

NSMM

Helsinki, May 29, 2007

RVVC treated with Mannose-Binding Lectin (MBL)

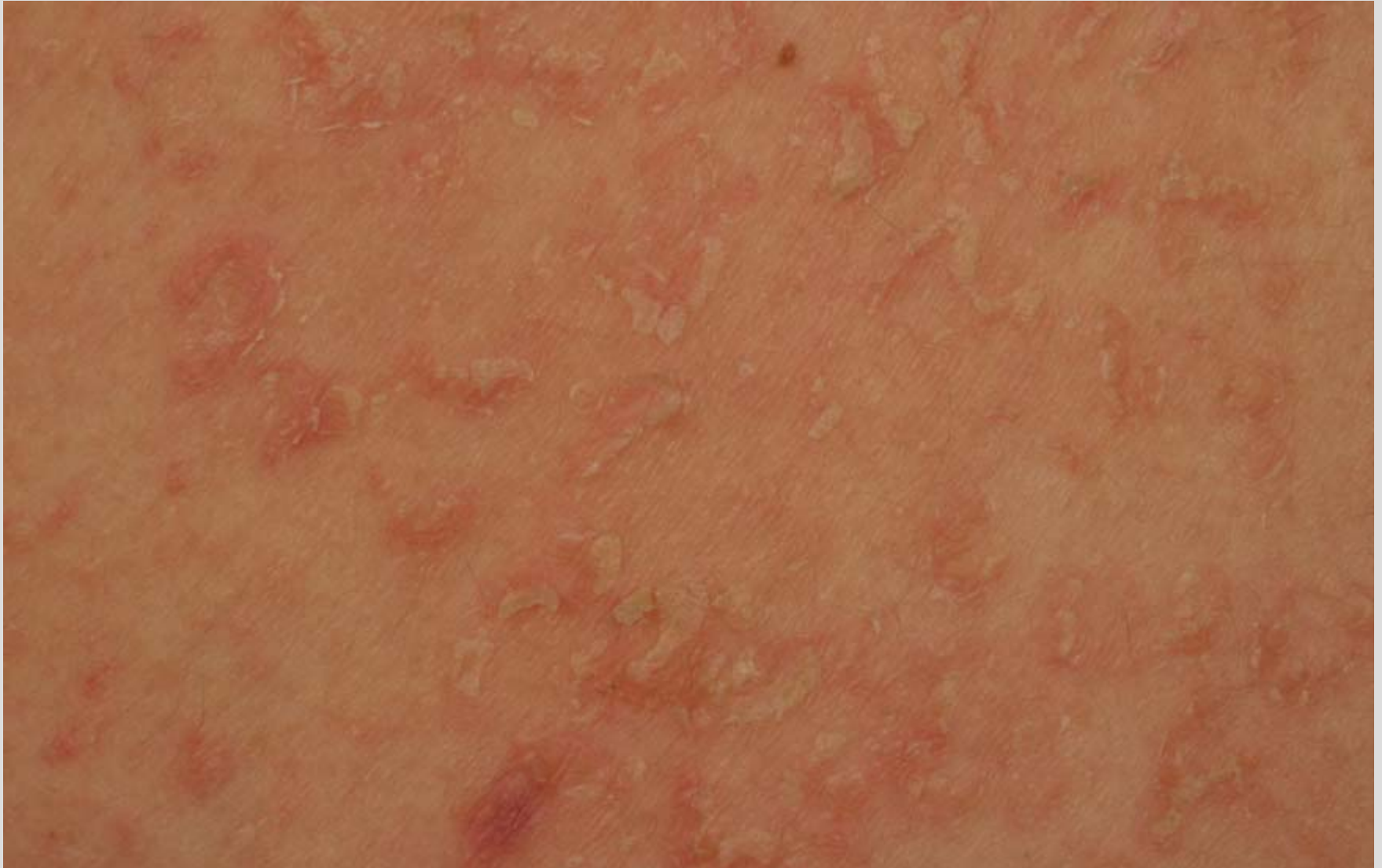
Efficacy in a patient with Netherton Syndrome and low serum MBL

