Appendix 8

Thyroid Cancer of Belarusians having been Exposed as Children or Adolescents as a Result of the Chernobyl Accident

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1. Introduction

Within post Chernobyl period (1986-2002) the majority of patients who were operated on for thyroid malignancies lived in Minsk region and Minsk city where the index of population density is higher than in other regions.

The current trends in incidence are revealed as follows:

- 1. By now childhood cases became rare, but the incidence is still enhanced as compared with pre Chernobyl period
- 2. Adolescent thyroid cancer incidence is gradually decreasing since 2001
- 3. The incidence index increases for the group of young adults

2. Patients and admissions

The study period includes time interval between June, 1, 1986 and December, 31, 2002. Within the observed period 1957 patients were enrolled into study. Of them 1917 (group I) were under 18 (1967 – 1986 years of birth) at the time of Chernobyl disaster (exposed or possibly exposed cases to ¹³¹I) and 40 pediatric patients were recognized as completely conformed to sporadic thyroid cancer (group II, 1987 – 1994 years of birth).

All patients enrolled into group I at the time of the accident lived in Belarus and were born before or at the time of the disaster. On the contrary, no one patient from the group II could be exposed to radiation. Those all were born after ¹³¹I decay.

Patients' data for the selected group I and group II are presented in table 1.

For the data obtained enrolled patients were predominantly females with the mean age between 18 and 19.

Group I consisted mostly of the patients who lived in Gomel and Brest regions of Belarus. Group II presented mainly the cases from Minsk-city.

Tumors spread and cancer pathology were assessed according to generally accepted TNM UICC and WHO pathological classification [1, annex 1].

Table 1

Variables	Group I	Group II	Total
Ι	II	III	IV
Total cases	1917 (100%)	40 (100%)	1957 (100%)
Gender: female	1314	28	1342
male	e 603	12	615
Age at Chernobyl			
min	-0.62*	-7.78	-7.78
max	x 18.99	-0.72	18.99
mear	n 7.5±5.88	-2.86±1.55	7.29 ± 6.00
under 5 years old	1 23 (1.2%)	not state	23 (1.2%)
from 5 to 10) 858 (44.8%)	not state	858 (43.8%)
from 10 to 1.	5 398 (20.8%)	not state	398 (20.3%)
from 15 to 20) 347 (18.1%)	not state	347 (17.7%)

Enrolled cases

Ι	II	III	IV
Age at therapy			
min	4.17	5.43	4.17
max	35.34	15.76	35.34
mean	18.69 ± 7.00	11.67±2.73	18.54 ± 7.01
under 5 years old	8 (0.4%)	0 (0.0%)	8 (0.4%)
from 5 to 10	158 (8.2%)	9 (22.5%)	167 (8.5%)
from 10 to 15	529 (27.6%)	26 (65.0%)	555 (28.4%)
from 15 to 20	487 (25.4%)	5 (12.5%)	492 (25.1%)
older than 20	735 (38.3%)	0 (0.0%)	735 (37.6%)
Regions of abode			
Brest	373 (19.5%)	7 (17.5%)	380 (19.4%)
Vitebsk	107 (5.6%)	2 (5.0%)	109 (5.6%)
Gomel	736 (38.4%)	8 (20.0%)	744 (38.0%)
Grodno	101 (5.3%)	2 (5.0%)	103 (5.3%)
Minsk	173 (9.0%)	4 (10.0%)	177 (9.0%)
Minsk-city	237 (12.4%)	12 (30.0%)	249 (12.7%)
Mogilev	190 (10.0%)	5 (13.0%)	195 (10.0%)

Continuation of table 1

Note: * in utero cases

3. Results

3.1. Pathological classification of available thyroid cancer cases after the Chernobyl accident

Papillary histology was the main pathological type of thyroid carcinoma in complete population of enrolled patients. Less common were follicular carcinomas proven in 82 (4.2%) cases. Other types presented by C-cell (medullary) and anaplastic (or undifferentiated) cancer were diagnosed only in 17 (0.9%) and 2 (0.1%) patients respectively.

There was no statistically significant difference in the structure of pathological types between group I and group II (Fig.1).

