

Sporadic Pheochromocytoma

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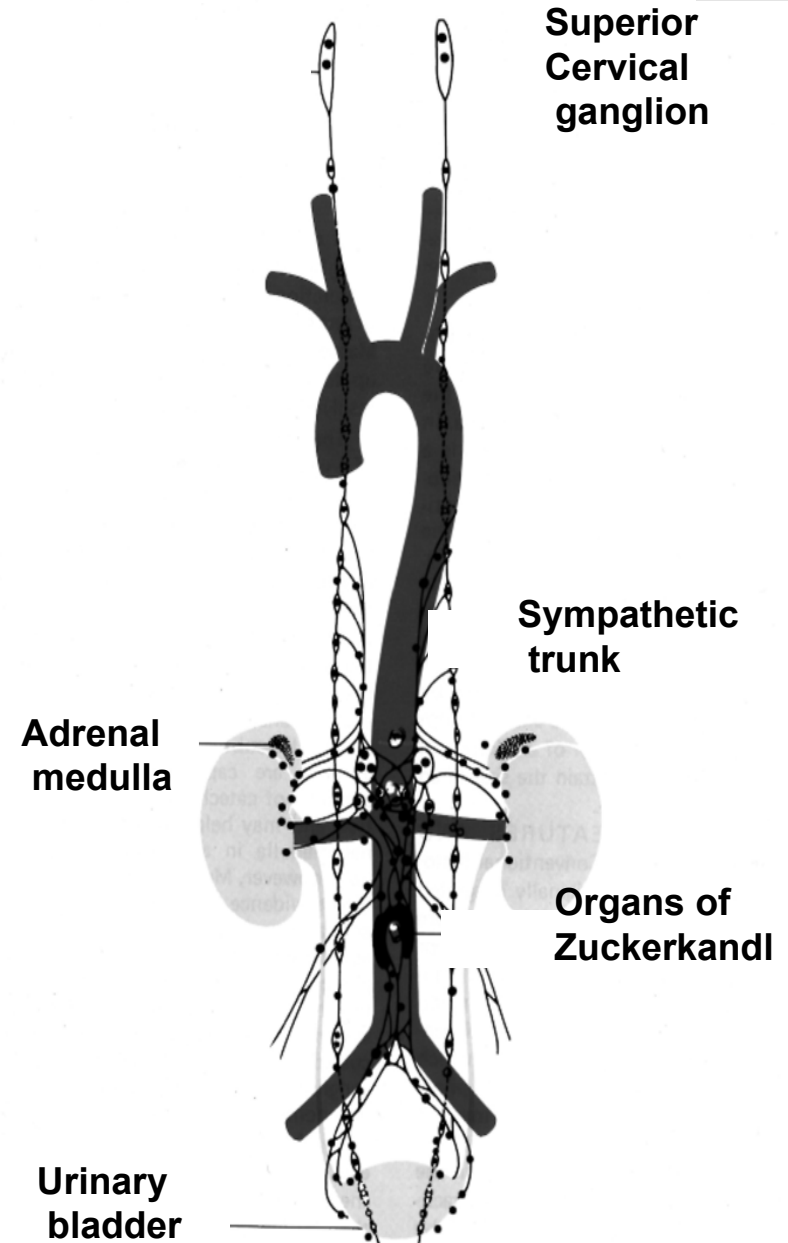
Pheochromocytoma

- **Anatomy, physiology and pathology**
- **Symptoms and diagnosis**
 - **Plasma metanephrines**
- **Pretreatment and surgical considerations**
- **Malignant pheochromocytoma**
 - **New markers help?**
- **Sporadic or familial? - Next talk**
- **Conclusions**



Paraganglioma

- Tumors arising from paraganglia occurring from the skull base to the bladder
- Many paraganglioma produce catecholamines, dopamine, noradrenaline and/or adrenaline
- Adrenal paraganglioma = pheochromocytoma
- Extra-adrenal pheochromocytoma often used



