

## MEN2: kliniek

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internist-endocrinoloog



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## Multiple Endocrine Neoplasia 2

### MEN2a

- medullary thyroid cancer
- pheochromocytoma
- hyperparathyroidism

### MEN2b

- medullary thyroid cancer
- pheochromocytoma
- mucosal neuromas
- intestinal ganglioneuromas



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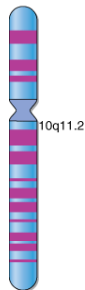
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## RET Proto-oncogene mutation

- chromosome 10
- autosomal dominant
- genotype-phenotype relation



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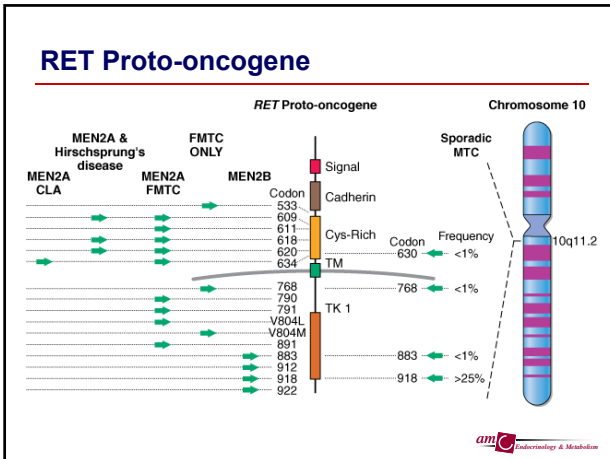
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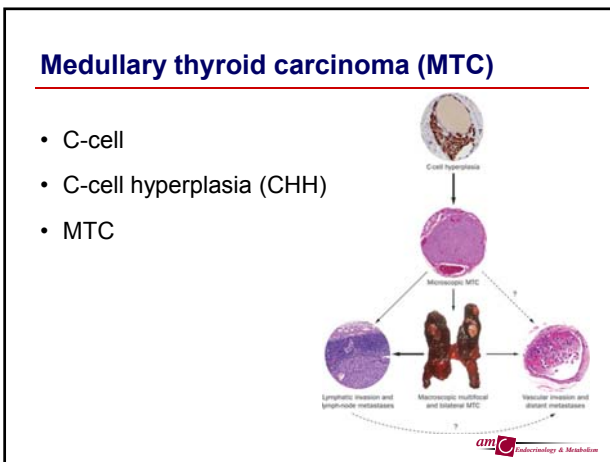
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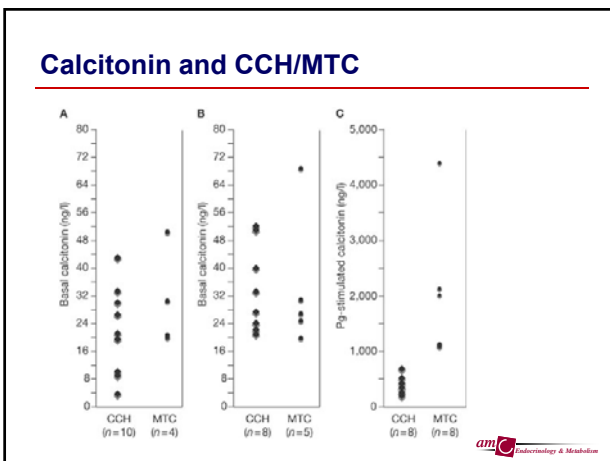
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### Pentagastrin stimulation

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Stimulated calcitonin peak (ng/l)	Clinical significance
<10	Absence of C-cell disease
>10 but <100	Indeterminate (probable false-positive result)
>100 but <500	Probable C-cell hyperplasia
>500 but <1,000	Probable medullary thyroid carcinoma
>1,000	Medullary thyroid carcinoma



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### MTC treatment

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#### Surgery

- thyroidectomy + median lymph node dissection
- lateral neck dissection



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### MTC follow-up

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- calcitonin & CEA
- imaging (CT, MRI)



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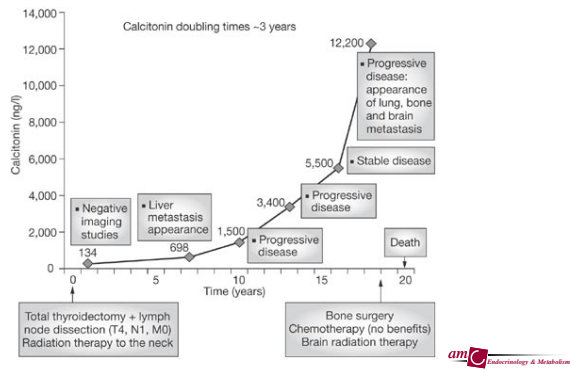
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### Calcitonin and disease progression




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### Pheochromocytoma



am Endocrinology & Metabolism

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### Terminologie

- Parasympathisch paraganglioom
  - hoofd/hals
- Sympathisch paraganglioom
  - buik, borstholte, hart, blaas
- Feochromocytoom
  - bijnier

am Endocrinology & Metabolism

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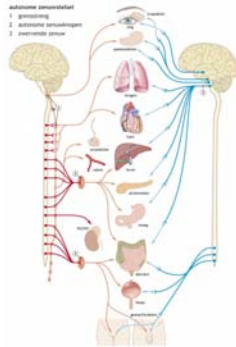
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## Het autonome zenuwstelsel



### Sympathische zenuwstelsel

#### catecholamines

- fright (angst)
- fight (vechten)
- flight (vluchten)

