

## Gestational Trophoblastic Diseases

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### STAGING

In 1991, FIGO added non-surgical-pathologic prognostic risk factors to the classic anatomical staging system. These include urinary hCG levels >100000 mIU/ml and/or serum  $\beta$ -hCG >40000 mIU/ml and the duration of an antecedent pregnancy being >6 months.

Since gestational trophoblastic diseases (GTD) have a very high cure rate in virtually all patients, the ultimate goal of staging is to differentiate patients who

are likely to respond to less intensive chemotherapeutic protocols, from those who will require more intensive chemotherapy in order to achieve remission.

Staging should be based on history, clinical examination, and appropriate laboratory and radiological studies. Since hCG and  $\beta$ -hCG titers accurately reflect clinical disease, histologic verification is not required for diagnosis, although it may aid in therapy.

Table 1  
GTD: FIGO nomenclature (Singapore 1991)

Stage I	Disease confined to the uterus
Ia	Disease confined to the uterus with no risk factors
Ib	Disease confined to the uterus with one risk factor
Ic	Disease confined to the uterus with two risk factors
Stage II	GTD extends outside of the uterus, but is limited to the genital structures (adnexa, vagina, broad ligament)
IIa	GTD involving genital structures without risk factors
IIb	GTD extends outside of the uterus, but is limited to genital structures with one risk factor
IIc	GTD extends outside of the uterus, but is limited to the genital structures with two risk factors
Stage III	GTD extends to the lungs, with or without known genital tract involvement
IIIa	GTD extends to the lungs, with or without genital tract involvement and with no risk factors
IIIb	GTD extends to the lungs, with or without genital tract involvement and with one risk factor
IIIc	GTD extends to the lungs, with or without genital tract involvement and with two risk factors
Stage IV	All other metastatic sites
IVa	All other metastatic sites, without risk factors
IVb	All other metastatic sites, with one risk factor
IVc	All other metastatic sites, with two risk factors

Table 2  
GTD: Stage grouping for GTD

FIGO stage	UICC		
	T	N	Risk factors
Ia	T1a	M0	None
Ib	T1b	M0	One
Ic	T1c	M0	Two
IIa	T2a	M0	None
IIb	T2b	M0	One
IIc	T2c	M0	Two
IIIa	Any T	M1a	None
IIIb	Any T	M1a	One
IIIc	Any T	M1a	Two
IVa	Any T	M1b	None
IVb	Any T	M1b	One
IVc	Any T	M1b	Two

Risk factors affecting staging include the following:

- (i) Urinary hCG >100000 mIU/ml (or serum  $\beta$ -hCG >40,000 mIU/ml)
- (ii) Duration of disease >6 months from termination of the antecedent pregnancy

The following factors should be considered and noted in reporting:

- (i) Prior chemotherapy for known GTD
- (ii) Placental site tumors should be reported separately
- (iii) Histological verification of disease is not required

### DEFINITIONS OF TREATMENTS

Treatment definitions are given in Table 3.

## DATA ANALYSIS

### Summary and comments

In the staging of gestational trophoblastic neoplasia (GTN), the FIGO 1991 staging has still been used in the current Annual Report. With the increase in the number of contributing centers, the number of GTN reported was more than double that in the previous report (Table 9). Same as before, the majority of patients had Stage I disease. Excluding the 202 cases with missing data, 76% had Stage I, 5% had Stage II, 15% had Stage III and 4% had Stage IV disease which were quite similar to that of 1993–5 (Table 10).

The predominance of GTN in women under 30 was more obvious in this Report, with 64% compared to 49% in the data on patients treated in 1993–95 (Fig. 1). It is important that these patients be managed correctly to ensure a near 100% survival.

The main stay of treatment was chemotherapy, though more patients received both chemotherapy and surgery

in Stage IV disease (Tables 5–8). For all stages, 66% of patients were treated with chemotherapy with or without surgery (Table 11). Even for choriocarcinoma, 90% were treated with chemotherapy with (52%) or without (38%) surgery (Table 12).