Catecholamine secretion

- **Dopamine only is found in some paraganglioma and does not give hemodynamic symptoms**
- **Noradrenaline is secreted from all adrenal pheochromocytoma and many extraadrenal paraganglioma**
- **Adrenaline is secreted from some adrenal pheochromocytoma including MEN 2**
- **Adrenaline secretion indicates adrenal localization as cortisol is needed for PNMT(phenylethanolamine N-methyl transferase) gene expression**
- **Chromogranins and NPY can be used as general markers but of limited practical use**



Biochemical diagnosis

- **Urinary catecholamines or metanephrines are widely used for diagnosis. Slight increase (2x) may be due to physical or psychic stress. 12 h over night sampling may be more sensitive than 24 h sampling.**
- **Plasma catecholamines have a very short halftime in blood and not suitable for routine analysis. Plasma normetanephrine and metanephrine may be more specific for pheochromocytoma diagnosis (Eisenhofer et al NEJM 340:1872 1999)**

Presentation

Pheochromocytoma
is like a



- **Pheochromocytoma are giving symptoms for a long time before diagnosis, in our material mean time being 3 years, range 0-20 years**
- **Hypertension following minor trauma: a rare presentation of pheochromocytoma(Dueck et al 1999)**
 - 16 year old boy after minor blunt abdominal trauma
- **Noncardiogenic pulmonary edema as the chief manifestation of a pheochromocytoma, a case report of MEN 2 A(Okada et al 1999)**
 - 30 year old man who turned out to be index case to a MEN 2 family



**Pheochromocytoma
is like a**

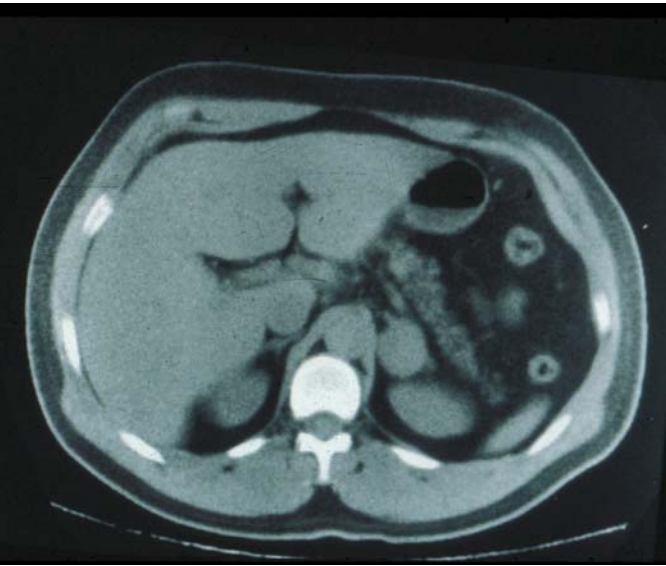


Diagnostic hints for the surgeon

- **Patients with previous thyroid surgery(MTC?)**
- **Unexpected blood pressure rise at premedication or induction of anesthesia**
- **Unexpected blood pressure rise on invasive procedures angiography, needle aspiration**
- **Previously healthy patients with hypotension and pulmonary edema**
- **Patients surviving a severe attack may end up in ICU with multi-organ failure**

