

Anhang 3

**Morphologic analysis of thyroid carcinomas
selected for carrying out investigations in
the framework of StSch4299 project**

**MORPHOLOGIC ANALYSIS OF THYROID CARCINOMAS
SELECTED FOR CARRYING OUT INVESTIGATIONS IN THE FRAMEWORK
OF StSch4299 PROJECT**

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Investigations according to the Project provide for the study of 191 cases of thyroid cancer reported among residents of Kiev, Chernigov, and Zhytomir regions, born in 1968-1985, and 202 cases of thyroid cancer found in residents of the City of Kiev within the same age group for the period 1990-1999. These cases have been selected from clinico-morphological Register, which has been established at the Institute of Endocrinology and Metabolism of the Academy of Medical Sciences of Ukraine in 1992 on the base of statistical reports on the number of thyroid cancer cases in subjects aged 0-18 years at the time of the Chernobyl accident in all 27 regions of Ukraine, and on a review of medical records of patients having undergone surgical or postoperative treatment at the Hospital of the Institute of Endocrinology [N.D.Tronko et al., 1999, 2002, 2002].

The detailed morphological characteristics for this report have been estimated by means of a histological analysis of carcinomas obtained after surgical treatment of thyroid cancer patients at the Institute of Endocrinology and Metabolism of the Academy of Medical Sciences of Ukraine, or based on material (paraffin blocks, histological specimens) forwarded to the Laboratory of Morphology of the Institute for consultative conclusion. Pathology diagnoses were based on WHO classification [Chr.Hedinger et al., 1988]. Most of the cases have been additionally studied by international experts. The diagnosis of carcinoma has been confirmed in all the cases under study.

Out of 191 cases reported in the three above regions, we have carried out a morphologic analysis of 147 cases, or 77.0% (**Table 1**). 131 cases out of 147 (89.1%) have been operated at the Institute of Endocrinology, and 16 cases (10.9%) have been received from other clinics for additional verification of pathologic diagnoses.

In 92 cases the tumours were removed in children aged up to 15 years, in 20 cases of adolescents aged 15 to 18, and in 35 cases of young adults aged 19 to 31 years.

The data obtained point out that the overwhelming majority of thyroid cancer cases in the series under study represented a papillary carcinoma: 97.8% of cases in children, 100% in adolescents, and 97.1% among young adults.

A follicular carcinoma has been reported in one case of a girl aged 14, and in one case of a female aged 21 years. In one boy aged 7 a papillary carcinoma (in one lobe) has been removed, as well as a medullary carcinoma (in the other lobe) a year later.

Out of 202 cases registered in the Kiev-city (**Table 2**), we have carried out a morphologic analysis of 96 cases (or 47.5%) having been operated at the Institute of Endocrinology (79 cases out of 96, i.e. 82.3%), or referred to the Laboratory for expert conclusion (17 cases, or 17.7%).

In 34 cases the tumours have been removed in children aged up to 15; 26 cases in adolescents aged 15 to 18, and 36 cases in young adults aged 19 to 31 years.

In this series papillary carcinoma is also dominant: 94.2% of cases in children, 84.6% in adolescents, and 88.9% in young adults; but the rate of papillary carcinoma among inhabitants of the City of Kiev is lower as compared to the residents of the three above regions, especially in adolescents and young adults. This is due to the fact that among 26 cases in adolescents one represents a follicular carcinoma, and two cases an anaplastic carcinoma. Among young adults 4 out of 36 cases represent a follicular carcinoma (11.1%). A wider range of morphologic types of thyroid carcinomas among inhabitants of the City of Kiev may be due - to a certain degree - to a higher spontaneous incidence rate of thyroid cancer, and, therefore, to a lesser part of "radiation" papillary cancers.

An analysis of both series showed (**Table 3**) that in all age groups more than 90% cases are represented by papillary carcinoma. Follicular carcinoma more often was revealed in young adults: in 7% of cases.

Tumour size and histological peculiarities have been analysed for thyroid carcinomas, when we had clear pathology information about tumour size. There were 130 cases for first series, 78 for second one, and 208 cases for both series. As to their size, the tumours of first series (**Table 4**) measured most often more than 1 cm in diameter. For all age groups, tumours from 1 to 2 cm in diameter were dominant: 61.2% for children, 52.6% for adolescents, and 46.2% of cases for young adults.

In all age groups, isolated cases of extensive tumours were reported, which affected one or both thyroid lobes.

Tumours up to 1 cm in diameter have been found in 7 cases of children, in 2 cases of adolescents, and in 1 cases of young adults, what makes up, respectively, 8.2, 10.3%, and 3.8% of cases in each age group, and 7.7% of all 130 cases under study.