Else Svejgaard

Dep of Dermatology

University Hospital of Copenhagen

**Netherton syndrome =
Ichthyosis congenita circumflexa**



Netherton Syndrome

- Defect Spink-5 gene
- overproduction of serine-protease inhibitor
- defective skin protein formation
- **Thin and fragile epidermis**
- **Hair abnormalities**
- **Atopy:**
- **Eczema, asthma, high IgE values**
- **Complications:**
Infections with *staph. aureus* and *strep. haemolyticus*

Netherton Syndrome intertriginous changes



Arm pit



Pubes

GD, born 1979

Disease Course

Age 0 – 12:

Multiple attacks of *staph/strep* infections

Frequent hospitalization

Age 13 – 22:

Stabile - symptoms tolerable

Age 23 and on:

**Development of severe dermatitis of external
genitals, bacterial infection and **RVVC****

Mycology and treatment

Year/mth	Patogen	Antimycotic
(Always combined with antibiotics)		
2002	<i>C. albicans</i>	fluconazole x 2
2003 feb-sep	<i>C. krusei</i>	itraconazole x 3
2003 nov-dec	<i>C. glabrata</i>	voriconazole x 2
2004 apr-may	<i>C. glabrata</i>	voriconazole x 2
- combined with MBL		

Immunology 2003

- **Lymphocyte populations: normal konc**
- **Lymphocyte stimulation: normal responses**
- **Total haemolytic complement:
normal classical and alternative pathway**
- **Ig A-G-M classes and subclasses: normal**
- **Ig E: 2578 kIU/L (n=<150)**

Mannose-Binding Lectin

April 2003

- MBL konc: 147 $\mu\text{g/L}$ (normal $> 500 \mu\text{g/L}$)

- MBL gene type: *A/0*

Known to be associated with reduced MBL levels

Mannose-Binding Lectin

- Plasma protein belonging to the innate immune system
- Part of the Complement System
- Binds to carbohydrates on the surface of micro-organisms
- Activates phagocytic cells: opsonization
- Activates complement
- 4% lack MBL (*O/O* homozygous)
- 30% low MBL levels (*A/O* heterozygous)

MBL and Infection

- **Low levels associated with opsonization defects and respiratory infections in children**

Koch et al: JAMA 2001,285:1316

- **Association between RVVC, vaginal concentrations of MBL and MBL polymorphism in Latvian women**

Babula et al: Clin inf dis 2003,37:733L

Results of MBL gene typing in RVVC

	Patients		Controls	
	Babula	Garred	Babula	Garred
	n= 42	n=46	n=43	n=250
AA	13	25	39	157
A0+0	29	21	9	93
	(69%)	(46%)	(9%)	(37%)

Treatment of GD with MBL SSI

- **MBL SSI:**

 - Plasma-derived product from
voluntary Danish blood donors

- **Procedure:**

 - infusion intravenously 3ml/min




- **Dosage:**

 - 0,2 mg /kg i.e. 10 mg

 - twice weekly/4 weeks

 - once weekly/4 weeks

Course of RVVC/MBL levels

	MBL iv	MBL $\mu\text{g}/\text{m}$
04 april-june	120 mg	from 147  to 1700
04 sep-dec	68 mg	from 358  to 1734
05 mar		457
06 feb		357
07 feb		374

**There have been no relapses of RVVC
since May 04**

MBL in RVVC

Conclusions

- **MBL polymorphism controls MBL levels**
- **Low MBL levels frequent in most populations**
- **RVVC may be associated with low MBL levels**
- needs confirmation in additional studies
- **Patient with Netherton Syndrome and treatment resistant RVVC had low MBL levels**
- **Two courses of iv MBL treatment associated with disappearance of *Candida***