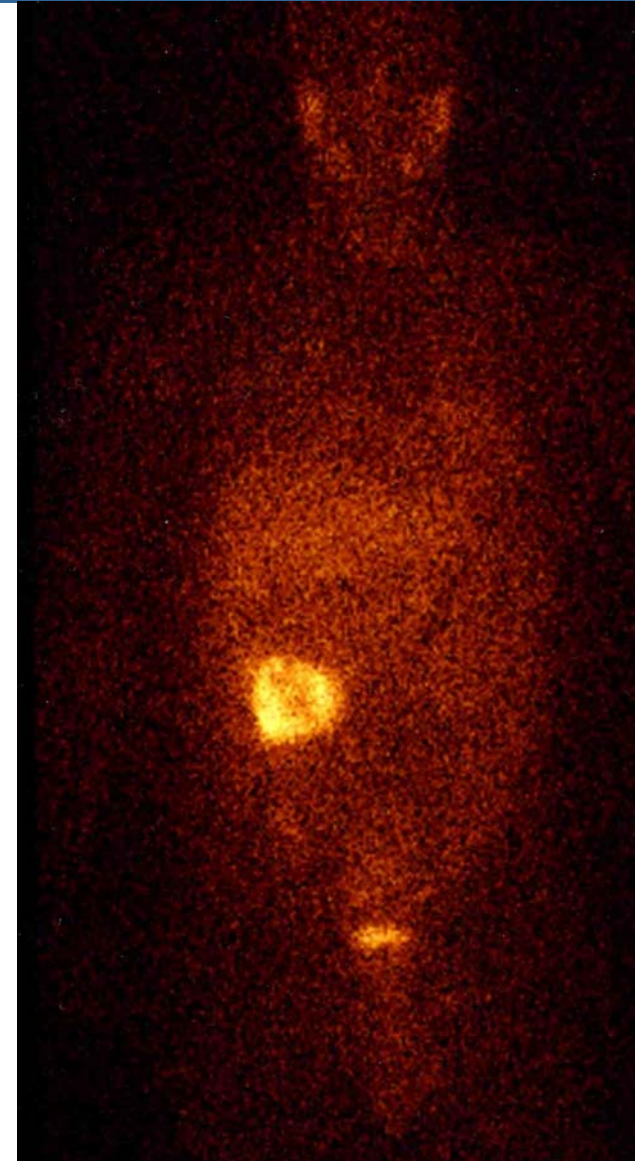


Localization



CT, MR US all have a high accuracy to find a pheochromocytoma. In straight forward cases further localization may not be necessary

MIBG has a high accuracy to find extraadrenal paraganglioma and metastatic disease and may be extremely useful in difficult cases



MRI of Pheochromocytoma

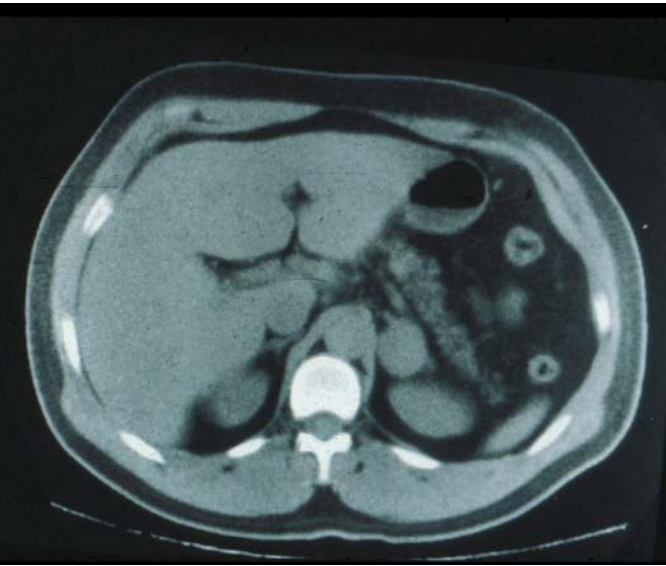
Table 1. Accuracy of MR imaging in characterization of adrenal masses.