It should be stressed (**Table 5**) that among inhabitants of the City of Kiev the percentage of carcinomas up to 1 cm in diameter is significantly lower in children's age group as compared to the residents of the above regions. This may be due both to a more thorough follow-up of children of the most contaminated Kiev, Chernigov, and Zhytomir regions, and to a lesser volume of morphologic analysis of cases of inhabitants of Kiev as compared to the volume of morphologic analysis of cases of residents of the 3 regions in question (47.5% versus 77.0% of cases). In addition, 5 tumours measuring more than 6 cm have been registered among inhabitants of the City of Kyiv. 4 out of them were extensively invasive papillary carcinomas, and one tumour represented an anaplastic carcinoma.

For both series (**Table 6**) tumours from 1 to 2 cm in diameter were also dominant: 57.0% for children, 42.1% for adolescents, and 42.8% of cases for young adults. Tumours up to 1 cm in diameter have been found in 8 cases of children, in 4 cases of adolescents, and in 5 cases of young adults, what makes up, respectively, 7.0, 10.5%, and 8.9% of cases in each age group, and 8.2% of all 208 cases under study for the 1990-1999 period.

At the same time, it should be noted that in 1994-1996, and in 1997-1999 the percentage of these "small" carcinomas was increasing. If in 1990-1993 only one "small" tumour out of 38 thyroid carcinomas (2.6%) were registered, in 1994-1996 their number has increased up to 4 out of 70 (5.7%), exceeding by 2.2 times the previous indicator, and in 1997-1999 their number has increased up to 12 out of 100 (12.0%), exceeding by 4.6 times the indicator for 1990-1993 (**Table 7**). An increase of number and percentage of "small" tumours may be connected with intensification of screening, because in the process of special screening examinations in the framework of the Ukraine-U.S. Thyroid Project the percentage of such "small" tumours was 23.3% during 1st screening (10 cases out of 43 thyroid carcinomas, revealed in 1998-2000 in 13227 screened subjects), and 38.1% during 2nd one ([M.D.Tronko et al., 2003]).

An analysis of the signs of extrathyroid spreading of carcinomas (T4 category by TNM classification) depending on tumour size shows that among children of the above regions or Kiev-city tumours with any size referred to T4 category were more often reported than among adolescents and young adults (**Table 8,9**).

For both series (**Table 10**) 60.5% of cases of children were referred to T4 category as a whole. Among tumours up to 1 cm, 4 out of 8 carcinomas (50.0%) spread outside thyroid capsule and were referred to T4 category; the remaining 4 tumours corresponded to T1 category. Practically for any size of tumour more than 1 cm among children under study most of carcinomas belonged to T4 category. Among adolescents and young adults bigger tumours measuring up to 5 cm and more were referred more often to T4 category. So, extrathyroid spreading depended on age of operated patients.

It should be stressed that minimum tumour size - up to 1 cm - does not exclude the development of regional metastases, especially in children. A high rate of regional metastases is also noted for tumours measuring from 1.1 to 2 cm (**Table 11-13**). Tumours exceeding 3 cm in size are characterized in most of cases by the presence of metastases to regional lymph nodes in all age groups. The highest percentage of regional metastases (**Table 13**) was observed in children (57.9%). So, presence of regional metastases, as well as extrathyroid spreading of the papillary carcinomas, depended on age of operated patients.

CONCLUSIONS

- In both series for all age groups papillary carcinomas are dominant, but their rate is lower among inhabitants of the City of Kiev as compared to residents of Kiev, Chernigov, and Zhytomir regions, at the expense of a wider range of morphologic types of thyroid carcinomas.
- An increase in percentage of tumors measuring up to 10 mm was registered with increasing time elapsed after the Chernobyl accident.
- Extrathyroid spreading and presence of regional metastases depended on the age of operated patients. These indicators were highest in children.

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**Table 1. Main types of the thyroid carcinoma
in patients who were born in 1968-1985
(Kiev, Chernigov, Zhytomir oblasts, aggregate data, 147 cases for 1990-1999 period)**

Histological type	Children		Adolescents		Young adults	
	Number	%	Number	%	Number	%
Papillary carcinoma	90	97.8	20	100	34	97.1
Follicular carcinoma	1	1.1	-	-	1	2.9
Medullary carcinoma	1*	1.1	-	-	-	-
Oxyphilic cell carcinoma	-	-	-	-	-	-
Anaplastic carcinoma	-	-	-	-	-	-
Total	92		20		35	

* - 1 case PTC+MTC (a same case)

**Table 2. Main types of the thyroid carcinoma
in patients who were born in 1968-1985
(Kiev-city, aggregate data, 96 cases for 1990-1999 period)**

Histological type	Children		Adolescents		Young adults	
	Number	%	Number	%	Number	%
Papillary carcinoma	32	94.2	22	84.6	32	88.9
Follicular carcinoma	1	2.9	2	7.7	4	11.1
Medullary carcinoma	1	2.9	-	-	-	-
Oxyphilic cell carcinoma	-	-	-	-	-	-
Anaplastic carcinoma	-	-	2	7.7	-	-
Total	34		26		36	

