

# Barnaspítali Hringins

## Æðabólgusjúkdómar barna

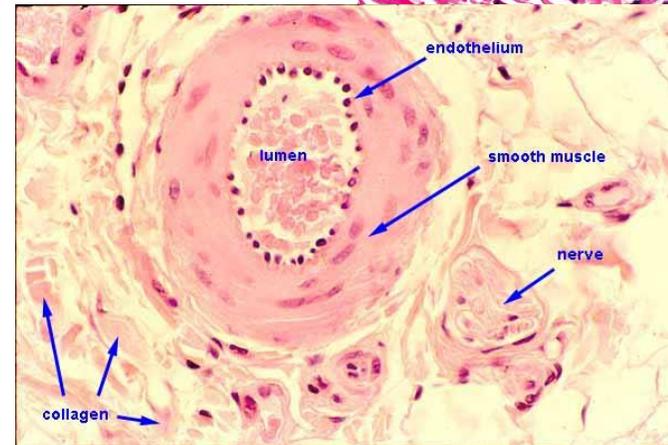
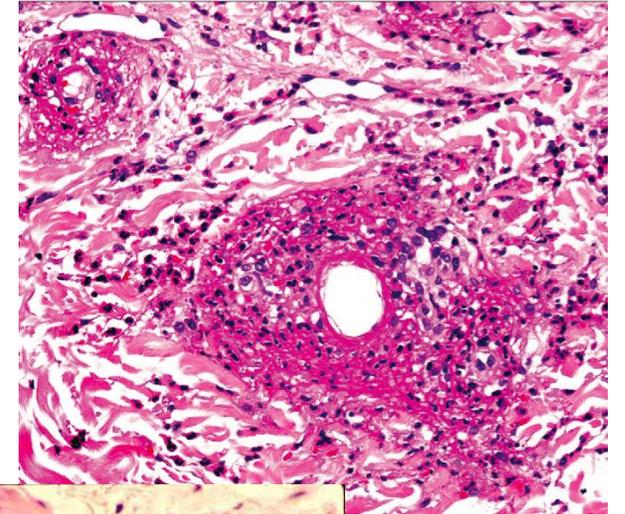
**Judith Amalía Guðmundsdóttir**

**Barnalæknir**



# ÆÐABÓLGUSJÚKDÓMAR BARNA

- Bólga í æðavegg
  - Primer vs sekunder
  - Einkennamynd tengd gerð, staðsetningu, bólgumagni og æðaskemmdum
- Nýgengi 20/100.000/ár
- Einkenni oft ósértæk
  - Hiti, slappleiki, húðbreytingar, hækkanir bólguparametra...
- Vasculitis mimics algengari!