Finding	Number of adrenal masses	Sensitivity (%)	Specificity	Accuracy (%)
Malignant neoplasms	25	89	99	93,9
Adenoma	136	96,2	89,8	93,9
Pheochromocytoma	45	93,3	98,4	97,4
Carcinoma	10	93,2	100	97,8
Metastasis	8	84	100	97,4

How accurate is MR imaging in characterisation of adrenal masses: update of a long-term study Selma ^{et}Hönigschnabl ^{al} [European Journal of Radiology](#) **Volume 41, Issue 2** 113-122 2003

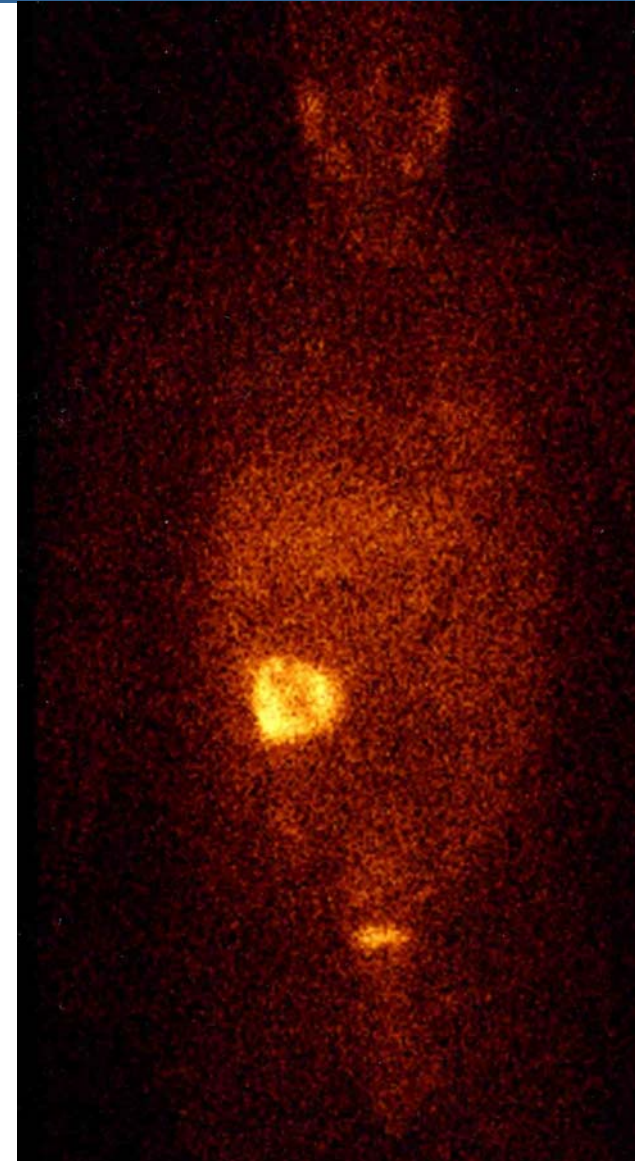


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CT-PET is very helpful if localization problems occur or metastatic disease is suspected

Dopamine-PET, DOPA-PET, Hydroxyephedrine-PET



Preoperative treatment

- **α -receptor blocking agents**
 - **Phenoxybenzamine up to 100 mg daily**
 - **Other α -receptor blocking agents like doxazosine, which is at present our first choice**
- **β -receptor blocking agents if needed, propranolol 40-120 mg daily**
- **Fluid supplementation not needed**
- **Is preoperative treatment necessary at all if you have an experienced anaesthesiologist?**

What to do when you peroperatively find a tumor highly suspicious for pheochromocytoma

- **Is the textbook recommendation to close when a possible pheochromocytoma is unexpectedly found peroperatively valid?**
- **Find an experienced anesthesiologist who can handle hypertension and hypotension perioperatively**



Blood pressure control during operation

- **The anaesthesiologist must be prepared to handle hyper- and hypotension promptly**
- **Central venous line and arterial line is mandatory**
- **In patients with cardiomyopathy an transoesophageal echocardiography is helpful**
- **For lowering blood pressure many drugs can be used, nitroprusside, nitroglycerine, adenosine and magnesium. Phentolamine is less suitable**
- **Noradrenaline may be needed for hypotensive periods and when the tumor is out**

