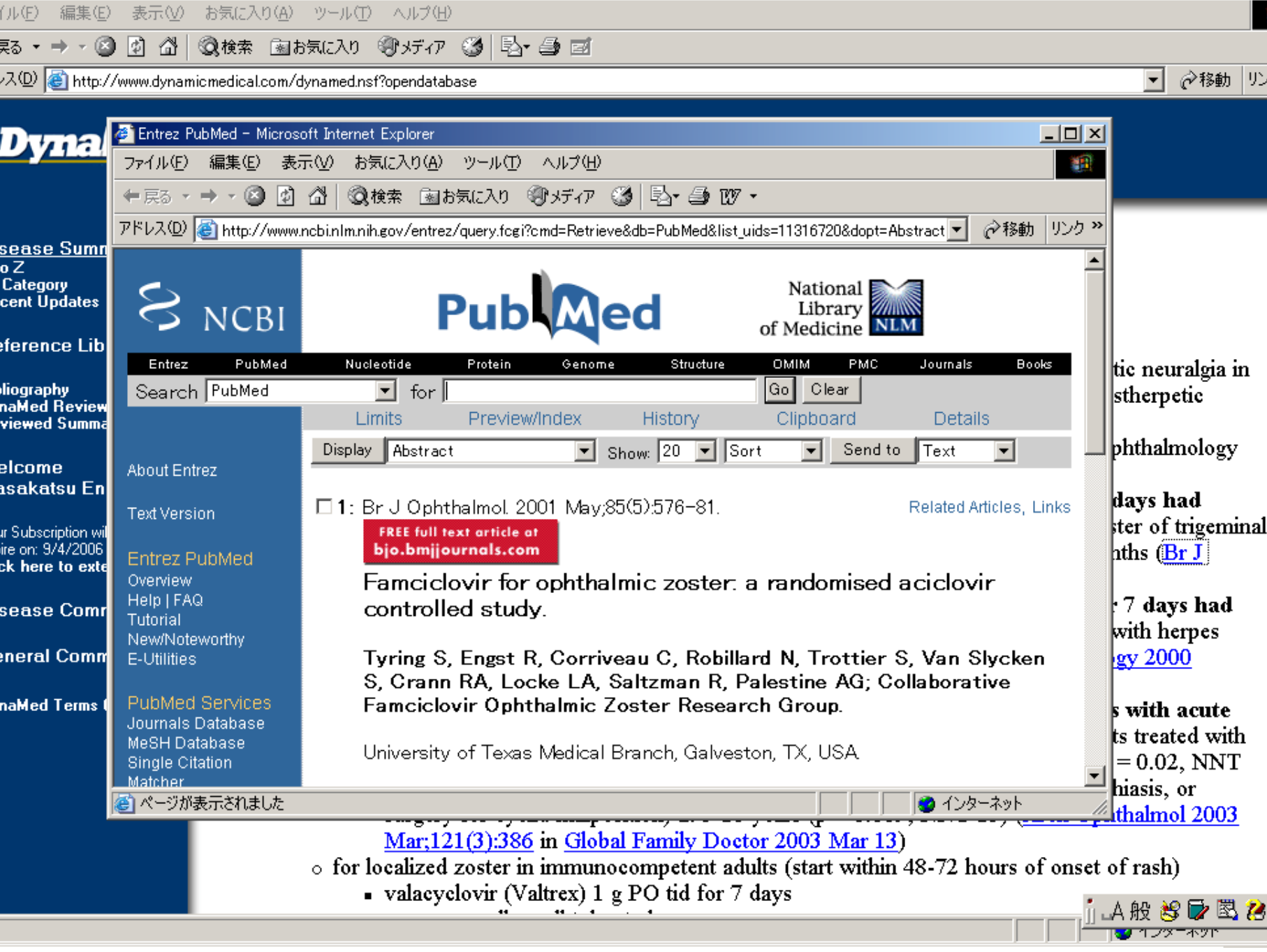
Updated 06/05/2004 07:40 AM : patient information handout from Patient UK
low-dose tricyclic antidepressants effective in adults (Cochrane Library 2003 Issue 3)
30-day costs (Treatment Guidelines from The Medical Letter 2003 Jul)

- general information
 - previous response to TCA or family history of TCA efficacy may be predictive of benefit
 - in elderly start low, go slow
 - terminal insomnia disappears first, predicts response
 - do not use if suicidal or sedating
 - monitor blood level
 - cardiovascular problems most dangerous but uncommon
 - contraindication - preexisting block
 - agents with more anticholinergic effects relatively contraindicated in narrow-angle glaucoma or BPH, recent myocardial infarction, active seizure disorder
 - choice based on mix of sedation, anticholinergic and orthostatic hypotension acceptable to patient
 - before beginning TCA treatment - checklist for contraindications: ECG for BBB or prolonged PR, LFTs, tonometry or screen for glaucoma, sitting + standing BP measurements, evaluate urinary obstructive symptoms + prostate size in men, assess

- valacyclovir (Valtrex) 1 g PO tid for 7 days

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1: Br J Ophthalmol. 2001 May;85(5):576-81. [Related Articles, Links](#)

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Famciclovir for ophthalmic zoster: a randomised aciclovir controlled study.

