Asymptomatic hypogammaglobulininemic patients

Do we need immunoglobulins?

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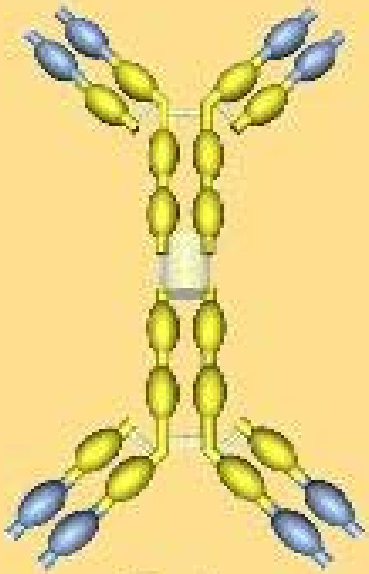
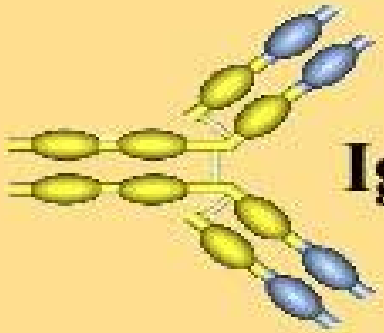


IgA



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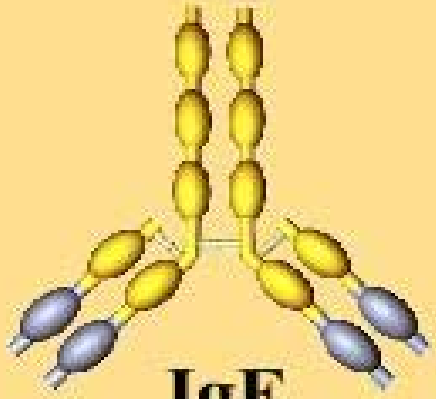
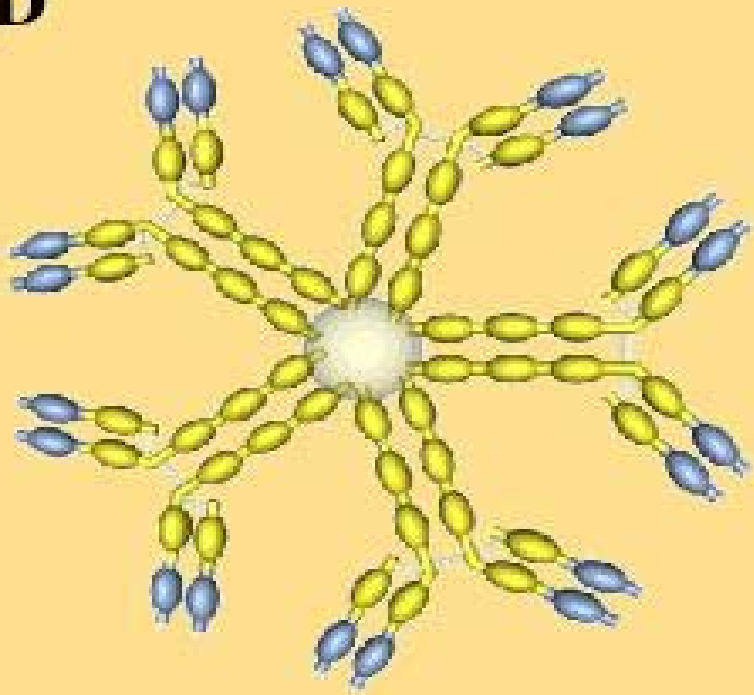
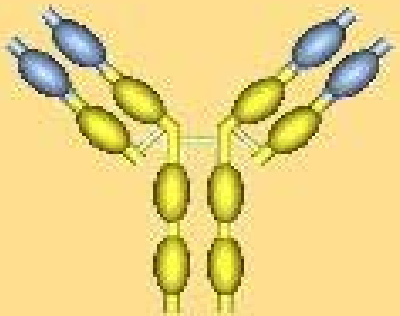


IgE



IgM



IgG

Biological functions of immunoglobulins

- Activation of complement system (IgG, IgM)
- Opsonization (namely IgG)
- Neuralization of antigens (IgG, IgA, IgM)
- Adesion interference (IgA, IgG)
- Aglutination, precipittion (IgG, IgM)
- Degranution of mast cells (IgE
- Imunoregulation (namely IgG)

Clinical manifestation of immunoglobulin deficiency

- Frequent and complicated infections of the respiratory tract.
- Patients suffer from recurrent attacks of bronchitis, sinusitis, pneumonia, otitis.
- Infections are caused namely by encapsulated bacteria: *Heamohilus sp.*, *Str. pmeumoniae*, *St. aureus.*
- Typical complications are bronchiectasis and/or lung fibrosis.