### Parasympatisch

- spijsvertering
- slapen




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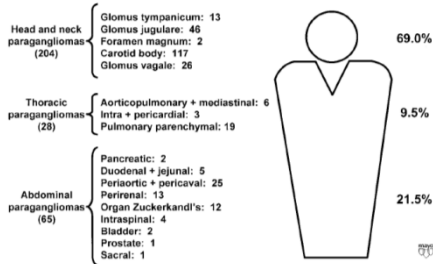
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## Lokalisatie bij SDHD mutaties




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## Catecholamines

- Catecholamines
  - adrenaline
  - noradrenaline
  - (dopamine)
- Hoofd/hals paraganglioom (5-15%)
- Sympathisch paraganglioom (80-100%)
- Feochromocytom (>95%)




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### Feochromocytoom

- 80 – 85% in medulla v.d. bijnier
- Prevalentie
  - 0.05% in autopsie studies
  - 0.1 – 0.6% in hypertensieve patienten
- Incidentaloom
  - 5% feochromocytoom
  - 25% pheochromocytomen bij toeval ontdekt




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### Genetische predispositie

	<u>feo present</u>
• MEN2	50%
• von Hippel-Lindau	10 – 20%
• SDHD/SDHB	3 – 11%
• neurofibromatosis	<5%




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### Klinische symptomen (symptomatische patienten)

• Hoofdpijn	60 – 90%
• Palpaties	50 – 70%
• Zweten	55 – 75%




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### Bloeddruk

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- Hypertensie
  - continue
  - paroxismaal
  - geen



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### Diagnose

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1. Aantonen catecholamine exces
2. Lokalisatie (CT, MRI, scintigrafie)



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### Preoperatieve behandeling

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- $\alpha$ -antagonist
- ( $\beta$ -antagonist)
- repletie intra-vasculair volume

Mortaliteit 13-45% → 0-3%



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**Catecholamine effect op  $\alpha$ - and  $\beta$ -adrenoceptors**

$\alpha$ 1	Vasoconstrictie (veneus & arterieel), stimulatie glycogenolyse	NE
$\alpha$ 2	Inhibitie NE uitscheiding (presynaptic), vasoconstrictie	E & NE
$\beta$ 1	Positief chronotroop, dromotroop en inotroop, stimulatie renine uitscheiding	E & NE
$\beta$ 2	Vasodilatatie (spier), bronchodilatatie	E




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**Plasma metanefrines: cut-off waarden**

- Metanefrines <0,30 nmol/L
- Normetanefrine <0,60 nmol/L
  
- Sensitiviteit 99%
- Specificiteit 89%




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**Urine metanefrines: referentiewaarden**

- Metanefrine
- Man <1,52  $\mu$ mol/24 uur
  - Vrouw <0,92  $\mu$ mol/24 uur
- Normetanefrine
- 20-29 jaar <1,89  $\mu$ mol/24 uur
  - 30-39 jaar <2,30  $\mu$ mol/24 uur
  - 40-49 jaar <2,84  $\mu$ mol/24 uur
  - 50-59 jaar <3,26  $\mu$ mol/24 uur
  - 60-69 jaar <2,96  $\mu$ mol/24 uur




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### Update referentiewaarden

	N	Age (years)			Normetanephrine (nmol/L)			Metanephrine (nmol/L)		
		Median	97.5 percentile	2.5 percentile	Median	97.5 percentile	2.5 percentile			
All subjects	1226	41.0	0.298	0.706	0.120	0.147	0.325	0.031		
Women	679	40.2	0.293	0.710	0.125	0.132*	0.315	0.035		
Men	547	41.0	0.302	0.704	0.120	0.170†	0.329	0.030		
5-17 y	116	13.2	0.248*	0.470	0.048	0.172†	0.333	0.045		
18-29 y	229	24.7	0.251*	0.588	0.118	0.137*	0.264	0.034		
30-39 y	232	34.5	0.273*†	0.618	0.126	0.138*	0.304	0.014		
40-49 y	283	45.0	0.300†	0.687	0.115	0.147*†	0.324	0.031		
50-59 y	241	53.0	0.362‡	0.747	0.136	0.157†	0.375	0.046		
>60 y	125	65.4	0.355§	1.047	0.137	0.163†	0.358	0.051		

Eisenhofer et al, Ann Clin Biochemistry 2013




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### Age-adjusted cut-off waarden

Model	Upper cut-offs (nmol/L)		Test performance	
	NMN	MN	Sensitivity (%)	Specificity (%)
Fixed - 97.5 percentiles	0.706	0.325	93.9*	88.3*
Age-dependent linear model	Variable	0.325	93.9*	91.2†
Age-dependent curvilinear model	Variable	0.325	93.7*	93.6‡
Age-dependent curvilinear model	Variable	0.446	93.6*	96.0*
Age-adjusted score model	NA	NA	79.5†	99.9‡

Eisenhofer et al, Ann Clin Biochemistry 2013




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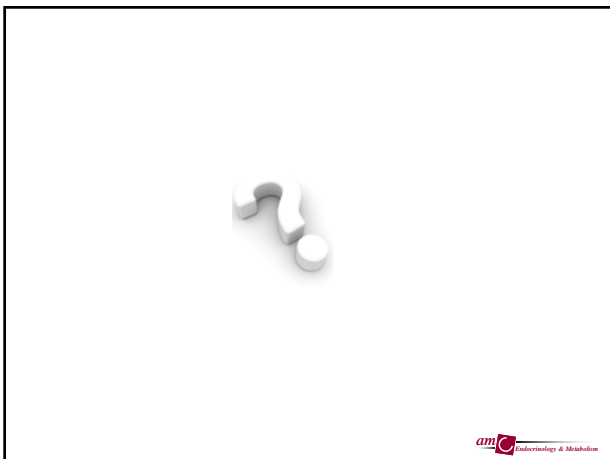
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