# ÆÐABÓLGUSJÚKDÓMAR BARNA



- Kawasaki disease



© 2015 Kawasaki Disease Canada

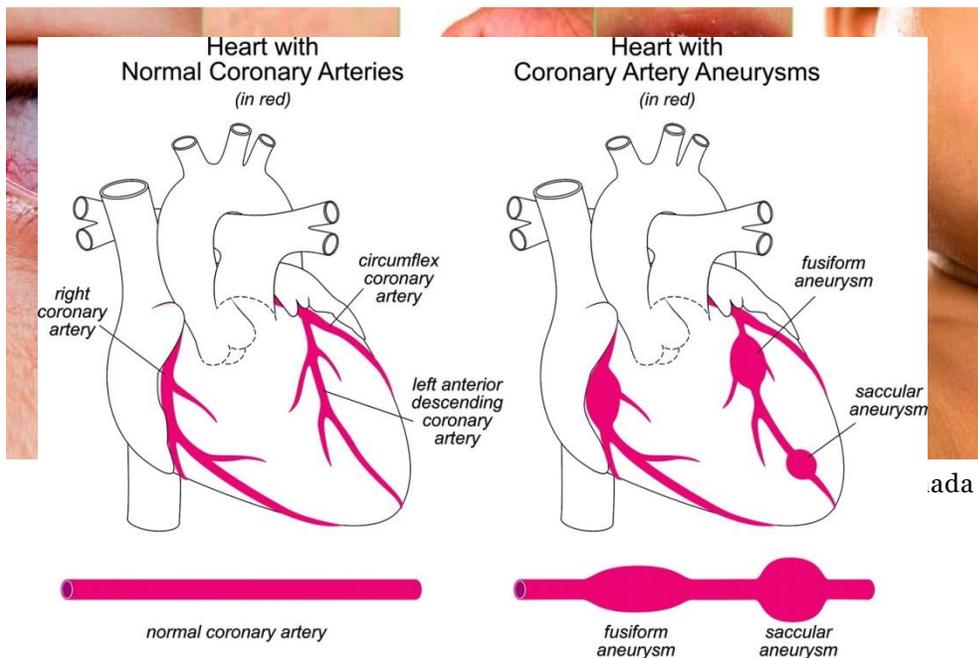
- Henoch Schönleins purpura



- Aðrir æðabólgusjúkdómar sjaldséðir

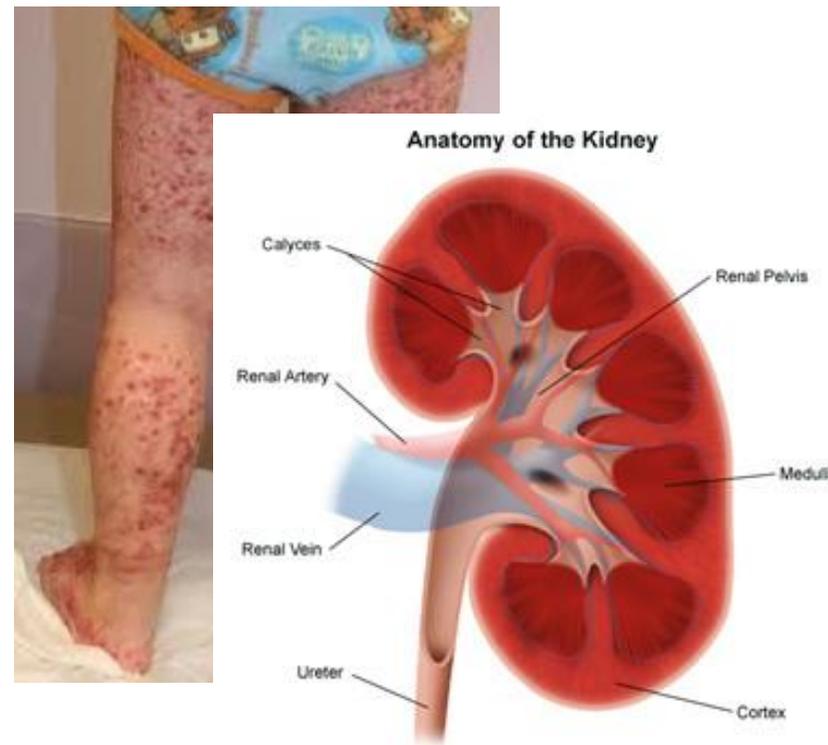


- Kawasaki disease



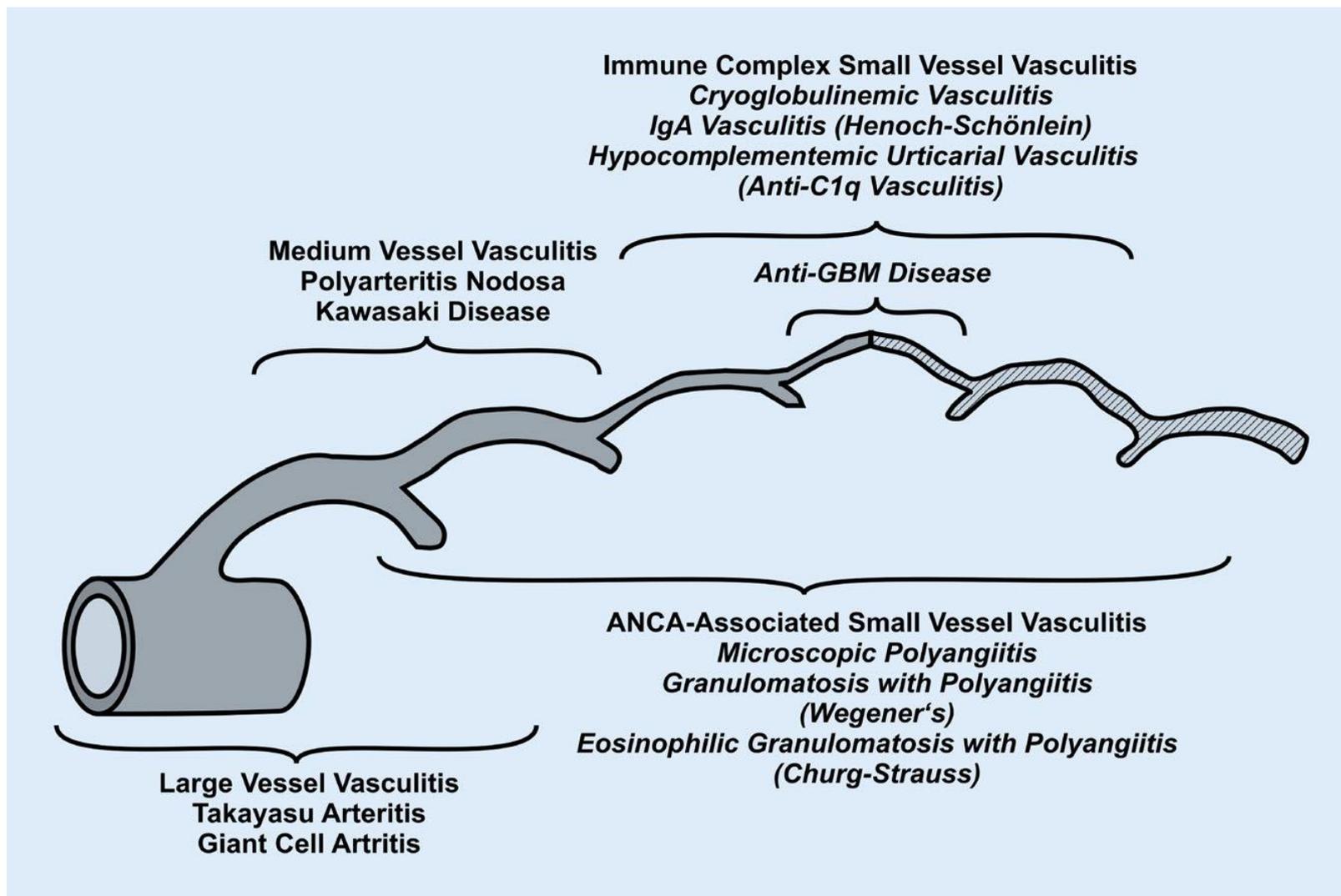
Baker, Newburger, Kawasaki Disease, Circulation 2008

- Henoch Schönleins purpura



www.renal-diseases.org





## Æðabólgur í börnum – flokkun Eular/Printo/Pres 2008

Stórar æðar	Takayasus Arterit
Meðalstórar	Polyarteritis Nodosa (systemic, húð) Kawasaki
Litlar	<p>Granulomatous:</p> <ul style="list-style-type: none"> <li>Granulomatosis with polyangitis GPA</li> <li>Eosinophil granulomatosis with polyangitis EGPA</li> </ul> <p>Ekki granulomatous:</p> <ul style="list-style-type: none"> <li>Microscopic polyangitis MPA</li> <li>Henoch Schönlein Purpura</li> <li>Leukocytoclastic skin vasculitis</li> <li>Urticarial hypocomplementemic vasculitis</li> </ul>
Annað	<p>Behcet</p> <p>Afleiddir – sýkingar, illkynja, bandvefssjkd., lyf</p> <p>CNS æðabólga</p> <p>Cogans sjkd. (augu, innra eyra)</p>