Patient No. 1 (born 1974)

- Family History: negative
- 12 years: skin rash, gradually disappeared
- The patient never suffered from frequent/severe infections.
- 24 years: delivered twins. Liver function test were abnormal. Electrophoresis showed low gamma-fraction.

Patient No. 1 (24 years) - laboratory investigations

- IgG: 3.31 g/l (7-16)
- IgA: <0.08 g/l
- IgM<0.08 g/l
- anti-tetanic toxoid: 0.080 IU/ml (>0.120) after vaccination 0.158 IU/ml
- anti-HIB: 0.04 mg/l (0,09-17.7)
- anti-PCP: 1.4 mg/l (>15.0)
- Isohemagglutinis anti-A, anti-B: titre 1:2

Patient no I. (born 1974)

- Aged 25: hypothyreosis
- Decrease of IgG was documented (2.8 g/l), treatment by intramuscular immunoglobulin 1.2 g/week was initiated.
- Currently: 30 years, IgG: 3.0-3.5 g/l. She does not suffer from frequent infections.

Patient No. 2 (born 1981)

- Family history: negative
- Frequent respiratory tract infections from childhood, repeated sinusitis, 2x pneumonia,
- 13 years: tonsillectomy for chronic tonsillitis.
- 13 years: first immunological investigation: IgG: 3.7 g/l, IgA: 0.15 g/l, IgM: 1.04 g/l, Treatment by IMIG was introduced, frequent infections disappeared (with the exception of rhinitis)

Patient No 2 – (aged 20)

- IgG: 2.80 g/l
- IgA: 0.04g/l
- IgM: 0.49 g/l
- anti-tet-tox: 0,111 IU/ml (>0.120),
- anti-HIB: 0.16 mg/l (0.09-17.7)
- anti-PCP: 12,1 mg/l (> 15.4)
- Isohaemaglutinins: anti-A: 1:32, anti-B 1:16
- No frequent infections.
- Treatment: IMIG 1.2 g IMIG/2 weeks.

Patient no. 2 (1981)

- Aged 22 – spent 18 months in USA and Japan, without any treatment.
- She had no clinical problems, even her chronic rhintiis disappeared.
- No abnormalitieses in HRCT an lung function tests were observed.

Patient No 2 laboratory investigations at the age of 23

- IgG 2.17 g/l (7.00-16.00)
- IgA <0.01 g/l (0.70-4.00)
- IgM 0.45 g/l (0.40-2.30)
- a-tet. tox: 0.054 IU/ml (>0.120), afrer vaccination 0.123 IU/ml
- a-HIB: 0.143 mg/l (>0.090)
- a-PCP: 2.7 mg/l (>15.4)

Patient No 3 (born 1967)

- Family history: negative
- No frequent infections during childhood
- 21 years: delivered a boy, pneumonia after delivery.
- The next two pregnacies without complications.
- The patient "did not visit a doctor because of infection during the last 10 years".
- 36 years: miscarriage at 11th week of pregnancy.

Patient no 3 (born 1967)

- After miscarriage blood group was determined, no anti-B isohemagglutinins were detected.
- IgG: 2.60 g/l
- IgA: <0,01 g/l
- IgM: 0,16 g/l
- anti-tet-tox: 0,069 IU/ml (ref. >0,120), after immunisation 10.931 IU/ml
- anti-PCP: 5,5 mg/l (ref. >15,5), after immunisation 6,6 mg/l
- anti-HIB: 1,863 mg/l (ref. > 0,09)

To treat or not to treat ?

Possible complications in untreated hypogammaglobulinemic patients

- Life-threatening pneumonia
- Meningitis
- Irrevesible lung damage: fibrosis and/or bronchiectasis
- Other severe infections

Patient with X-LA

- Negative family history
- By 12 months no frequent or severe infections.
- At 12 months phlegmona of the left cheek.
- At 18/12 otogenic meningitis with septicemia, irreversible deafness.
- First pneumonia at 2 years.
- Antromastoidectomy at 3 years
- Diagnosis of X-LA was made at 4 years.

Patient with CVID (born 1964)

- No frequent infections during childhood
- Meningitis at 15 years
- 19 years: pneumonia, first immunological investigation was performed: IgG: 1.72 g/l, IgA: 0.34 g/l, IgM: 0.11 g/l
- After initiation of immunoglobulin treament he does not suffer from frequent infections but one pneumonia occurred.