GTN is a chemosensitive disease. Excluding 296 cases with missing data, 85% achieved complete response (Table 13). Only 11 relapses were reported (Table 14). The overall 5-year survival rate of all subjects was 97.2% (Fig. 3). Based on FIGO anatomical stage alone, the 5-year survival rates of Stages II and III were quite similar, though Stage IV disease had a lower survival rate than the rest (Fig. 4). With the addition of the 8 prognostic factors in the FIGO 2000 staging, analysis on their significance would be possible in the future to better discriminate high risk Stage II/III disease from low risk one. However, it would be very important to have all data provided by contributing centers in order to have a meaningful analysis.

Table 3  
GTD: Definitions of treatments

Treatment	Definition
None	No treatment.
Chemotherapy	Performed either as a prophylactic treatment or as primary treatment following D&C with residual disease (uterine or extrauterine).
Surgery alone	Only hysterectomy (because of GTD), with normalization of serum $\beta$ -hCG levels, performed on patients who did not undergo chemotherapy before and/or after hysterectomy.
Chemotherapy + surgery	Chemotherapy plus surgery (abdominal and/or pelvic surgery, craniotomy, lobectomy of the lung, etc.) with the intention to treat GTD. Please note that chemotherapy can be given before and/or after surgery.

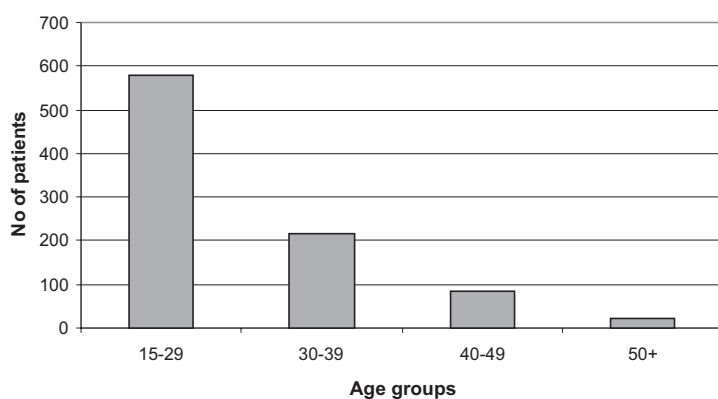


Fig. 1. GTD: patients treated in 1996–98. Distribution by age groups.

Age groups	Patients (n)	Percentage (%)
15–29	578	64.2
30–39	216	24.0
40–49	85	9.4
50+	22	2.4
Total	901	100.0

Table 4  
GTD: patients treated in 1996–98. Distribution of patients by center and stage