**Tengdir  
ANCA**

**HSP+Kawasaki >95% - Hver barnagigtlaeknir greinir <1 árlega af öðrum æðabólgu**



# ERFIÐ GREINING

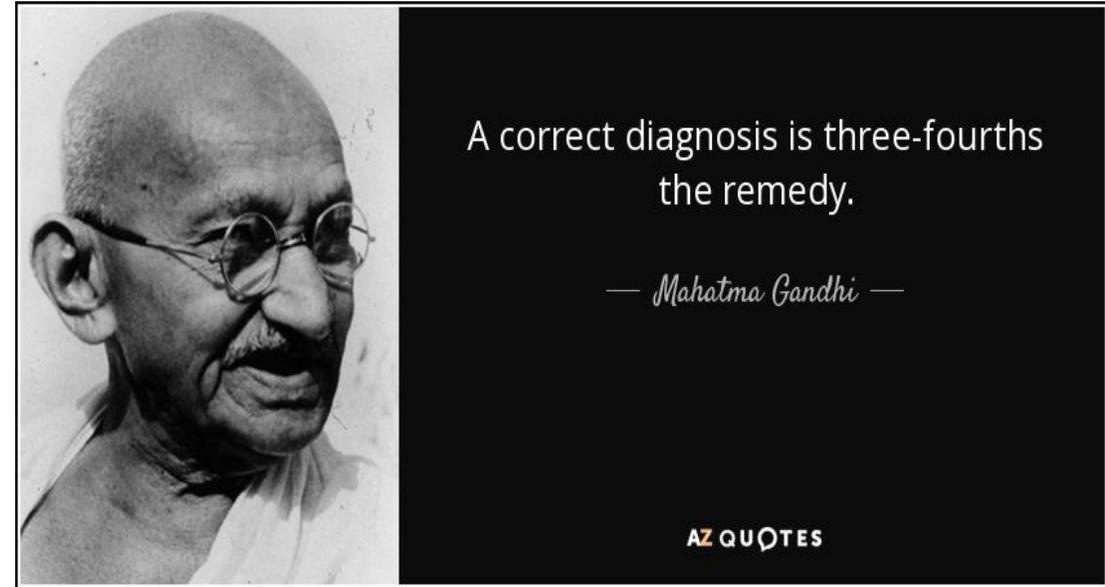
## MARGVÍSLEG EINKENNI ÁSAMT SKÖRUN AÐABÓLGUSJÚKDÓMA

Almenn	• Hiti, þróttleysi, þyngdartap
Nýru	• Stix, nefrit, nefrosa, nýrnabilun
Lungu	• Mæði, hósti, blæðing
HNE	• Sinusit, stenosur, rhinit, blæðing
Augu	• Retinopathy, bólgubreytingar
Húð	• Útbrot, raynauds, livedo reticularis
Melting	• Kviðverkir, ógleði
Stoðkerfi	• Stoðkerfisverkir, liðbólгур, myosit
Miðtaugakerfi	• Höfuðverkur, stroke, blæðing, neurit
Hjarta og æðar	• Háþrýstingur, occlusion, skert blóðflæði



## MEÐFERÐ - ALMENNT

- Rétt greining!
- Hve alvarlegur er sjúkdómurinn
- Know the natural course of the disease
- Áhætta mót kostum meðferðar
- Virkur sjúkdómur eða afleiðingar?
- Induction, maintenance, relapse, refractory

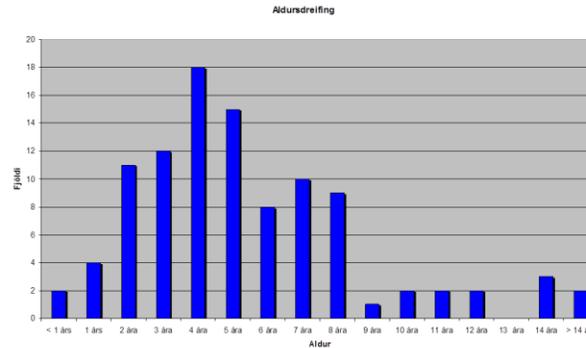


- Anti-histamín, NSAIDS
- Ónæmisbælandi lyf
  - Sterar
  - Cyclofosfamíð, mycophenolat mofetil (MMF)...
  - Líftæknilyf (TNF-alfa blokkar, IL-6 blokkar...)



