



WILMS' TUMOR

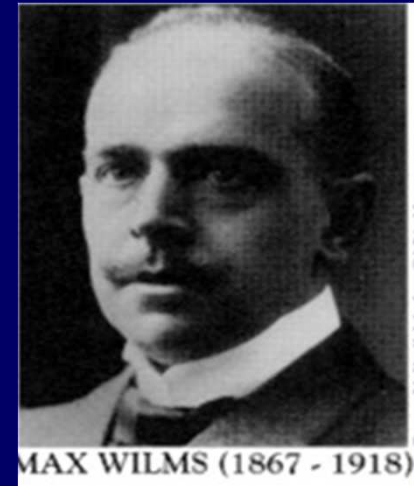
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HISTORY

- German Surgeon
- Childhood renal tumors
- Burns . tuberculosis
- Radiation
- Co-author of Surgical text book
- Died taking care of a patient



WILMS' TUMOR

- First solid malignancy in which the value of adjuvant chemotherapy was established.
- Multimodality treatment has resulted in a significant improvement in outcome from ~30% in the 1930s to > 85% in the modern era.
- Although the NWTSG & SIOP differ philosophically regarding the merits of preoperative CT, outcomes of patients treated with either up-front nephrectomy or preoperative CT have been excellent.
- The goal of current clinical trials is to reduce therapy for children with low-risk tumors, thereby avoiding acute and long-term toxicities

NWTS FAMILY



Giulio D'Angio, MD Daniel Green, MD Audrey Evans, MD J. Bruce Beckwith, MD Norman Breslow, PhD

SIOP FAMILY

On 3 July 1967, a small group of paediatricians, surgeons, pathologists and others met in the Paediatric Department "Service Milhit" of the Institut Gustave Roussy (IGR) in Villejuif/Paris, France. Everyone there knew SIOP's now Honorary Member, Dr Odile Schweisguth, and shared a keen interest in paediatric oncology. The Founding Members of the Society, who were present at the founding meeting of the Society in Madrid and voted for the constitution, were Doctors Bouchon, Boureau, Brunat, Carton, Delemarre, Gerard-Marchant, Gompel, Gubler, Hitzig, Hurtado, Kaser, Lemerle, Massimo, Maurus, Monero, Neidhardt, Noel, Pages, Payan, Pellerin, Pluss, Orsini, Raybaud, Schlienger, Schweisguth, Sullivan, Voûte and Wagner - this category of membership is still in existence and is held in high esteem, although it is purely historically derived!

WILMS' TUMOR

- Origin: “Metanephric Blastema”
- ⑩ Rarely arises in extra renal tissues
- ⑩ Sex ratio is 1:1
- ⑩ Median age at diagnosis 39 months for unilateral & 26 months of bilateral tumor
- ⑩ 1 % cases are familial
- ⑩ “Two- Hit” mutation model suggests loss of functioning gene by mutation at homologous loci (11p13),(11p15)

CLINICAL FEATURES

CLINICAL PRESENTATION:

⑩ Abdominal mass	68 %
⑩ Abd. Pain	29 %
⑩ Haematuria	25 %
⑩ Hypertension	25 %
⑩ Fever	18 %
⑩ Anorexia, vomiting, lassitude	14 %
⑩ Metastatic disease	15 %
• Lung (85%), Liver (15%)	
• Bone, Brain	

WILMS' TUMOUR - ASSOCIATIONS

CONGENITAL ANOMALIES:

Intrinsic Renal Abnormalities

Nephroblastomatosis
Darsh Syndrome
Multi cystic kidney

Genito Urinary

Hypospadias
Cryptorchism
Pseudohermophrodism
Horse shoe kidney
Double collecting sys
Ambiguous genitalia

Sporadic
Aniridia
(11 p -)

WILM'S tumor

Other

WAGAR

Hamartomas

Nevi

Growth Excess

Beckweth Wiedman
Hemihypertrophy
Klippel Trenaunay

Skeletal

Klippel Fiel
Club feet

IMAGING OF WILMS'

- Ultrasound abdomen with dopplor
- CT-abdomen with contrast.
- Chest x-ray – concordant and discordant
- CT-Chest
- Bone scan (CCSK)
- CT brain (RTK, CCSK)

PATHOLOGY OF WILMS' TUMOR

■ MICROSCOPIC:

Tri/Bi/Monophasic with undiff.

Spindle cells surrounding epithelial tubules, sometimes forming abortive glomerulus

■ NWTs (Beckwith palmer)