Tyring S, Engst R, Coriveau C, Robillard N, Trottier S, Van Slycken S, Crann RA, Locke LA, Saltzman R, Palestine AG; Collaborative Famciclovir Ophthalmic Zoster Research Group.

University of Texas Medical Branch, Galveston, TX, USA

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Level of Evidence Labeling in DynaMed

DynaMed has introduced level of evidence/strength of recommendation labeling as of March 2004.

Individual evidence reports will be labeled as one of the following:

level 1 (likely reliable) evidence -- representing the most valid reports addressing patient-oriented outcomes. Examples include randomized trials with at least 80% follow-up, inception cohort studies for prognostic information, and systematic reviews of level 1 evidence reports. These examples are only presented as brief examples. Achieving a level 1 evidence label means that specific quality criteria were met based on the study type.

level 2 (mid-level) evidence -- representing reports addressing patient-oriented outcomes, and using some method of scientific investigation, yet not meeting the quality criteria to achieve level 1 evidence labeling. Examples include non-randomized trials with less than 80% follow-up, non-randomized comparative studies, and diagnostic studies with out...

- creatinine clearance 20-39 mL/minute - 500 mg qd
- creatinine clearance < 20 mL/minute - 250 mg qd

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- 20/20 vs. 20/70 had adverse outcomes (visual acuity 20/200 or worse, strabismus, or surgery for eyelid malposition) at 5-10 years (p = 0.009, NNT 15) ([Arch Ophthalmol 2003 Mar;121\(3\):386](#) in [Global Family Doctor 2003 Mar 13](#))
- o for localized zoster in immunocompetent adults (start within 48-72 hours of onset of rash)
 - valacyclovir (Valtrex) 1 g PO tid for 7 days
 - generally well tolerated
 - adverse effects may include gastrointestinal symptoms, headache, rash, hallucinations, confusion
 - renal dosing (7-day course)
 - creatinine clearance 30-49 mL/minute - 1 g q12h
 - creatinine clearance 10-29 mL/minute - 1 g q24h
 - creatinine clearance < 10 mL/minute - 500 mg q24h
 - **valacyclovir associated with earlier pain relief than acyclovir (level 1 [likely reliable] evidence)**; 1,141 immunocompetent adults > 50 years old with zoster randomized to valacyclovir 1 g PO tid for 7 or 14 days vs. acyclovir 800 mg PO 5 times daily for 7 days and followed for 6 months; median duration of zoster-associated pain was 38 or 44 days vs. 51 days; comparing both valacyclovir groups vs. acyclovir group, 19.3% vs. 25.7% had postherpetic neuralgia at 6 months (NNT 16); no significant differences in pain intensity, quality of life, or adverse events ([Antimicrob Agents Chemother 1995 Jul;39\(7\):1546 PDF](#))
 - famciclovir (Famvir) 500 mg PO tid for 7 days
 - generally well tolerated
 - adverse effects may include headache, nausea, diarrhea
 - renal dosing
 - creatinine clearance 40-59 mL/minute - 500 mg q12h
 - creatinine clearance 20-39 mL/minute - 500 mg qd
 - creatinine clearance < 20 mL/minute - 250 mg qd



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case presentation of disseminated herpes zoster (Mayo Clin Proc 2004 Aug)
topical application of povidone-iodine associated with rapid crusting and pain resolution in case report (Lancet 2004 Aug 7)