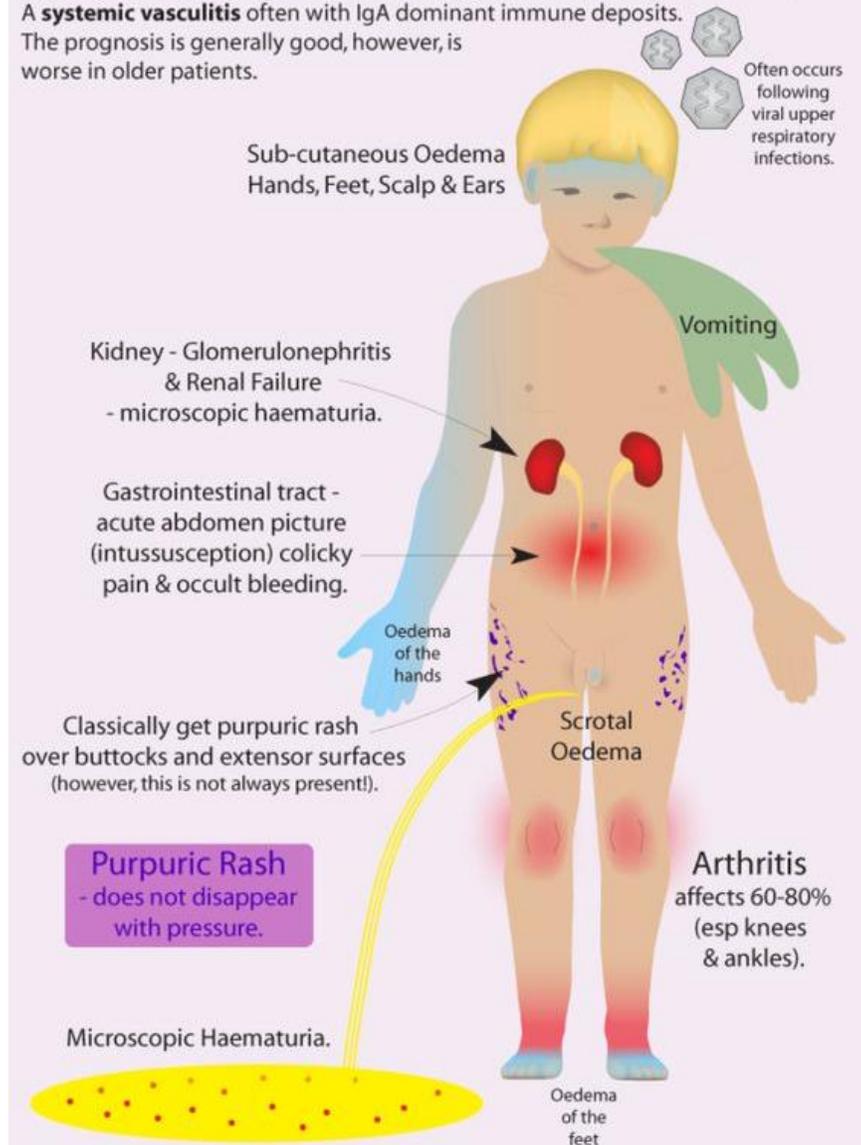
# HENOCH SCHÖNLEIN PURPURA

- Algengast
  - Nýgengi 10/100.000
  - Strákar > stelpur, 2:1
  - 3-10 ára
- IgA vasculitis
- Purpura eða petechiae án blóðflögufæðar meira á neðri útlimum auk:
  - Kviðverkir
  - Liðbólga eða liðverkir
  - Leukocytoclastic vasculitis eða proliferative glomerulonephritis with predominant IgA deposition
  - Nýrnaáhrif (hematuria, rauðkornaafsteypur, proteinuria)



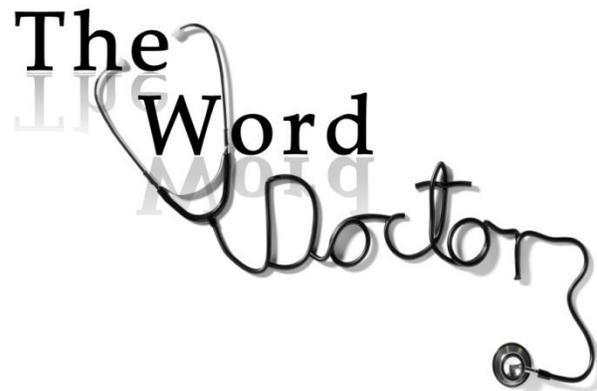
## Henoch Schonlein Purpura

Typically a young boy. Often occurs following upper respiratory tract infection. A **systemic vasculitis** often with IgA dominant immune deposits. The prognosis is generally good, however, is worse in older patients.



## GREINING OG RANNSÓKNIR

- Mjög þakklát klínísk greining...
  - Aðrar æðabólgur, fjölkerfagigt, kawasaki
  - Húðsýni til vefjagreiningar
- Fræðsla mikilvæg

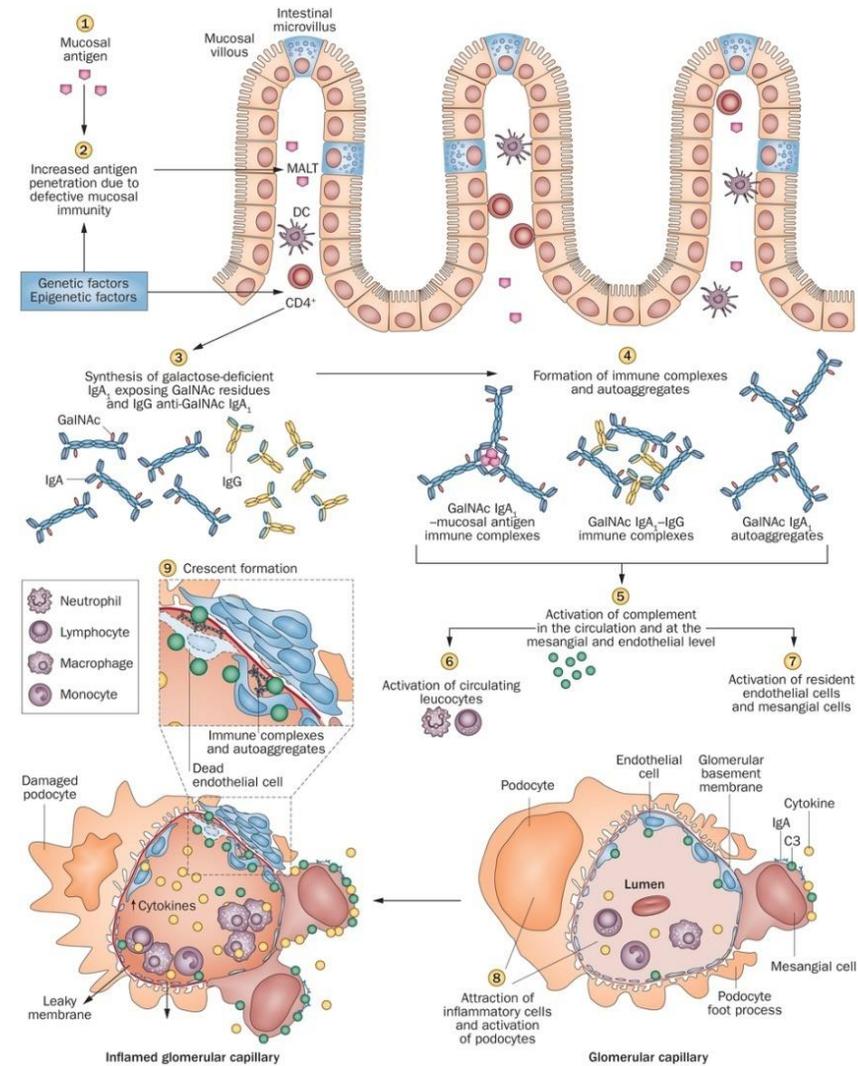


- Hvaða prufur skyldi taka?
  - Blóðhagur
    - Flögur
  - Þvagstatus
  - Kreatínín
  
  - Hvít, sökk, IgA, IgM, komplement, ANA, blæðingarprufur...
- Og hvað oft?