Three of 17 medullary thyroid carcinomas had genetic predisposition (1 MEN2B and 2 MEN2A syndromes). Other 14 cases of this tumor could be assessed as sporadic form of the disease.

Two anaplastic carcinomas developed in patients with prolonged history of thyroid nodules. It is necessary to emphasize that no one case of undifferentiated carcinoma was diagnosed in patients under 15 years old at therapy.

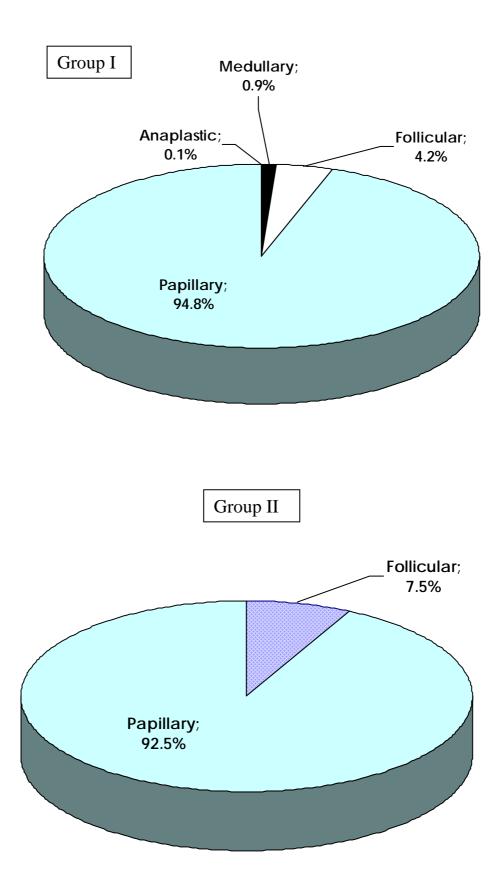


Fig.1 Distribution on tumor histology for group I and II

3.2. Analysis of time, age and gender for different types of thyroid tumors

Per year patients' distribution of therapy revealed no significant difference for follicular, medullary and anaplastic carcinomas in both groups of the patients. The mentioned pathological types were much rarer than predominant papillary cancer.

In exposed group the gradual increase of annual cases became evident since 1990, most distinct in females. There is no clear enhancing of thyroid carcinomas cases in group II before 2000. It is essential that the last year of study demonstrate unexpectedly enhanced level of female thyroid carcinomas (table 2).

Table 2

Year at		Pathology								
therapy *	Pap	illary	Follicular		Medullary		Anaj	plastic		
	males	females	males	females	males	females	males	females		
	Group I									
1986	1	2	0	0	0	0	0	0		
1987	2	9	0	0	0	0	0	0		
1988	4	3	1	2	0	0	0	0		
1989	5	7	0	2	0	0	0	0		
1990	16	16	2	3	1	0	0	0		
1991	20	45	3	8	0	0	0	1		
1992	41	51	1	2	0	2	0	0		
1993	29	87	0	0	0	1	0	0		
1994	46	96	2	4	0	1	0	1		
1995	44	91	4	4	0	0	0	0		
1996	41	106	1	5	1	3	0	0		
1997	50	102	0	3	0	0	0	0		
1998	48	111	4	1	1	2	0	0		
1999	63	132	2	8	2	0	0	0		
2000	53	116	1	5	0	0	0	0		
2001	56	116	1	2	0	1	0	0		
2002	55	155	1	7	0	2	0	0		
Total	574	1245	23	56	5	12	0	2		

Distribution on pathology and gender in dependence on year of therapy

Continuation of table 2

	Group II										
1994	1	0	0	0	0	0	0	0			
1995	0	1	0	0	0	0	0	0			
1996	1	0	0	0	0	0	0	0			
1997	0	1	0	0	0	0	0	0			
1998	1	0	0	0	0	0	0	0			
1999	2	1	0	0	0	0	0	0			
2000	3	6	0	2	0	0	0	0			
2001	2	5	0	1	0	0	0	0			
2002	2	11	0	0	0	0	0	0			
Total	12	25	0	3	0	0	0	0			

Note: * Four patients refused from therapy. The pathological diagnosis for them was based on the results of fine needle aspiration biopsy but not on histological study of removed thyroid tissue.