Operative planning

- **Laparoscopic approach when**
 - **Tumor below 5-7 cm in size**
 - **No suspicion of malignancy**
 - **No concomitant surgery planned**
- **Always make sure you are informed on arterial pressure and stop manipulating when BP over 200**
- **Peroperative fluid restriction important**
- **Postoperative supervision focused on BP, diuresis and oxygenation and monitoring blood glucose**

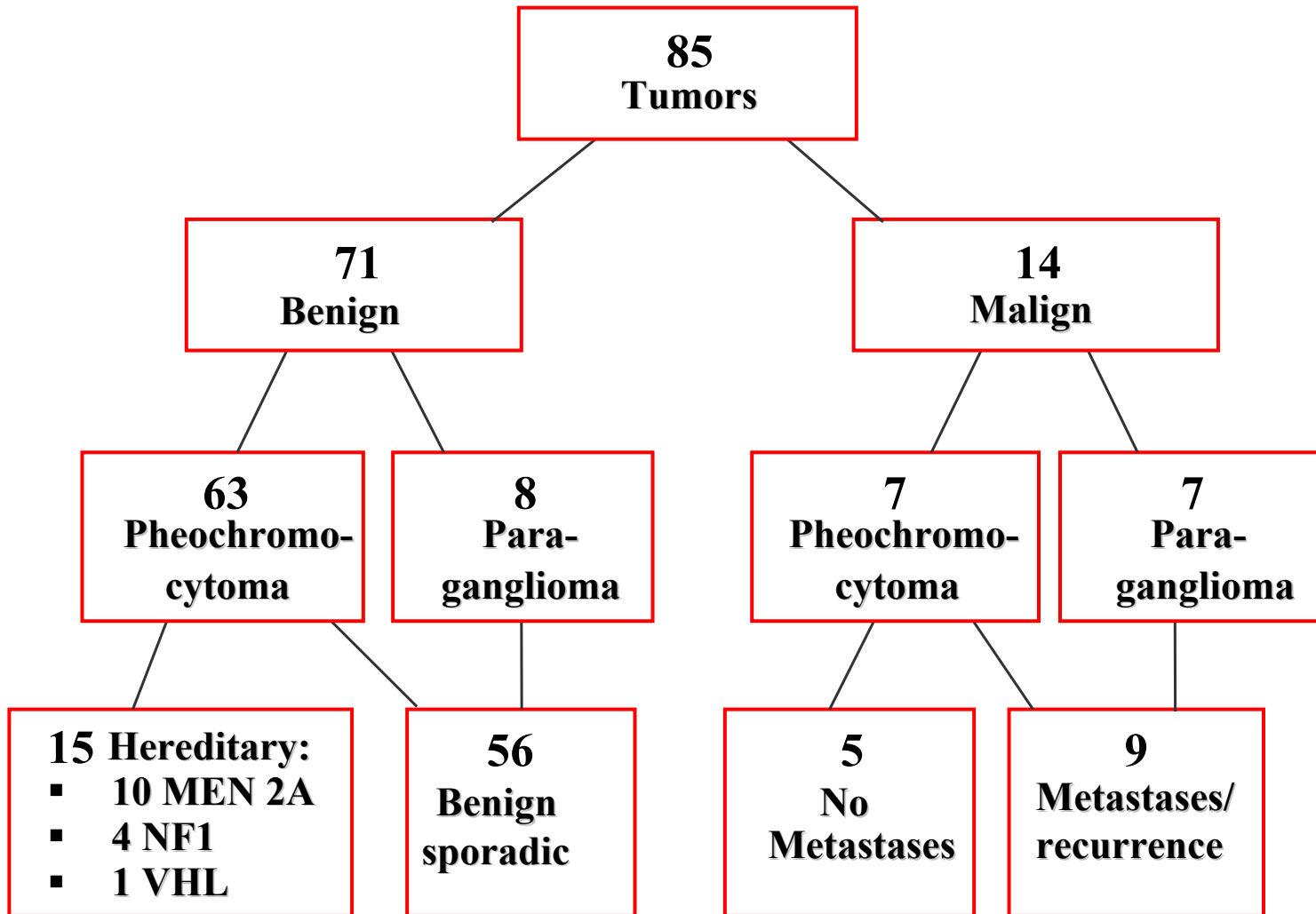


Malignancy

- **Difficult diagnosis often not found until after the surgical procedure**
- **Also after histopathology the diagnosis is difficult without obvious metastatic growth**