		All	Not available	Stage I	Stage II	Stage III	Stage IV
All centers		901	202	529	34	106	30
South Africa	Pretoria (G Lindeque)	4	1	2	1	–	–
Argentina	Buenos Aires (R Testa)	3	–	3	–	–	–
	Neuquén (GH Focaccia)	3	–	3	–	–	–
	Santa Fe (A Ellena)	6	–	6	–	–	–
Peru	Arequipa (L Medina Fernandez)	1	–	–	1	–	–
USA	Baltimore MA (F Montz, RE Bristow)	6	5	–	–	–	1
	New Haven CT (EI Kohorn)	10	–	7	–	3	–
	New York NY (R Barakat)	10	–	5	3	2	–
Uruguay	Montevideo (G Arribeltz)	7	–	7	–	–	–
China	Hong Kong (HSY Ngan)	52	2	31	–	10	9
	Hong Kong (VSY Yu)	14	–	14	–	–	–
India	Calicut (PK Sekharan)	280	192	83	5	–	–
	Bangalore (KU Devi)	20	–	6	–	13	1
Indonesia	Medan (M Fauzie Sahil)	4	–	3	–	1	–
Japan	Kumamoto (H Okamura)	12	–	12	–	–	–
	Nagasaki (T Ishimaru)	14	–	9	–	5	–
	Osaka (A Suzuki)	2	–	2	–	–	–
	Tokyo (K Kinoshita)	5	–	5	–	–	–
	Sagamihara (H Kuramoto)	7	–	4	–	3	–
Korea	Seoul (HP Lee)	18	–	12	–	6	–
	Seoul (JE Mok)	7	–	7	–	–	–
Philippines	Manila (IB Benitez)	13	1	8	2	2	–
	Manila (AM Manalo)	65	–	36	3	18	8
Thailand	Bangkok (V Linasmita)	25	–	19	1	5	–
	Songkhla (V Wootipoom)	25	–	11	3	10	1
Turkey	Sivas (T Guvenal)	4	–	4	–	–	–
Austria	Graz (R Winter)	2	–	2	–	–	–
	Innsbruck (C Marth)	11	–	10	–	–	1
Croatia	Zagreb (S Jukić)	27	–	25	1	–	1
Finland	Turku (T Salmi)	3	1	2	–	–	–
France	Bordeaux (ML Campo)	3	–	2	–	1	–
Germany	Kiel (D Weisner)	1	–	1	–	–	–
Portugal	Coimbra (C Freire de Oliveira)	5	–	4	1	–	–
	Porto (MT Osorio)	3	–	1	1	–	1
Spain	Barcelona (J Pahisa Fabregas)	2	–	2	–	–	–
	Madrid (F Calero Cuerda)	2	–	2	–	–	–
Sweden	Örebro (B Sorbe)	5	–	5	–	–	–
Ukraine	Odessa (AA Zelinsky)	10	–	6	3	1	–
UK	London (ES Newlands)	210	–	168	9	26	7

Table 5

GTD: patients treated in 1996–98. Distribution of patients (%) by country and treatment (Stage I),  $n=529$ 

Country	Number of patients	First line of treatment (%)				
		None	CT	Surgery alone	CT + surgery	Other
All	529	10	69	3	12	1
South Africa	2	50	50	–	–	–
Argentina	12	17	42	8	–	–
USA	12	–	83	–	17	–
Uruguay	7	57	43	–	–	–
China	45	27	71	–	2	–
India	89	2	85	1	11	–
Indonesia	3	–	33	–	67	–
Japan	32	53	25	9	6	6
Korea	19	5	47	37	11	–
Philippines	44	2	50	2	45	–
Thailand	30	–	80	3	17	–
Turkey	4	25	–	–	–	75
Austria	12	83	17	–	–	–
Croatia	25	–	–	–	20	–
Finland	2	–	100	–	–	–
France	2	–	50	50	–	–
Germany	1	–	–	–	100	–
Portugal	5	20	60	–	20	–
Spain	4	25	25	–	50	–
Sweden	5	20	80	–	–	–
Ukraine	6	–	50	17	17	17
UK	168	–	95	–	5	–

Table 6

GTD: patients treated in 1996–98. Distribution of patients (%) by country and treatment (Stage II),  $n=34$ 

Country	Number of patients	First line of treatment (%)				
		None	CT	Surgery alone	CT + surgery	Other
All	34	9	62	3	24	0
South Africa	1	–	100	–	–	–
Peru	1	–	100	–	–	–
USA	3	–	33	33	33	–
India	5	–	60	–	40	–
Philippines	5	–	40	–	60	–
Thailand	4	–	50	–	50	–
Croatia	1	–	–	–	–	–
Portugal	2	–	100	–	–	–
Ukraine	3	100	–	–	–	–
UK	9	–	100	–	–	–

Table 7

GTD: patients treated in 1996–98. Distribution of patients (%) by country and treatment (Stage III),  $n=106$ 