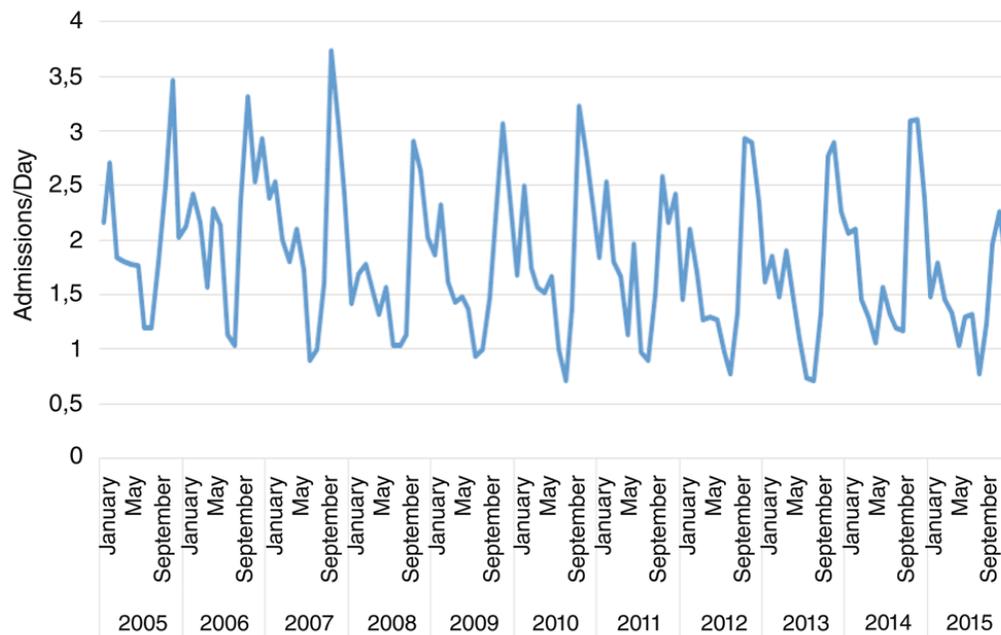


# MEINGERÐ HENOCH SCHÖNLEIN PURPURA

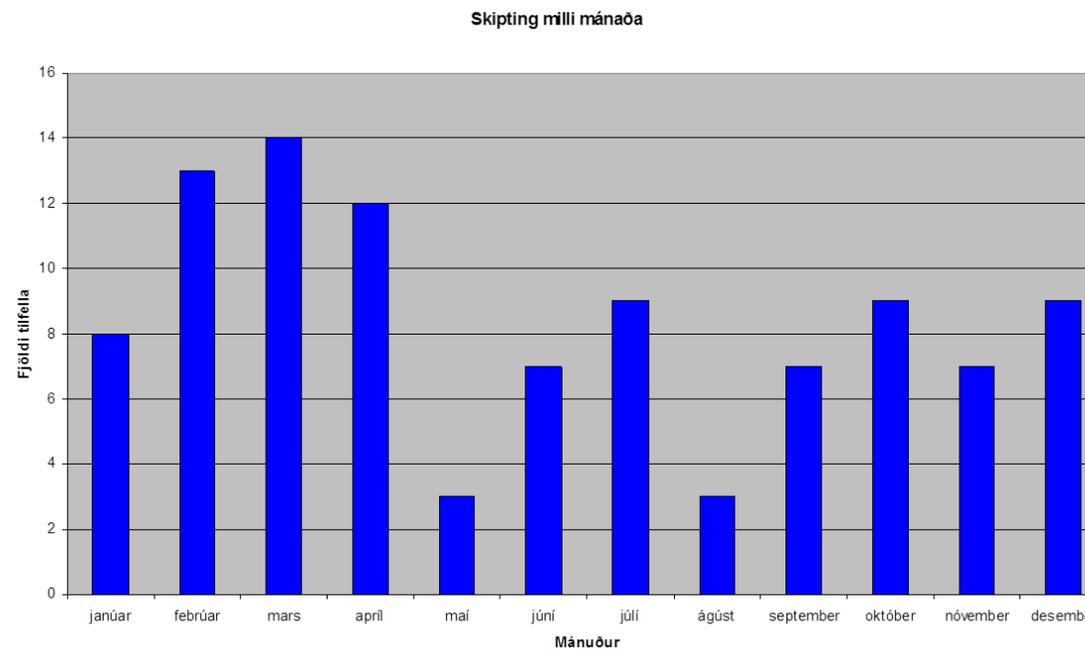
- Infectious trigger
  - mjög oft
- Genetic susceptibility
  - C1GALT1; thombopoesis, nýrnastarfsemi
  - CCL2; cytokine/chemoattractant; susceptibility
  - CCL5; cytokine/chemoattractant; severity, nýrnaáhrif
  - Regulation of endothelial function, ICAM-1, vascular endothelial growth factor, MEFV...
  - HLADRB1 01, 07, 11



# BREYTILEIKI NÝGENGIS



Riancho-Zarrabeitia, Santurtún, Cutaneous vasculitis in children: a nationwide epidemiological study in Spain, F1000Research 2017

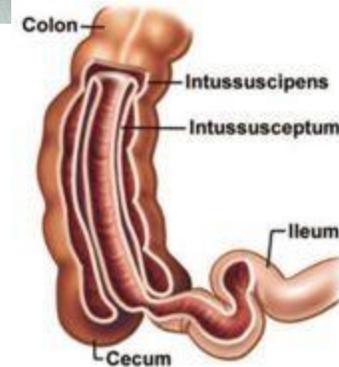
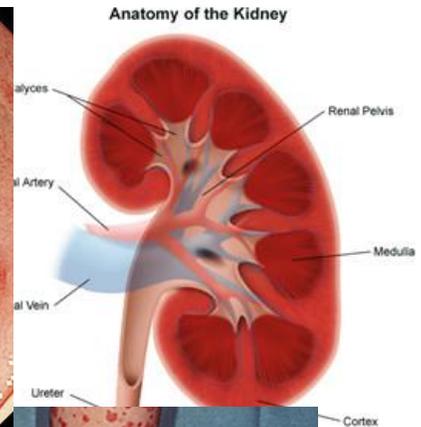
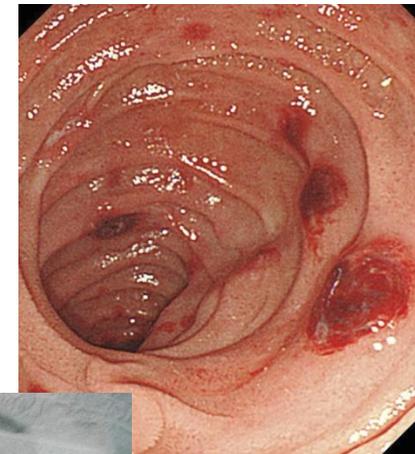