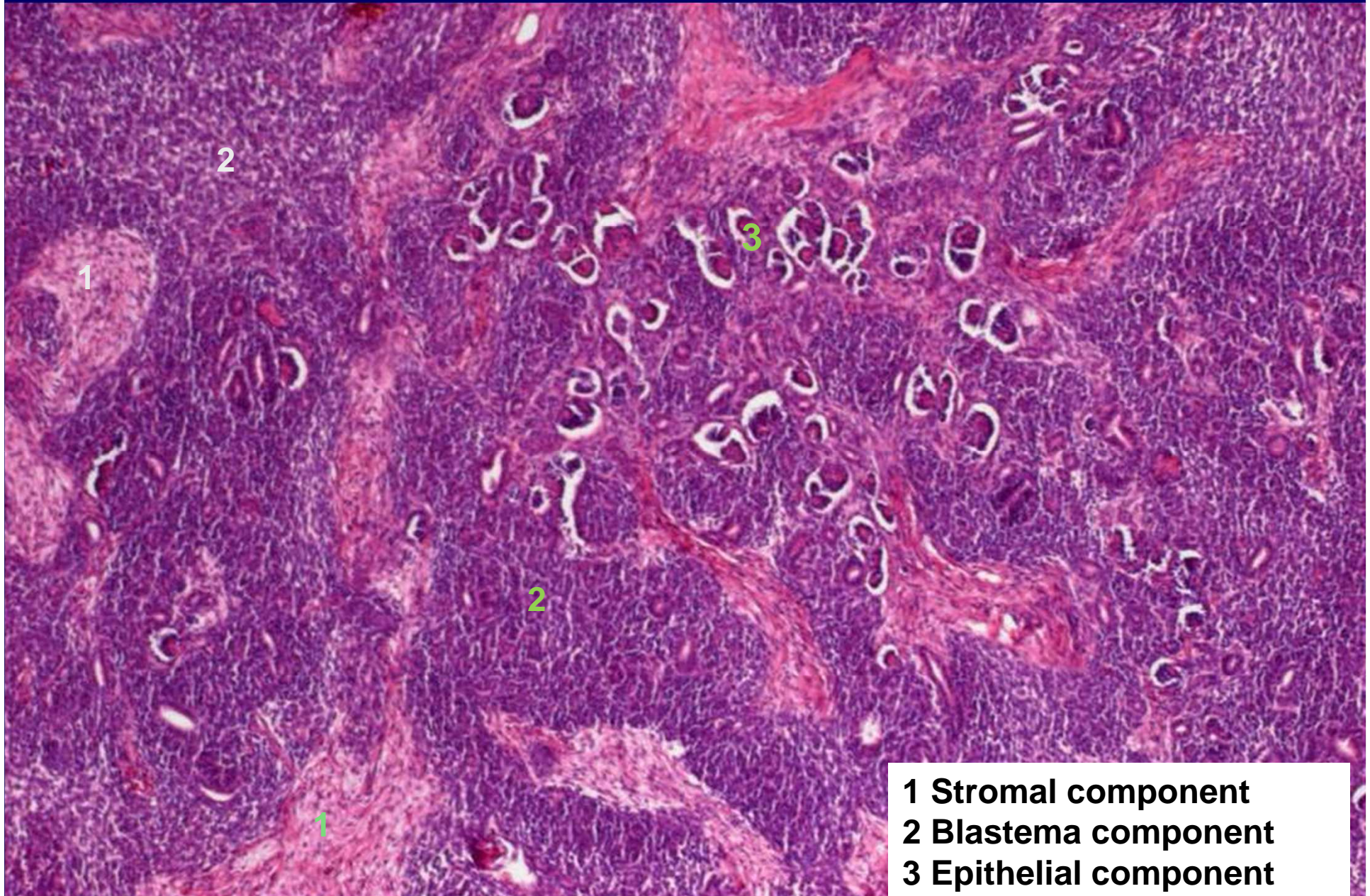
1. Favourable (FH)

2. Unfavourable (UH)

- Anaplastic – hyperchromasia, Increased size, mitosis

* Clear Cell Sarcoma

Wilms' tumour (nephroblastoma)



STAGING OF WILMS' TUMOR - NWTs

STAGE I : Tumor limited to kidney and
completely excised

STAGE II : Tumor extends beyond the
kidney but is completely excised

STAGE III : Residual non-haematogenous
tumor confined to the abdomen

STAGE IV : Haematogenous metastasis

STAGE V : Bilateral renal involvement at
diagnosis.

DIFFERENTIAL DIAGNOSIS FROM NEUROBLASTOMA

- Crossing midline - NB
- Hypertension - WT
- Calcification on plain x-ray - NB
- Kidney Pushed down (drooping lily appearance) - NB
- Pelvicalyceal system distortion - WT
- VMA - NB

TREATMENT PLAN

MANAGEMENT : MULTIMODAL

- Surgery - Radical Nephrectomy
- Radiotherapy
- Chemotherapy

Table 3. Primary conclusions from NWTSG studies of Wilms' tumor with favorable histologic features

Study	Stage/group	Chemotherapy	Radiation therapy
NWTS-1 [97] (1969–1973)	I	–	Unnecessary for children <2 years (when treated with chemotherapy)
	II and III	Vincristine and dactinomycin combination better than either drug alone	–
NWTS-2 [92] (1974–1978)	I	6 months of vincristine and dactinomycin sufficient	Unnecessary
	II, III, and IV	Addition of doxorubicin increased RFS rate	–
NWTS-3 [92] (1979–1986)	I	11 weeks of vincristine and dactinomycin sufficient	–
	II	Doxorubicin unnecessary	Unnecessary
	III	Doxorubicin necessary	With 1,000-cGy abdominal irradiation
	IV	Doxorubicin unnecessary	With 2,000-cGy abdominal irradiation
		No benefit to the addition of cyclophosphamide	–
NWTS-4 [93, 98] (1986–1994)	I–IV	“Pulse-intensive” chemotherapy as effective, less toxic, and less expensive	–
	II, III, and IV	6 months of chemotherapy sufficient	–
NWTS-5 (1995–2001)	I	Without chemotherapy, 2-year OS rate remained 100% but RFS rate was 86% – arm closed	–
	All stages	Loss of heterozygosity at chromosomes 1p AND 16q is an adverse prognostic indicator	