The distribution of thyroid carcinoma cases per year of therapy represents a certain interest. Within the observed period only 8 patients were younger than 5. All of them have been diagnosed and underwent surgery between 1987 and 1991. Later no one patient had thyroid malignancy.

According to IARC data based on the analysis of world cancer registries there were only four officially accepted cases of thyroid carcinomas in children aged from 0 to 4 for two decades or even more [3]. Belarus was never included into these calculations.

The second point of interest is that patients aged between 5 and 10 were significantly frequent at the beginning of 90-s. The majority of cases for both groups were for the age group from 10 to 15. Since 1995 thyroid carcinomas became relatively frequent at age groups older than 15 in adolescents and young adults.

The evidence of shift towards older ages for papillary carcinomas is presented in table 3.

The data received for follicular, medullary and anaplastic carcinomas look less systematic. The majority of follicular and medullary carcinomas were diagnosed for the age group between 10 and 25 with no evident peeks per year (tables 4 and 5).

Year at	Patients' age (years old)							
therapy	<5	5 - 10	10 -15	15-20	20-25	25-30	30-35	
			Group	ρI				
1986	0	1	0	2	0	0	0	
1987	1	0	2	8	0	0	0	
1988	0	2	3	2	0	0	0	
1989	1	1	6	3	1	0	0	
1990	5	16	6	3	2	0	0	
1991	1	28	20	9	7	0	0	
1992	0	29	36	9	18	0	0	
1993	0	38	42	21	13	2	0	
1994	0	24	53	28	27	10	0	
1995	0	11	71	27	16	10	0	
1996	0	1	79	23	21	23	0	
1997	0	0	64	34	18	32	4	
1998	0	0	46	39	34	34	6	
1999	0	0	46	52	33	43	22	
2000	0	0	21	63	19	38	27	
2001	0	0	4	78	30	31	29	
2002	0	0	0	69	41	41	59	
Total	8	151	499	470	280	264	147	
			Group	II				
1994	0	1	0	0	0	0	0	
1995	0	1	0	0	0	0	0	
`996	0	1	0	0	0	0	0	
1997	0	1	0	0	0	0	0	
1998	0	0	1	0	0	0	0	
1999	0	1	2	0	0	0	0	
2000	0	1	8	0	0	0	0	
2001	0	1	6	0	0	0	0	
2002	0	1	7	5	0	0	0	
Total	0	8	24	5	0	0	0	

Age distribution for **papillary** thyroid carcinomas

Year at			Pat	ients' ag	e (years	old)					
therapy	<5	5 - 10	10 - 15	15-20	20-25	25-30	30-35	+35			
	Group I										
1988	0	0	2	1	0	0	0	0			
1989	0	0	1	1	0	0	0	0			
1990	0	2	0	0	3	0	0	0			
1991	0	3	5	2	1	0	0	0			
1992	0	0	1	1	1	0	0	0			
1994	0	1	1	1	0	3	0	0			
1995	0	1	5	0	1	1	0	0			
1996	0	0	2	0	4	1	0	0			
1997	0	0	1	0	1	0	0	0			
1998	0	0	3	1	0	0	1	0			
1999	0	0	1	3	0	5	1	0			
2000	0	0	1	3	0	2	0	0			
2001	0	0	0	2	0	0	0	1			
2002	0	0	0	1	1	3	2	1			
Total	0	7	23	16	12	15	4	2			
			Gr	oup II							
2000	0	1	1	0	0	0	0	0			
2001	0	0	1	0	0	0	0	0			
Total	0	1	2	0	0	0	0	0			

Age distribution for **follicular** thyroid carcinomas

Table 5

Age distribution for **medullary** thyroid carcinomas

Year at	Patients' age (years old)									
therapy	<5	5 - 10	10 -15	15-20	20-25	25-30	30-35	+35		
	Group I									
1990	0	0	0	1	0	0	0	0		
1992	0	0	1	0	1	0	0	0		
1993	0	0	0	0	1	0	0	0		
1994	0	0	0	0	0	1	0	0		
1996	0	0	1	2	1	0	0	0		
1997	0	0	0	0	0	0	0	0		
1998	0	0	1	1	1	0	0	0		
1999	0	0	0	0	2	0	0	0		
2001	0	0	0	0	1	0	0	0		
2002	0	0	0	1	0	0	1	0		
Total	0	0	3	5	7	1	1	0		