Thors, et al, Henoch-Schönlein purpura, patients admitted to Landspítali University Hospital 1984-2000, Læknablaðið 2002

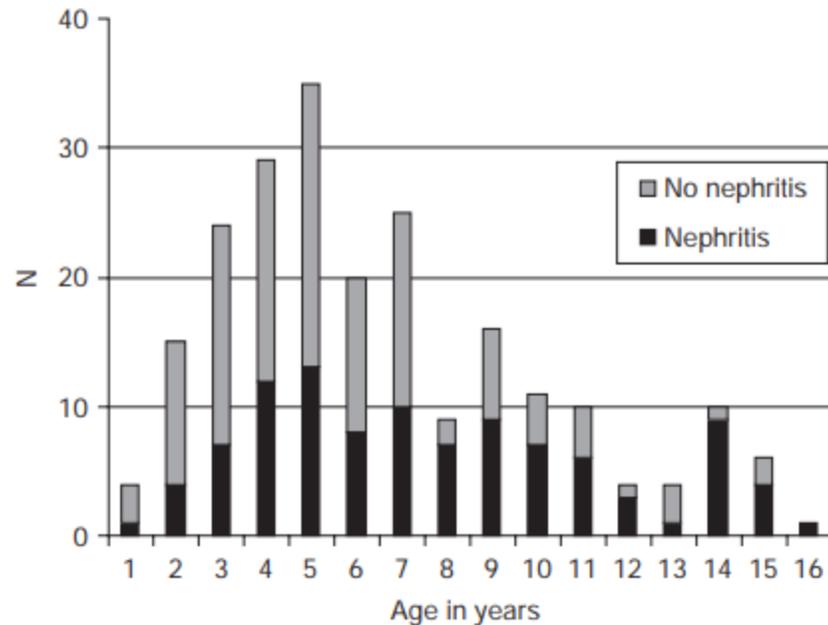


# HENOCH SCHÖNLEIN PURPURA – HORFUR OG MEÐFERÐ

- 20% recurrent
  - Oftast fyrstu vikurnar
- 5% chronic
- Nýru
  - Bíða...
  - Hematuria, proteinuria, háþrýstingur...
- Meðferð
  - Paracetamol
  - Nsaid
  - Sterar
    - Cochrane review
    - 2-3 vikur, start 1-2 mg/kg/dag
    - Ábending: GI einkenni



## EFTIRLIT - HORFUR



**Figure 1** Age distribution and occurrence of nephritis in 223 children with Henoch-Schönlein purpura.

Jauhola et al., Renal manifestations of HSP in a 6 month prospective study of 223 children. Arch dis Child 2010

- HSP án nefrit:
  - Þvagstix viku 0, 2, 4, 8, 12 og 26
- Ef nefrit
  - Lengra eftirlit
  - Bx – bara ef persistent
  - Nephritis, nephrotic syndrome
    - 15% ESRD
  - Háþrýstingur
    - ACE inhibitor, ARB
  - Sterar
    - Púls, niðurtröppun



## GREINING KAWASAKI

- Hiti í minnst 5 daga auk 4/5:
  - 1
  - 2
  - 3
  - 4
  - 5



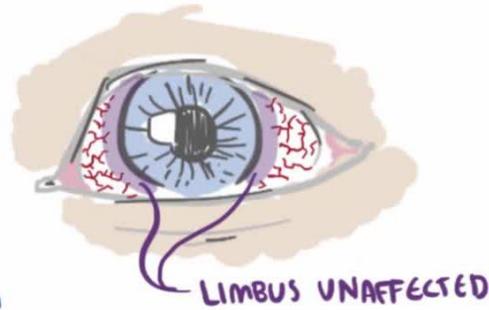
# KAWASAKI DISEASE

- Hiti í minnst 5 daga auk 4/5:

## KAWASAKI DISEASE

### \* CLASSIC SYMPTOMS \*

- Conjunctivitis (sparing limbus)
- Rash ~ all body parts  
Polymorphous → <sup>flakes</sup> desquamation
- Adenopathy ~ enlarged lymph nodes (cervical)
- Strawberry tongue ~  + RED MOUTH & THROAT
- Hands & feet ~ Swollen + rash