- **WHO classification only distant metastasis**
- **AFIP distant metastasis and/or local invasion**



Patient material Karolinska 1976-1999



Malignancy According to AFIP:

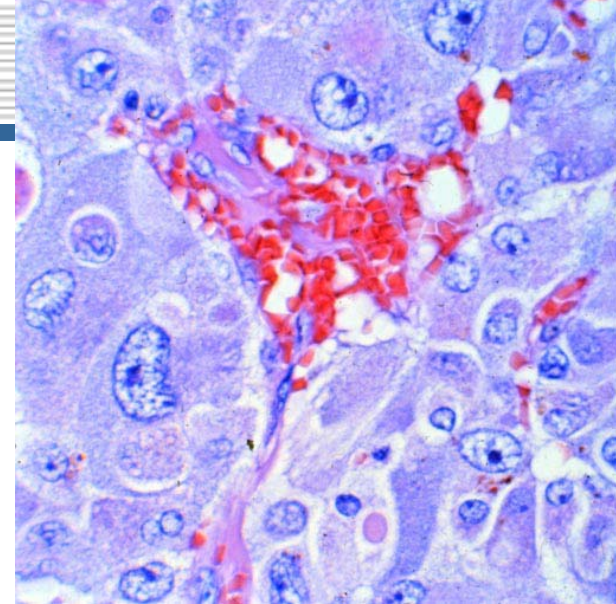
71 BENIGN

- No malignant recurrences after 144 months (7-287)
- 1 local recurrence of a bladder paraganglioma

14 MALIGN

- 5 with metastatic disease at diagnosis
- 4 rec 36-107 months postop
- 5 no rec after 11, 40-78 mån

- Patients with benign tumors according to AFIP have a very small risk for recurrence and life long follow up may be questioned



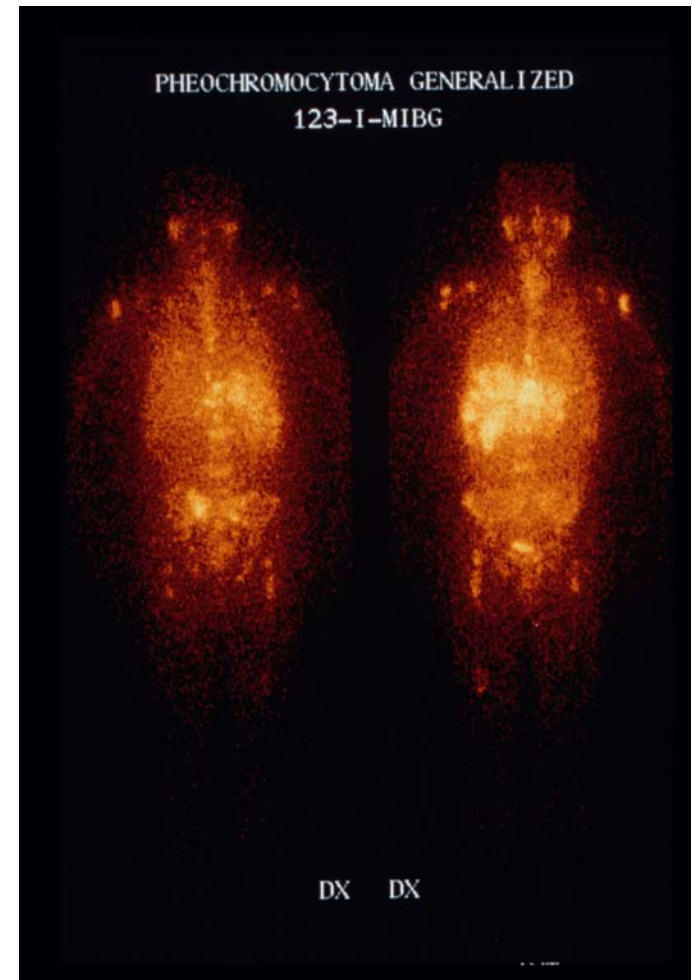
New markers for malignancy?