Country	Number of patients	First line of treatment (%)				
		None	CT	Surgery alone	CT + surgery	Other
All	106	–	71	2	25	2
USA	5	–	20	–	80	–
China	10	–	100	–	–	–
India	13	–	85	–	15	–
Indonesia	1	–	100	–	–	–
Japan	8	–	38	–	38	25
Korea	6	–	50	–	50	–
Philippines	20	–	55	5	40	–
Thailand	15	–	67	–	33	–
France	1	–	100	–	–	–
Ukraine	1	–	–	100	–	–
UK	26	–	92	–	8	–

Table 8

GTD: patients treated in 1996–98. Distribution of patients (%) by country and treatment (Stage IV),  $n=30$ 

Country	Number of patients	First line of treatment (%)				
		None	CT	Surgery alone	CT + surgery	Other
All	30	–	47	–	43	7
USA	1	–	–	–	100	–
China	9	–	78	–	11	11
India	1	–	–	–	100	–
Philippines	8	–	13	–	75	–
Thailand	1	–	–	–	100	–
Austria	1	–	–	–	100	–
Croatia	1	–	–	–	–	100
Portugal	1	–	–	–	100	–
UK	7	–	86	–	14	–

Table 9

GTD: patients treated in 1996–98. Review of the data collection of the last *Annual Report* volumes

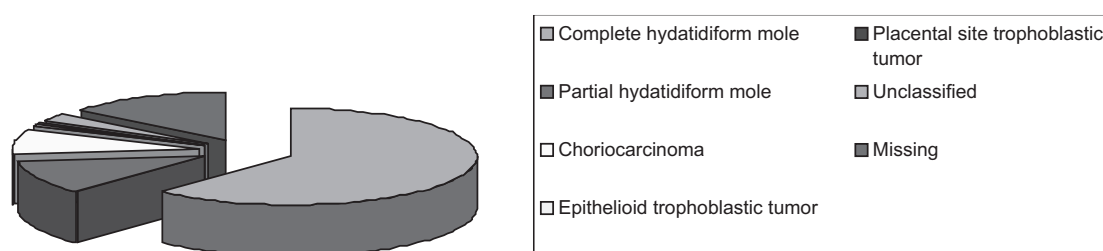
Vol.	Year	Patients ( $n$ )	Contributing centers
19	1976–78	1688 <sup>a</sup>	21
20	1979–81	1938 <sup>a</sup>	22
21	1982–86	996 <sup>a</sup>	24
22	1987–89	408	15
23	1990–92	234	22
24	1993–95	411	31
<b>25</b>	<b>1996–98</b>	<b>901</b>	<b>39</b>
<b>Total</b>		<b>6576</b>	

<sup>a</sup>These figures include cases that had been collected in wider time intervals compared with the period of data collection of those volumes, or that might be already present in the data reported in previous volumes.

Table 10

GTD: patients treated in 1996–98. Distribution by FIGO stage

FIGO stage	Patients ( $n$ )	Percentage (%)
I	529	58.7
II	34	3.8
III	106	11.8
IV	30	3.3
Missing	202	22.4
All	901	100.0



Histotype	All	%	Missing	I	II	III	IV
Complete hydatidiform mole	552	61.3	184	327	8	30	3
Partial hydatidiform mole	78	8.7	8	62	2	3	3
Choriocarcinoma	115	12.8	3	43	18	32	19
Epithelioid trophoblastic tumor	6	0.7	0	5	0	1	0
Placental site trophoblastic tumor	8	0.9	1	3	0	4	0
Unclassified	20	2.2	1	14	2	3	0
Missing	122	13.5	5	75	4	33	5
All	901	100	202	529	34	106	30

Fig. 2. GTD: patients treated in 1996–98. Histopathology by FIGO stage.