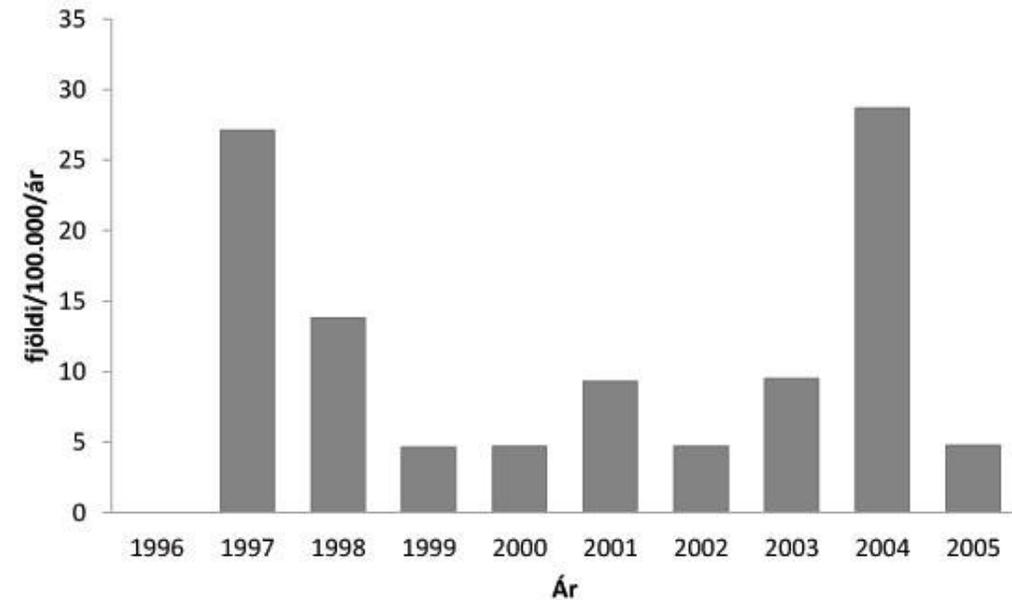
## KAWASAKI DISEASE

- Bráður vasculitis ungra barna
  - >90% yngri en 5 ára
  - Drengir > stúlkur, 2:1
- Meðalstórar æðar
- Hiti í minnst 5 daga auk 4/5:
  - Conjunctivitis
  - Slímhúðir í munni (rauðar varir, roði í koki, roði á tungu)
  - Bólgnar hendur og fætur, flögnun
  - Húðútbrot (polymorphous)
  - Eitlastækkarir



## KAWASAKI FARALDSFRÆÐI

- 10/100.000
  - Japan 260/10.000
- Trigger, árstíðabundið, epidemiur
- Acute, subacute and convalescent phase
- Genetic susceptibility
  - ITPKC, CASP<sub>3</sub>, TGF-beta signal pathway, B lymphoid tyrosine kinase, FCGR<sub>2A</sub>, KCNN<sub>2</sub> Th17/Treg imbalance



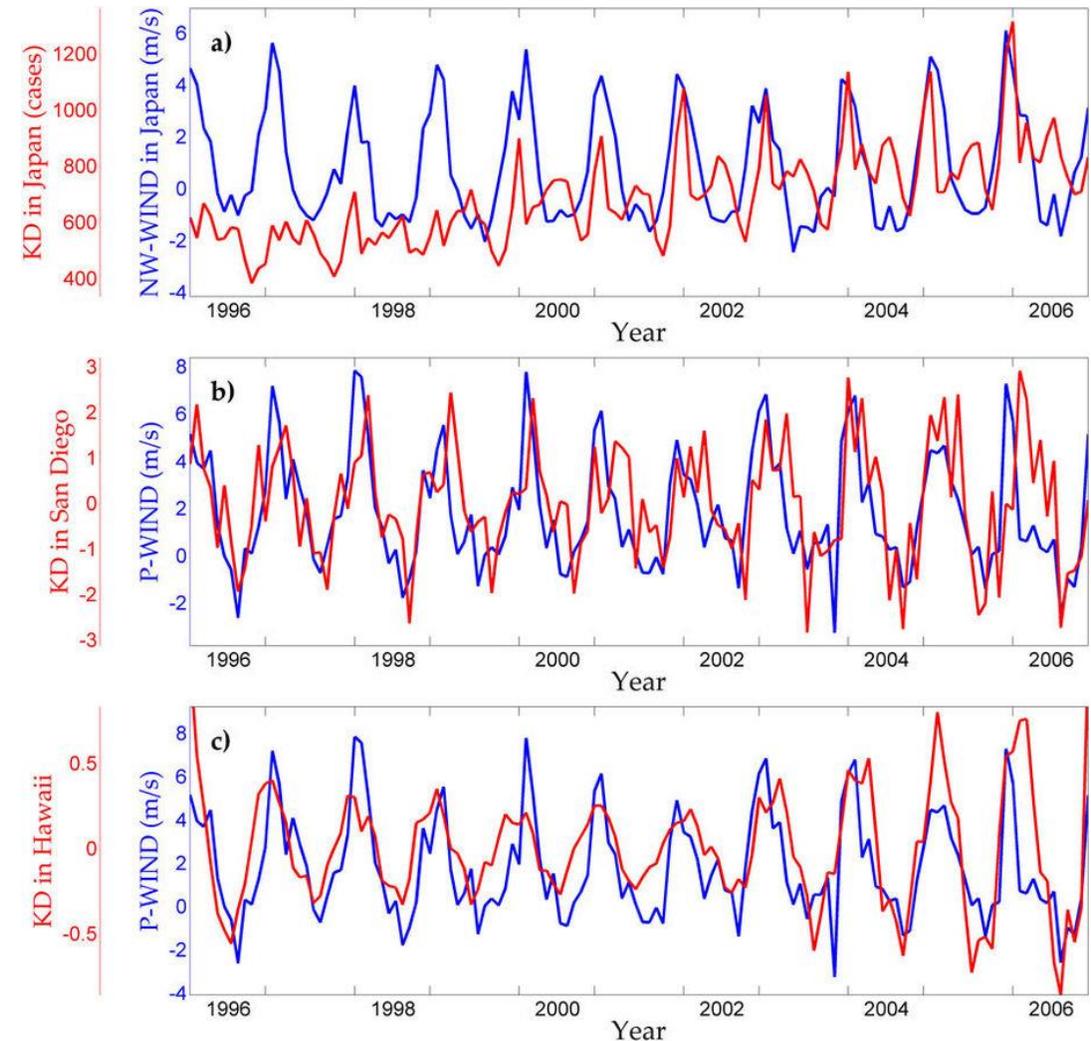
**Mynd 2.** Nýgengi Kawasaki-sjúkdóms á Íslandi hjá börnum <5 ára 1996-2005.