- **Telomerase activity determined as hTERT (human telomerase reverse transcriptase) expression is a sensitive tumor marker**
- **Ki-67/MIB-1 immunoreactivity reflects proliferative activity**
- **Combination Ki-67/MIB-1 and hTERT expression had a 90 % specificity and sensitivity to discriminate benign and malignant paraganglioma**
- **New markers e.g. VEGF(vascular endothelial growth factor) may become important for prognostic information**

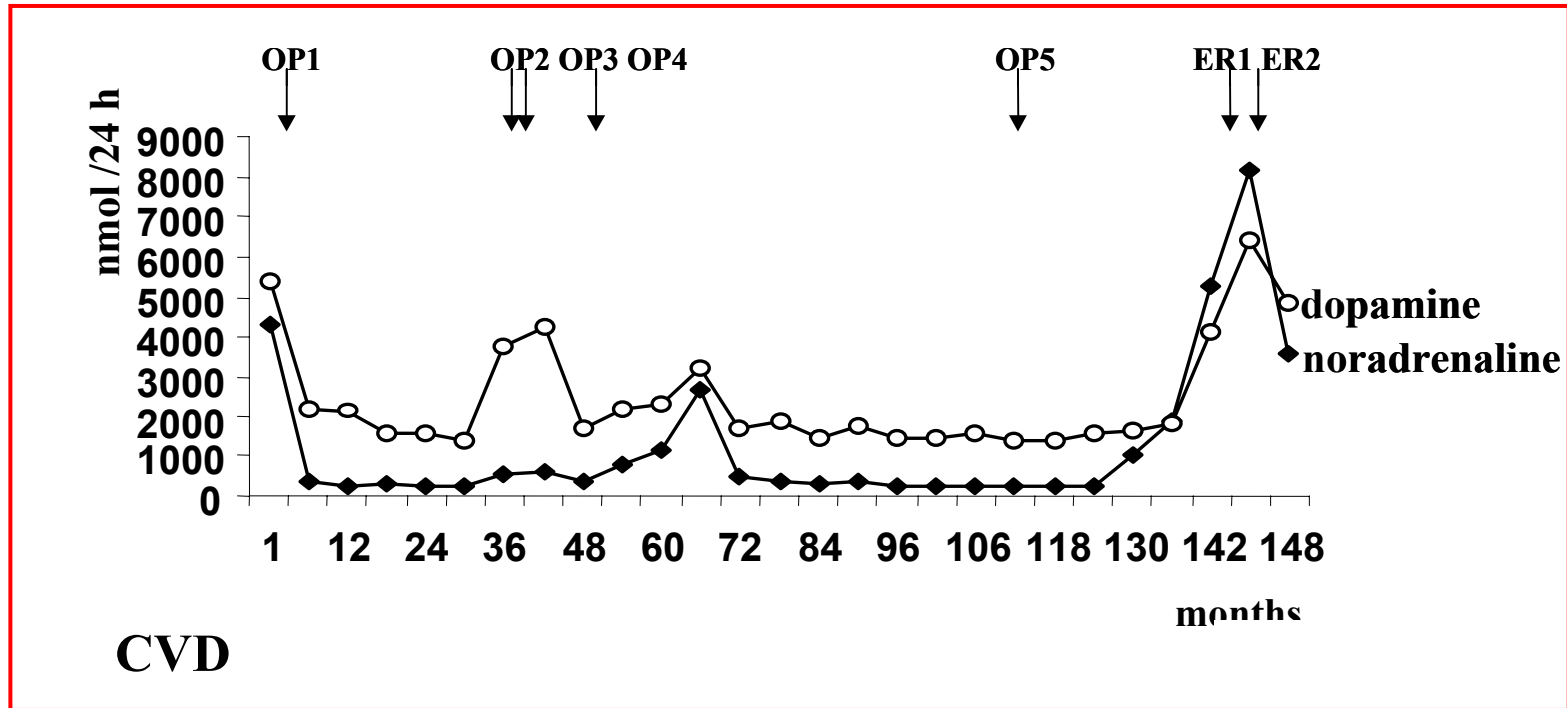


Treatment of malignant pheochromocytoma and paraganglioma

- **Operative removal of as much as possible and repeatedly**
- **^{131}I -MIBG**
- **Chemotherapy**
- **Radiotherapy for local symptomatic lesions**
- **Drugs: α -methyl tyrosine**