Table 11

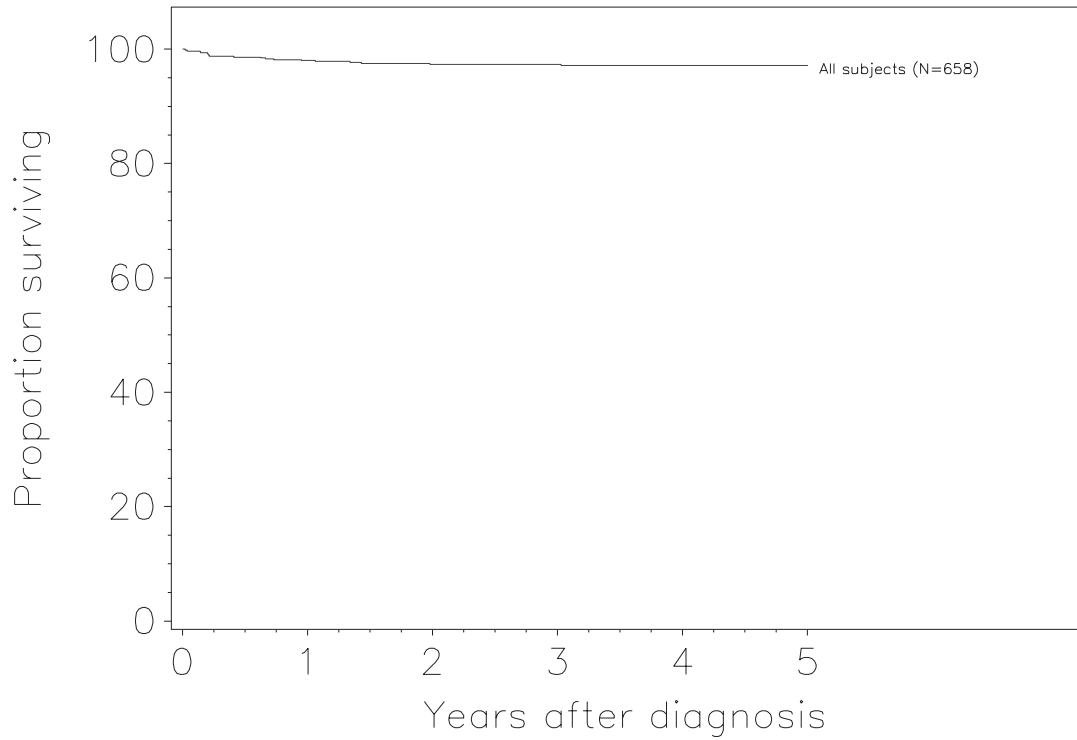
GTD: patients treated in 1996–98. Distribution of patients by mode of treatment and FIGO stage

Treatment	All	%	Missing	I	II	III	IV
No treatment	251	27.9	194	54	3	0	0
CT	480	53.3	3	367	21	75	14
Surgery alone	20	2.2	1	16	1	2	0
CT + surgery	114	12.7	4	62	8	27	13
Other non-standard	10	1.1	0	6	0	2	2
Missing	26	2.9	0	24	1	0	1
All	901	100.0	202	529	34	106	30

Table 12

GTD: patients treated in 1996–98. Distribution of patients by mode of treatment and histotype

Treatment	Complete hydatidiform mole	Partial hydatidiform mole	Chorio-carcinoma	Epithelioid trophoblastic tumor	Placental site trophoblastic tumor	Unclassified	Missing
No treatment	214	29	3	0	0	1	4
CT	291	30	44	2	3	3	107
Surgery alone	9	1	2	1	2	5	0
CT + surgery	27	2	59	3	3	11	9
Other non-standard	3	0	6	0	0	0	1
Missing	8	16	1	0	0	0	1
All	552	78	115	6	8	20	122