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- ▶ **Complications and Associated Conditions**
- ▶ **History**
- ▶ **Physical**
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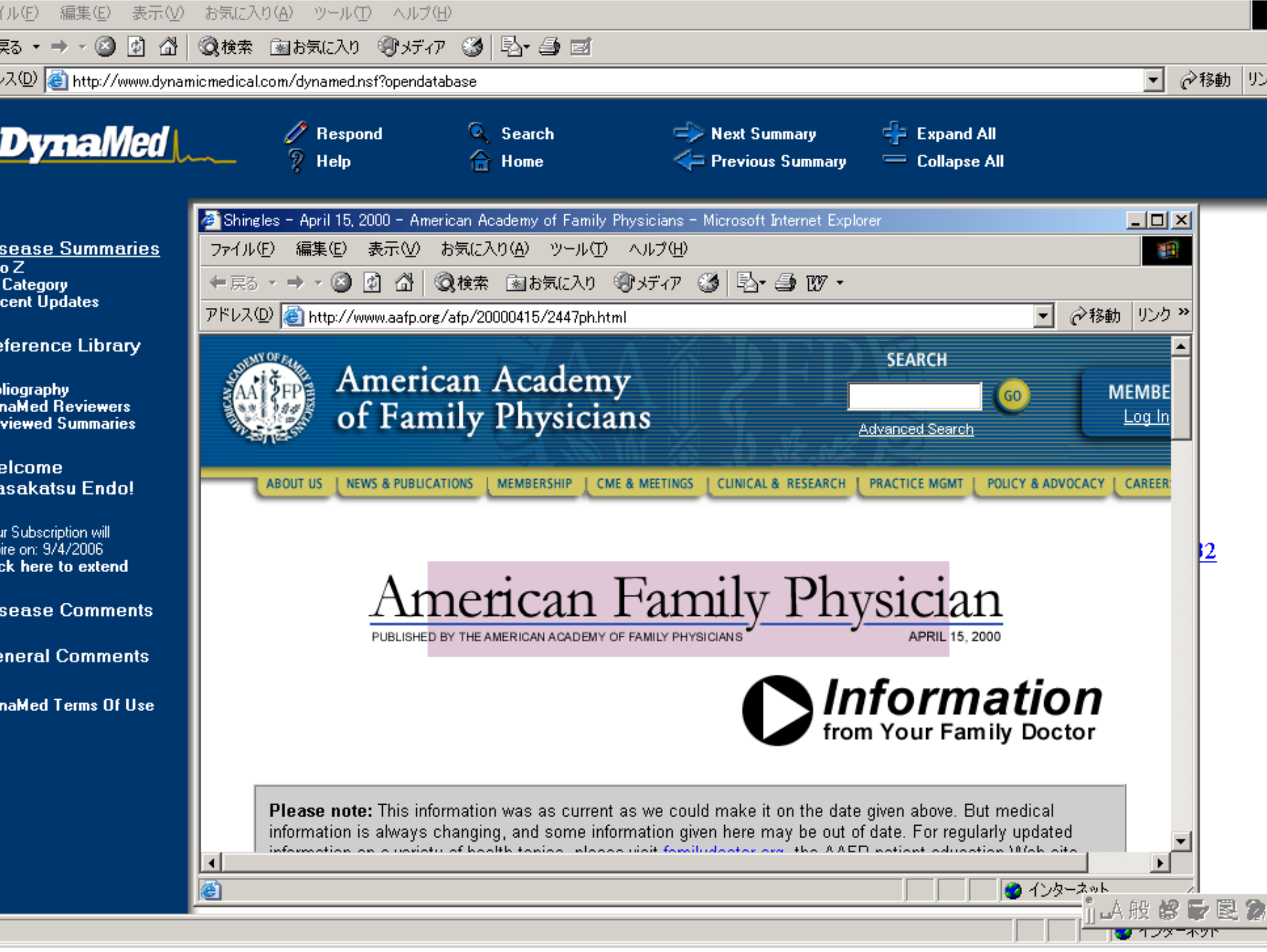
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- patient information brochure from [American Academy of Dermatology](#)
- handout can be found in [Postgrad Med 2003 Jun;113\(6\):87](#)
- handout on herpes zoster ophthalmicus can be found in [Am Fam Physician 2002 Nov 1;66\(9\):1732](#)
- patient notes on neuropathic pain can be found in [Postgrad Med 1999 Nov;106\(6\):261](#)
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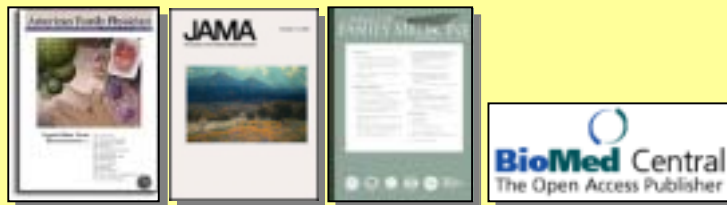
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主要ジャーナル、レビューサービスの査読

Relativity

- (1) 患者のQOLに直接的に影響をもたらすか？
- (2) 臨床でのディシジョンメイキングにとって有益か
- (3) 臨床の現場において、広く議論されている情報か？
- (4) DynaMedの収録形態に沿った情報か？
- (5) 多くの人が関心を寄せている情報か？

Validity

- ・ リサーチ方法、サンプルサイズなどの吟味
- ・ エビデンスレベルの付与
- ・ 既存収録エビデンスとの比較 (Best “Available”かどうか)

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