**Table 3. Main types of the thyroid carcinoma
in patients who were born in 1968-1985**

(Kiev, Chernigov, Zhytomir oblasts, and Kiev-city, aggregate data, 243 cases for 1990-1999)

Histological type	Children		Adolescents		Young adults	
	Number	%	Number	%	Number	%
Papillary carcinoma	122	96.8	42	91.4	66	93.0
Follicular carcinoma	2	1.6	2	4.3	5	7.0
Medullary carcinoma	2*	1.6	-	-	-	-
Oxyphilic cell carcinoma	-	-	-	-	-	-
Anaplastic carcinoma	-	-	2	4.3	-	-
Total	126		46		71	

* - 1 case PTC+MTC (a same case)

**Table 4. Size of thyroid carcinomas
in patients who were born in 1968-1985
(Kiev, Chernigov, Zhytomir oblasts, aggregate data, 130 cases for 1990-1999 period)**

Size of the tumour	Children		Adolescents		Young adults	
	Number	%	Number	%	Number	%
< = 1cm	7	8.2	2	10.5	1	3.8
1.1 - 2 cm	52	61.2	10	52.6	12	46.2
2.1 – 3 cm	11	12.9	2	10.5	9	34.7
3.1 – 4 cm	6	7.1	4	21.1	2	7.7
4.1 – 5 cm	6	7.1	-	-	1	3.3
5.1 – 6 cm	3	3.5	1	5.3	1	3.8
> 6 cm	-	-			-	
Total	85		19		26	

**Table 5. Size of thyroid carcinomas
in patients who were born in 1968-1985
(Kiev-city, aggregate data, 78 cases for 1990-1999 period)**

Size of the tumour	Children		Adolescents		Young adults	
	Number	%	Number	%	Number	%
< = 1cm	1	3.4	2	10.5	4	13.3
1.1 - 2 cm	13	44.9	6	31.6	12	40.0
2.1 – 3 cm	9	31.1	5	26.3	7	23.4
3.1 – 4 cm	1	3.4	2	10.5	3	10.0
4.1 – 5 cm	3	10.3	1	5.3	2	6.7
5.1 – 6 cm	-	-	1	5.3	1	3.3
> 6 cm	2	6.9	2	10.5	1	3.3
Total	29		19		30	

**Table 6. Size of thyroid carcinomas
in patients who were born in 1968-1985
(Kiev, Chernigov, Zhytomir oblasts, and Kiev-city, aggregate data, 208 cases for 1990-1999)**

Size of the tumour	Children		Adolescents		Young adults	
	Number	%	Number	%	Number	%
< = 1cm	8	7.0	4	10.5	5	8.9
1.1 - 2 cm	65	57.0	16	42.1	24	42.8
2.1 – 3 cm	20	17.6	7	18.4	16	28.6
3.1 – 4 cm	7	6.1	6	15.8	5	8.9
4.1 – 5 cm	9	7.9	1	2.6	3	5.4
5.1 – 6 cm	3	2.6	2	5.3	2	3.6
> 6 cm	2	1.8	2	5.3	1	1.8
Total	114		38		56	

**Table 7. Time dependence of size of thyroid carcinomas
in patients who were born in 1968-1985**

(Kiev, Chernigov, Zhytomir oblasts, and Kiev-city, aggregate data, 208 cases for 1990-1999)

Size of the tumour	1990-1993		1994-1996		1997-1999	
	Num	%	Num	%	Num	%
< = 1cm	1	2.6	4	5.7	12	12.0
1.1 - 2 cm	19	50.0	33	47.1	53	53.0
2.1 – 3 cm	10	26.3	17	24.2	16	16.0
3.1 – 4 cm	3	7.9	6	8.6	9	9.0
4.1 – 5 cm	3	7.9	6	8.6	4	4.0
5.1 – 6 cm	2	5.3	2	2.9	3	3.0
> 6 cm	-	-	2	2.9	3	3.0
Total	38	100	70	100	100	100

Table 8. Extra-thyroid spread (T4-category of TNM classification) and size of thyroid carcinomas in patients who were born in 1968-1985 (Kiev, Chernigov, Zhytomir oblasts, aggregate data, 130 cases for 1990-1999 period)

Size of the tumour	Children		Adolescents		Young adults	
	T4	%	T4	%	T4	%
< = 1cm	3/7	42.9	0/2	-	0/1	-
1.1 - 2 cm	30/52	57.7	5/10	50.0	2/12	16.7
2.1 – 3 cm	10/11	90.9	1/2		4/9	44.4
3.1 – 4 cm	5/6	83.3	0/4	-	1/2	
4.1 – 5 cm	4/6	66.7	-	-	1/1	
5.1 – 6 cm	2/3	66.7	0/1	-	1/1	
> 6 cm	-				-	
Total	54/85	63.5	6/19	31.6	9/26	34.6