Abbreviations: NWTS, National Wilms' Tumor Study; NWTSG, National Wilms' Tumor Study Group; OS, overall survival; RFS, relapse-free survival.

Table 5. Primary conclusions of SIOP studies of Wilms' tumor with favorable histologic features

Study	Stage	Therapy
SIOP-1 [101, 102] (1971–1974)	I, II, or III	There was no difference in survival rate between the preoperative radiation therapy and immediate surgery groups. Significantly fewer tumor ruptures occurred in the pretreated group, and the recurrence-free survival rate was lower for patients who experienced intraoperative rupture.
SIOP-2 [101] (1974–1976)	I, II, or III	Study confirmed that patients who receive preoperative radiation therapy with dactinomycin are less likely to experience tumor ruptures than are those who undergo immediate surgery. Six months of postoperative treatment was as effective as 15 months in terms of event-free and overall survival rates.
SIOP-5 [3, 103] (1977–1979)	I, II, or III	Preoperative chemotherapy with vincristine and dactinomycin was as effective as radiation therapy with actinomycin-D in preventing tumor rupture.
SIOP-6 [104] (1980–1986)	I II	Treatment with vincristine and dactinomycin was as effective for 17 weeks as for 38 weeks in terms of event-free and overall survival rates. Patients with negative lymph nodes who were assigned to receive no radiation therapy had a higher recurrence rate.
SIOP-9 [95] (1987–1993)	I, II, or III II	Preoperative vincristine and dactinomycin was as effective for 4 weeks as for 8 weeks in terms of stage distribution and tumor shrinkage. For patients with negative lymph nodes, the rate of relapse was reduced by treatment with epirubicin without radiation therapy.
SIOP 93-01 [12] (1993–2000)	I	Reduction of postoperative chemotherapy (for intermediate-risk and anaplastic Wilms' tumor) to four doses of vincristine and one dose of dactinomycin was not less effective than standard postoperative chemotherapy.

WILMS' TUMOUR DEFINITE INDICATIONS FOR PRE-OP CHEMOTHERAPY

- Histo/cytological Confirmation is a must

Indication:

- Large Wilms' tumour, technically difficult to deliver at surgery.
 - Metastatic disease
 - Wilms' tumour is a solitary kidney
 - Wilms' tumour in a horse kidney
 - Bilateral Wilms' tumour
 - Thrombus extending up to right atrium
- Plan: 4 weeks of CT (VCR + Act - D)



BILATERAL WILMS' TUMOR

- NWTS-5 recommends initial biopsy and local staging followed by chemotherapy (according to abdominal stage and histologic features) and second-look surgery at week 5
- If needed, additional CT or RT is given, but definitive surgery is recommended within 12 weeks of diagnosis to limit the risk of chemoresistant clonal expansion
- Failure of bilateral WT to respond to preopCT is often due not to anaplasia but to persistence of mature elements with a skeletal muscle component.
- In patients with anaplastic tumors, complete surgical excision is warranted, and in such cases the NWTSG favors tumor resection with a margin of renal tissue rather than enucleation.
- Long-term survival rates for patients with synchronous bilateral WT are approximately 70%–80%

FOLLOW UP OF WILMS'

1. Clinical examination once in 3 months.
2. Abdominal U/S Once in 6 months x 2 yrs.
3. Growth and development assessment

LONG TERM SEQUELAE OF TREATMENT

1. Cardio toxicity
2. Second Malignancy
3. Infertility
4. Growth retardation
5. Diabetes
6. Increased probability of death.

RECURRENT WILMS' TUMOR

1. Most recurrence within 2 years.
2. 15% of favorable histology recur
3. 50% of unfavorable histology recur
4. Sites of recurrence – Lung, Pleura (50-60%), Abdominal (30%), others(brain, bone 10-15%)
5. 5 year out comes in FH recurrence has improved from 25% - 60%

RISK STRATIFICATION

- Standard Risk - FH-WT relapse after 2 drug regime of vincristine and actinomycin 70 – 80% EFS, 30% of recurrences.
- High risk – FH-WT relapse after 3 drugs 40-50% EFS, 45-55% of recurrences
- Very High Risk – Anaplastic or blastemal predominant WT, EFS 10% and 10-15% of recurrences

TAKE HOME MESSAGE

- Second Common abdominal tumor
- 80 % occur below 5 years of age
- 95 % tumors are unilateral
- Favorable Histology in 95 %
- Pre-Op CT required in pts. with large tumor
- Multimodality treatment- survival > 90 %

THANK YOU