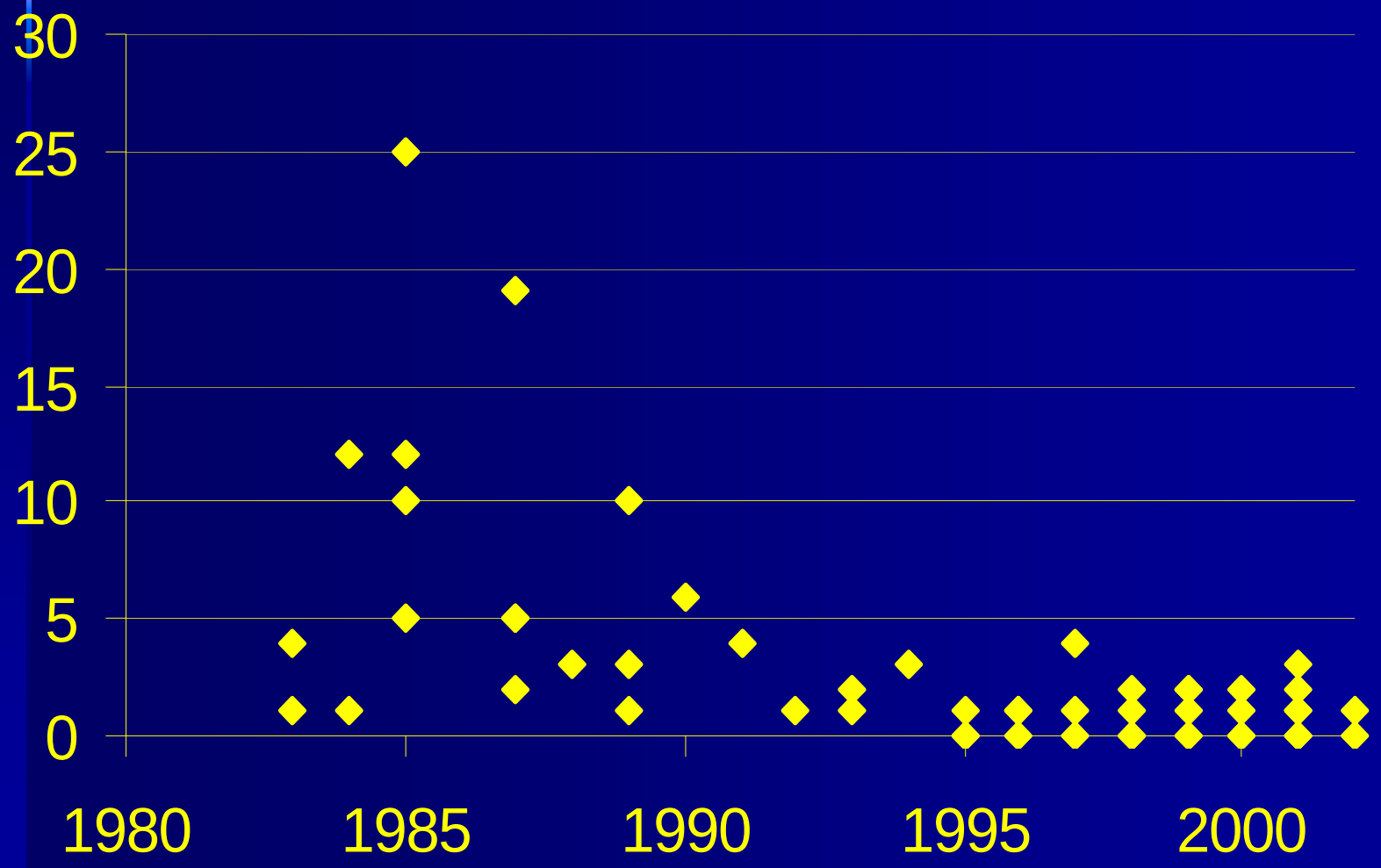
Patient with lung fibrosis (born 1970)

- Negative family history
- At 17 years „mild pneumonia“, but then without frequent infections
- Deliverd a baby at 29 years, afterwards increased frequency of respiratory tract infections for approximately 9 months.
- At 30 years - dyspnoea, lung fibrosis was diagnosed.
- At 31 years: IgG: 2.13 g/l, IgA: 0.14 g/l, IgM: 0.28 g/l

Causes of immunological investigation of new CVID patients in 1983-2004

- Total: 55
- Pneumonia: 37
- Frequent mild respiratory tract infections: 10
- Lung fibrosis: 3
- Other causes: 5

Number of episodes of pneumoniea before diagnosis of CVID was made (Dept. Clin. Immunol. Brno)



Number of pneumonisa before diagnosis of CVID was made
(Dept Clin Immunol, Brno)

	No.	Average	Median	Range
1983-1990	17	7,4	5	1-25
1991-1995	8	1,5	1	0-4
1996-2000	18	1,0	1	0-4
2001-2003	11	1,1	1	0-3

Criteria for introduction IVIG treatment

- IgG <2,5 g/l: all patients
- IgG 2,5-4 g/l: In patients with increased susceptibility to infections.
- IgG: 4-7 g/l: In patients with increased susceptibility to infections and antibody response deficiency.

(Zielen S, In: Wahn V (ed): Klinischer Einsatz von Intravenösen Immunoglobulinen, Uni-Med Verlag AG, 2000.)