Table 9. Extra-thyroid spread (T4-category of TNM classification) and size of thyroid carcinomas in patients who were born in 1968-1985 (Kiev-city, aggregate data, 78 cases for 1990-1999 period)

Size of the tumour	Children		Adolescents		Young adults	
	T4	%	T4	%	T4	%
< = 1cm	1/1		0/2	-	0/4	-
1.1 - 2 cm	5/13	38.4	3/6	50.0	1/12	8.3
2.1 – 3 cm	3/9	33.3	2/5	40.0	1/7	14.3
3.1 – 4 cm	1/1		0/2	-	1/3	33.3
4.1 – 5 cm	3/3		1/1		1/2	
5.1 – 6 cm	-	-	0/1	-	1/1	
> 6 cm	2/2		2/2		1/1	
Total	15/29	51.7	8/19	42.1	6/30	20.0

Table 10. Extra-thyroid spread (T4-category of TNM classification) and size of thyroid carcinomas in patients who were born in 1968-1985 (Kiev, Chernigov, Zhytomir oblasts, and Kiev-city. aggregate data, 208 cases for 1990-1999)

Size of the tumour	Children		Adolescents		Young adults	
	T4	%	T4	%	T4	%
< = 1cm	4/8	50.0	0/4	-	0/5	-
1.1 - 2 cm	35/65	53.8	8/16	50.0	3/24	12.5
2.1 – 3 cm	13/20	65.0	3/7	42.9	5/16	31.3
3.1 – 4 cm	6/7	85.7	0/6	-	2/5	40.0
4.1 – 5 cm	7/9	77.8	1/1		2/3	66.7
5.1 – 6 cm	2/3	66.7	0/2	-	2/2	
> 6 cm	2/2		2/2		1/1	
Total	69/114	69.5	14/38	36.8	15/56	26.8

Table 11. Presence of the regional metastasis (N1a,b - category of TNM classification) and size of thyroid carcinomas in patients who were born in 1968-1985 (Kiev, Chernigov, Zhytomir oblasts, aggregate data, 130 cases for 1990-1999 period)

Size of the tumour	Children		Adolescents		Young adults	
	N	%	N	%	N	%
<= 1cm	0/7	-	0/2	-	0/1	-
1.1 - 2 cm	30/52	57.7	4/10	40.0	4/12	33.3
2.1 – 3 cm	8/11	72.7	1/2		4/9	44.4
3.1 – 4 cm	5/6	83.3	2/4	50.0	1/2	
4.1 – 5 cm	4/6	66.7	-	-	1/1	
5.1 – 6 cm	2/3	66.7	1/1		1/1	
> 6 cm	-	-			-	
Total	49/85	57.6	8/19	42.1	11/26	42.3

Table 12. Presence of the regional metastasis (N1a,b - category of TNM classification) and size of thyroid carcinomas in patients who were born in 1968-1985 (Kiev-city, aggregate data, 78 cases for 1990-1999 period)

Size of the tumour	Children		Adolescents		Young adults	
	N	%	N	%	N	%
< = 1 cm	1/1		0/2	-	0/4	-
1.1 - 2 cm	7/13	53.8	1/6	16.7	6/12	50.0
2.1 – 3 cm	3/9	33.3	1/5	20.0	4/7	57.1
3.1 – 4 cm	1/1		1/2		0/3	-
4.1 – 5 cm	3/3		1/1		1/2	
5.1 – 6 cm	-	-	1/1		0/1	-
> 6 cm	2/2		1/2		1/1	
Total	17/29	58.6	6/19	31.6	12/30	40.0

Table 13. Presence of the regional metastasis (N1a,b - category of TNM classification) and size of thyroid carcinomas in patients who were born in 1968-1985 (Kiev, Chernigov, Zhytomir oblasts, and Kiev-city, aggregate data, 208 cases for 1990-1999)

Size of the tumour	Children		Adolescents		Young adults	
	N	%	N	%	N	%
< = 1cm	1/8	12.5	0/4	-	0/5	-
1.1 - 2 cm	37/65	56.9	5/16	31.3	10/24	41.7
2.1 – 3 cm	11/20	55.0	2/7	28.6	8/16	50.0
3.1 – 4 cm	6/7	85.7	3/6	50.0	1/5	20.0
4.1 – 5 cm	7/9	77.8	1/1		2/3	66.7
5.1 – 6 cm	2/3	66.7	2/2		1/2	
> 6 cm	2/2		1/2		1/1	
Total	66/114	57.9	14/38	36.8	23/56	41.1