

**Registration of APS I patients in EurAPS patient registry**

*To be filled in by the physician. Read the definitions carefully when you fill in the form.*

Physicians name: .....Phone: .....  
 E-mail: .....Fax: .....  
 Address: .....

Patient gender /M/F): .... Patient age: .....  
 Patient code (to be filled in by WP1-coordinator): .....

Manifestation	Y	Age	Manifestation	Y	Age
<b>Mucocutaneous candidiasis</b>			Autoimmune hepatitis		
oesophageal candidiasis			biopsy verified		
<b>Hypoparathyroidism</b>			Chronic diarrhoea/malabsorption		
magnesium deficiency			biopsy verified loss of entero-chromaffin cells?		
<b>Addison's disease</b>			Failure of exocrine pancreas (give details)		
Hypothyroidism			Severe obstipation		
Hyperthyroidism			Nephritis		
Diabetes mellitus type 1			biopsy verified		
Diabetes mellitus type 2			Hypertension		
Secondary ovarian failure (see def., give age at last menstruation)			Hypokalemia with apparent mineralo-corticoid excess/sensitivity		
Primary ovarian failure (see def.)			Asplenism		
Secondary testicular failure (see def.)			Keratoconjunctivitis		
Primary testicular failure (see def.)			Iridocyclitis		
Growth hormone deficiency			Dry eyes		
Central diabetes insipidus			Cataract		
Hypophysitis			Nail pitting		
Oral/oesophageal cancer			Vitiligo		
Celiac disease			Alopecia		
Cholelithiasis			Enamel dysplasia		
Cerebral calcifications			verified by dentist		
Connective tissue disease (specify)			Metaphyseal dysplasia		
Gastric parietal cell failure			Tympanic membrane dystrophy		
Atrophic autoimmune gastritis			Periodic rash with fever		

Other diseases (please specify all manifestations whether known to be related to APS1 or not):

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 .....  
 .....

Height .....cm weight.....kg. Blood pressure(mmHg, sitting): .....

For Children, weight percentile: ..... height percentile .....

Ethnic background: ..... Known mutations in AIRE .....

Medication: .....  
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Family history and other information of interest:  
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No. of siblings: ..... With APS-1 ..... No. of dead siblings (give details) .....  
.....  
.....

Date: ..... Physicians signature: .....

**The completed form is sent to:**

**Dr. Eystein Husebye  
Department of Medicine  
Haukeland University Hospital  
N-5021 Bergen  
Norway**

**Att: EurAPS registry**

## Diagnostic criteria for the different manifestations of APS I:

- Mucocutaneous candidiasis*: candida infections in the oral mucosa, skin or nails for more than 3 months. If oesophagus is involved, this is indicated separately.
- Hypoparathyroidism*: Subnormal calcium and supranormal plasma phosphate concentration and normal renal function. Mg-deficiency manifests as painful convulsions during normocalcemia and only relieved by Mg replacement (cf. Perheentupa JCEM 2006; 91,2843-50)
- Addison's disease*: subnormal serum cortisol together with elevated plasma ACTH concentrations, or failure to reach s-cortisol of 550 nmol/L 30 or 60 min in an i.v. ACTH stimulation test.
- Autoimmune thyroid disease*: Hyperthyroidism, suppressed TSH, elevated FT4; Hypothyroidism, Elevated TSH (> 5 mIE/L, and normal or low FT4).
- Diabetes mellitus type 1*: WHO criteria for type 1 diabetes.
- Diabetes mellitus type 2*: WHO criteria for type 2 diabetes.
- Secondary ovarian failure*: amenorrhoea with supranormal gonadotropin levels. Give the age at which the last menstrual bleeding occurred.
- Primary ovarian failure*: patient with absent, regressing or slow pubertal development (describe details under "Family history and other information of interest").
- Secondary testicular failure*: subnormal/normal gonadotropin levels, low testosterone values (morning sample).
- Primary testicular failure*: supranormal gonadotropin levels, low testosterone values (morning sample).
- Growth hormone deficiency*: Insufficient increase in growth hormone levels in response to arginine or insulin-induced hypoglycaemia, growth failure in childhood.
- Central diabetes insipidus*: Thirst, polyuria with U-osm < 200 mosm/L and S-osm > 287 mosm/L, typical pattern for central diabetes insipidus in response to thirst provocation.
- Hypophysitis*: Lymphocytic hypophysitis (cf. Caturegli et al, Endocrine Rev 2005; 26,599-614)
- Oral/oesophageal cancer*: verified by biopsy
- Celiac disease*: biopsy verified villous atrophy (cf. ESPGAN criteria, Walker-Smith et al, Arch Child Dis 1990; 65, 909-11)
- Cholelithiasis*: gallstones verified by imaging.
- Cerebral calcifications*: calcification verified by radiology.
- Connective tissue disease*: Give details under "Family history and other information of interest".
- Gastric parietal cell failure*: signs of functional vitamin B12 deficiency (low normal or subnormal serum cobalamine and high homocysteine and methylmalonate).
- Atrophic autoimmune gastritis*: atrophic gastritis verified by biopsy showing isolated fundal gastritis (type A autoimmune gastritis).
- Autoimmune hepatitis*: suspected if ALAT is chronically elevated (> 2-fold the upper reference limit) without substantial elevation of alkaline phosphatase without any other known cause (drugs, virus etc).  $\gamma$  globulins and IgG should be elevated and autoantibodies should be positive. Liver biopsy should be obtained and should show typical periportal or periseptal with predominantly lymphoplasmacytic necroinflammatory infiltrate. Diagnosis can be verified according to the revised criteria of the international autoimmune hepatitis study group (J Hepatol 1999; 31,929-938).
- Chronic diarrhoea/malabsorption*: episodes of diarrhoea and floating stools in combination with weight loss (> 10 percent of body weight). Biopsy may show loss of enterochromaffin serotonin-producing cells.
- Exocrine pancreatic failure*: Low fecal elastase (or if other tests are used, specify).
- Severe constipation*: Give details under "Family history and other information of interest".
- Nephritis*: tubulointerstitial nephritis verified by biopsy.
- Hypertension*: Blood pressure should be measured. For adults, hypertension is defined as >140/90 mmHg. For children the definition of hypertension varies according to age and height. Always give blood pressure for children.
- Hypokalemia with apparent mineralo-corticoid excess/sensitivity*: cf. Perheentupa JCEM 2006; 91,2843-50.
- Asplenism*: loss of spleen as determined by ultrasound or other imaging techniques.
- Keratokonjunktivitis*: Tear flow, intense sense of foreign body (sand) in the eyes, sensitivity to light, blepharospasm, conjunctival erythema and spotted staining of cornea with fluorescein. In absence of adequate therapy greyish corneal opacities appear with subsequent superficial neovascularization.
- Iridocyclitis*: iridocyclitis diagnosed by a ophthalmologist
- Dry eyes*: defined as dryness requiring treatment.
- Cataract*: opacities in the lens.
- Nail pitting*: 0.5 – 1 mm in diameter pits in several nails.
- Vitiligo*: depigmented skin areas.
- Alopecia*: partial or total loss of scalp and/or body hair.
- Enamel dysplasia*: affects permanent teeth only, often horizontal lines in otherwise normal enamel or pitting of the whole enamel.
- Metaphyseal dysplasia*: abnormalities of endochondrial ossification (cf Harris et al, JCEM 2003; 88,4576-85). Describe details under "Family history and other information of interest".
- Periodic rash with fever*: cf. Perheentupa JCEM 2006; 91,2843-50.