- **Future**
 - **new drugs**
 - **radiopharmaceuticals**



Treatment of malignant pheochromocytoma and paraganglioma



Chemotherapy: Cyclophosphamid, Vincristin, Dacarbazin (CVD) – effective on 3 of 4 pat.

Conclusions on pheochromocytoma

- **In relation to its incidence the tumor with the largest number of publications**
- **A potentially lethal, curable and usually benign adrenal tumor**
- **Often difficult to ascertain malignancy**
- **New treatment modalities for malignancy needed**

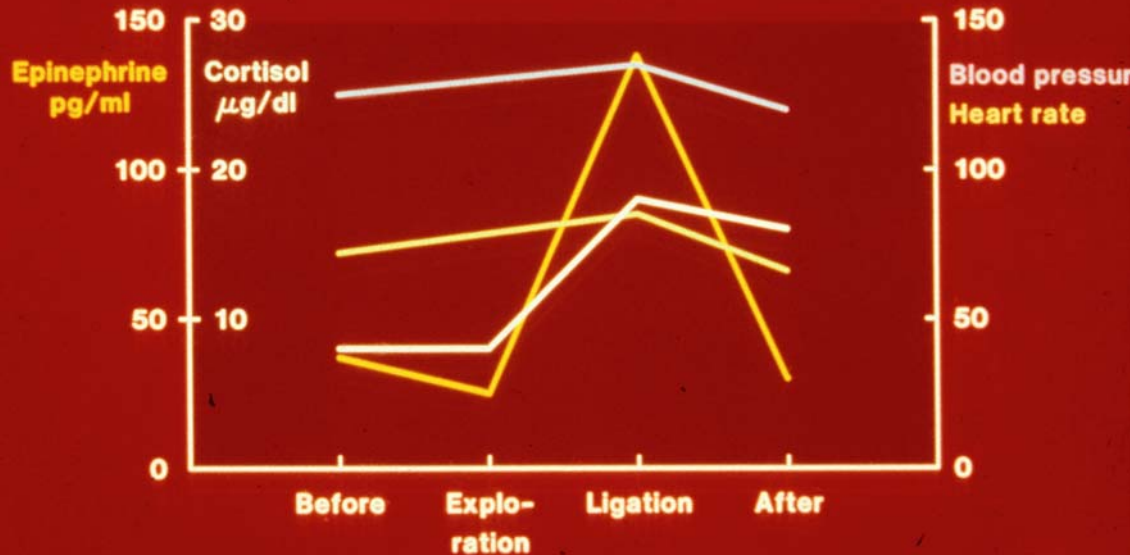
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Removing a right sided pheochromocytoma

SURGEON'S STRESS



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