Ólafsdóttir, HS. Kawasaki sjúkdómur á Íslandi 1996-2005  
Faraldsfræði og fylgikvillar, Læknablaðið 2012



# KAWASAKI FARALDSFRÆÐI

- 10/100.000
  - Japan 260/10.000
- Trigger, árstíðabundið, epidemiur
- Acute, subacute and convalescent phase
- Genetic susceptibility
  - ITPKC, CASP3, TGF-beta signal pathway, B lymphoid tyrosine kinase, FCGR2A, KCNN2
  - Th17/Treg imbalance



Rodó, Ballester, Cayan et al. Association of Kawasaki disease with tropospheric wind patterns. Nature Scientific reports 1;152 (2011)



# SJÚKDÓMSEINKENNI KAWASAKI

- Mismunagreiningar

- Sýkingar

- Skarlatssótt, mislingar, toxic shock syndrome, adeno, influenza, EBV, CMV

- Aðrar æðabólgur, SLE

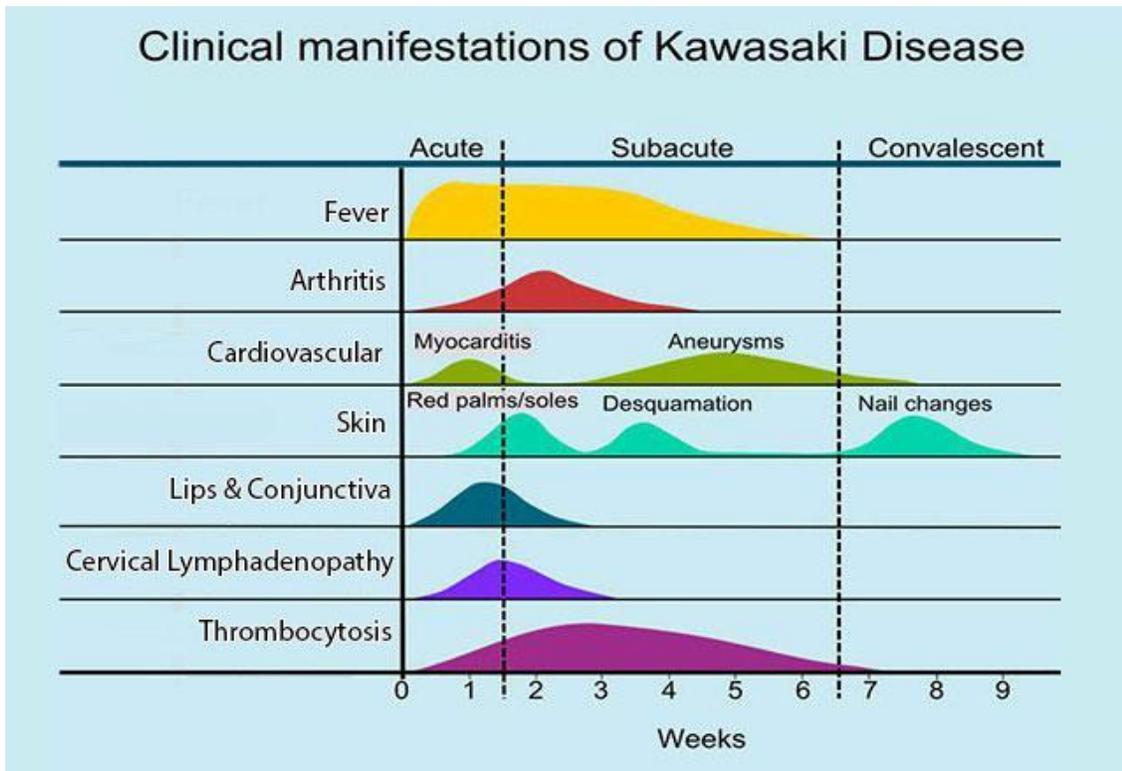
- Steven Johnson syndrome

- Fjölkerfagigt

- IL-18

**Önnur einkenni:**

Aseptic meningitis, niðurgangur, lifrabólga, þanin gallblaðra, urethritis, liðbólgur



Medscape



## BLÓÐ OG ÞVAGRANNSÓKNIR

Rannsókn	Fjöldi (n)	Hlutfall (%)
Hvít í þvagi	22/26	85
Prótein í þvagi	7/25	28
Hækkun lifrarprófa	19/28	68
Fjölgun blóðflagna	23/30	77
Fjölgun hvítra blóðkorna	20/30	67
Hækkað sökk	22/24	92
Hækkað CRP	26/29	90

Ólafsdóttir, HS. Kawasaki sjúkdómur á Íslandi 1996-2005 Faraldsfræði og fylgikvillar, Læknablaðið 2012



## KAWASAKI HORFUR

- Almennt góðar
  - Dánartíðni 1%
  - en...
- Algengasta ástæða áunnins hjartasjúkdóms
  - Æðasegi, blóðpurrðardrep, myocarditis, kransæðagúlar
- Kransæðagúlar
  - IVIG 20% => 4%
- Óhefðbundinn Kawasaki (incomplete)
  - 5 af 30 í Ólafsdóttir, 2012
  - Verri horfur
  - Erfiðari greining
  - Ung börn



## KAWASAKI - MEÐFERÐ

- IVIG
  - Áhrif á skamm- og langtímahorfur
  - 2 gr/kg, endurtaka eftir 36 tíma pn
  - 80% svara fyrstu meðferð
  - Áhrif á bólusetningu
- Ef svarar ekki meðferð
  - Sterapúls (methylprednisolon 30 mg/kg/dag)
  - TNF-alfa blokkar, calcineurin blokkar (ciclosporin, tacrolimus), rituximab, anakinra, plasmaskipti
- Acetylsalicylsýra
  - Skammtur 20-25 mg/kgx4 vs 3-5 mg/kg/dag



# KAWASAKI - EFTIRLIT

Athuga áhættuþætti hjarta og æðasjúkdóma, blóðfitu

Eðlileg ómun

Eftirlit 4-52v

ASA hætt 4-6v

Væg víkkun

Eftirlit áfram á 2-5 ára fresti, regress

ASA hætt 4-6v

Litlir til meðalstórir æðagúlar

Eftirlit áfram, áreynslupróf, angiography regress

ASA áfram

Stórir æðagúlar >8mm

Eftirlit 3 mán fresti, áreynslupróf, angiography

ASA áfram Warfarin eða LMWH



# LYKILATRÍÐI AÐ MUNA EFTIR ÞESSARI MISMUNAGREININGU





Takk fyrir