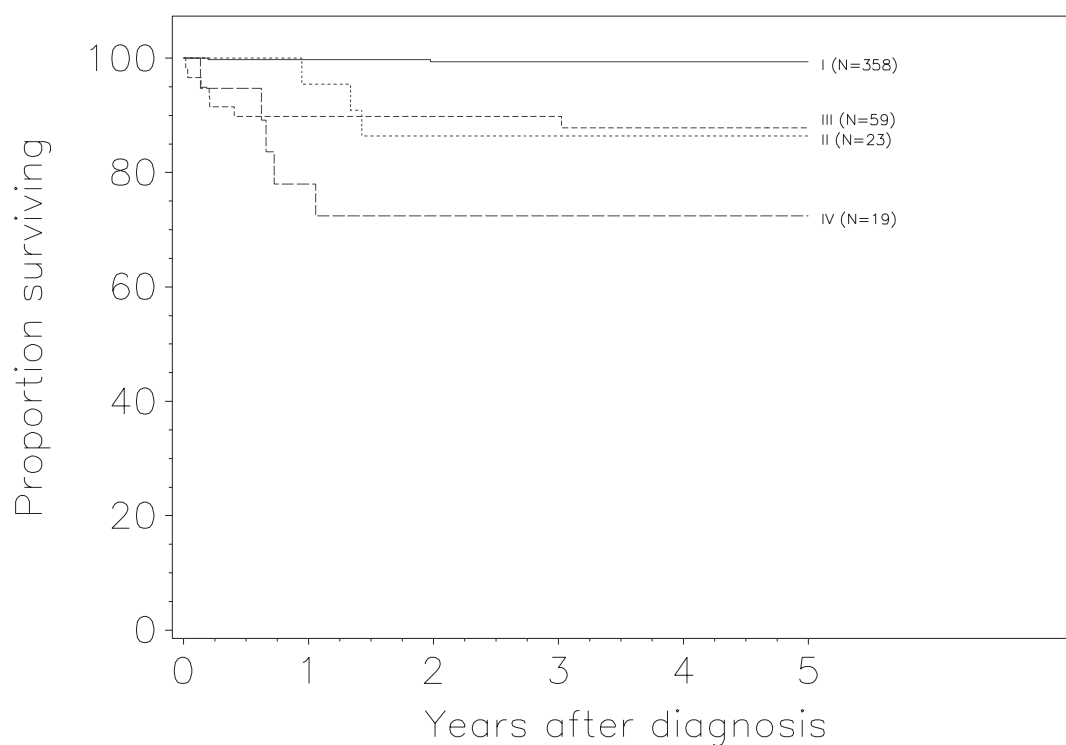


	Patients (n)	Mean age (yr)	Overall survival (%) at				
			1 year	2 years	3 years	4 years	5 years
All subjects	658	27.9	98.0%	97.4%	97.4%	97.2%	97.2%

Fig. 3. GTD: patients treated in 1996–98. Overall survival, n = 658.

Table 13  
GTD: patients treated in 1996–98. Response to treatment by FIGO stage

Response	All	Missing	I	II	III	IV
Missing	296	1	234	16	33	12
Complete response	515	194	240	15	56	10
Partial response	29	1	20	1	6	1
Stable disease	15	5	8	0	0	2
Progressive disease	9	0	3	1	3	2
Not assessable	37	1	24	1	8	3



Stage	Patients (n)	Mean age (yr)	Overall survival (%) at					Hazards ratio <sup>a</sup> (95% CI)
			1 year	2 years	3 years	4 years	5 years	
I	358	28.9	99.7	99.4	99.4	99.4	99.4	Reference
II	23	34.9	95.6	86.2	86.2	86.2	86.2	4.0 (0.6–29.1)
III	59	32.3	89.7	89.7	89.7	87.6	87.6	10.2 (2.3–45.0)
IV	19	33.0	78.4	72.6	72.6	72.6	72.6	30.9 (6.4–149.0)

<sup>a</sup>Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age, stage and country.

Fig. 4. GTD: patients treated in 1996–98. Survival by FIGO stage,  $n=459$ .

Table 14

GTD: patients treated in 1996–98. Relapses by FIGO stage

Site relapse	All	I	II	III	IV
Local (regional)	8	7	0	1	0
Metastatic	2	1	1	0	0
Local and metastatic	1	0	0	1	0
Missing site	533	252	15	60	11
Total	544	260	16	62	11