3.3. Tabulation of thyroid cancer cases

Thyroid cancer cases (both genders)

Veenef	Regions of Belarus								
Year of surgery	Brest	Vitebsk	Gomel	Grodno	Minsk	Minsk city	Mogilev		
			Gro	oup I					
1986	0	0	0	1	0	0	0		
1987	0	0	1	0	1	0	0		
1988	0	0	1	2	1	1	0		
1989	0	0	2	1	1	0	1		
1990	5	0	8	0	3	1	2		
1991	4	3	8	2	2	3	1		
1992	8	3	18	4	4	4	1		
1993	10	0	14	0	1	1	3		
1994	11	1	19	6	7	2	2		
1995	9	0	25	4	3	4	3		
1996	13	1	15	2	5	7	1		
1997	6	2	26	3	9	3	1		
1998	16	1	22	1	1	8	4		
1999	13	2	34	4	3	7	4		
2000	15	1	24	1	3	6	4		
2001	10	0	28	2	4	5	8		
2002	17	4	17	2	5	7	4		
Total	137	18	262	35	53	59	39		
			Gro	up II					
1994	0	0	0	0	0	0	1		
1995	0	0	0	0	0	0	0		
1996	0	0	0	0	0	1	0		
1997	0	0	0	0	0	0	0		
1998	0	0	0	0	0	1	0		
1999	0	0	0	0	0	2	0		
2000	1	0	1	0	0	1	0		
2001	0	1	0	0	0	0	1		
2002	0	0	1	0	0	1	0		
Total	1	1	2	0	0	6	2		

Veenef			Reg	ions of Bel	arus		
Year of surgery	Brest	Vitebsk	Gomel	Grodno	Minsk	Minsk city	Mogilev
			Gro	up I			
1986	0	1	0	0	1	0	0
1987	0	2	3	1	1	1	1
1988	1	0	2	0	1	1	0
1989	0	1	4	1	3	0	0
1990	5	2	6	1	0	5	0
1991	3	2	33	3	5	7	1
1992	12	6	17	7	7	4	2
1993	18	3	30	8	9	15	5
1994	19	5	40	5	8	14	11
1995	23	6	37	3	4	15	7
1996	30	5	46	5	7	13	7
1997	15	6	43	6	8	17	10
1998	23	5	30	7	11	28	10
1999	24	11	46	2	16	15	26
2000	18	5	45	6	11	11	25
2001	10	10	55	4	12	10	18
2002	35	19	37	7	16	22	28
Total	236	89	474	66	120	178	151
			Gro	up II			
1994	0	0	0	0	0	0	0
1995	0	0	1	0	0	0	0
1996	0	0	0	0	0	0	0
1997	1	0	0	0	0	0	0
1998	0	0	0	0	0	0	0
1999	0	0	0	0	1	0	0
2000	0	0	4	1	0	2	1
2001	2	0	0	1	1	1	1
2002	3	1	1	0	2	3	1
Total	6	1	6	2	4	6	3

Thyroid cancer cases (females)

Thyroid cancer	cases divided	by year of birth	(group I)
ingioid cuncer		by your or on an	(Group I)

Year of	Gender				Region				Total
birth	Gender	Brest	Vitebsk	Gomel	Grodno	Minsk	Minsk city	Mogilev	Total
1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
	Males	0	1	1	0	0	2	1	5
1967	Females	4	1	5	2	7	6	6	31
	Both	4	2	6	2	7	8	7	36 *
	Males	2	0	5	1	3	1	3	15
1968	Females	6	5	10	3	7	17	21	69
	Both	8	5	15	4	10	18	24	84
	Males	5	2	4	2	3	3	5	24
1969	Females	3	7	17	2	14	13	7	63
	Both	8	9	21	4	17	16	12	87
	Males	4	1	6	1	1	4	0	17
1970	Females	11	9	17	4	8	10	6	65
	Both	15	10	23	5	9	14	6	82
1971	Males	5	1	4	1	1	2	1	15
	Females	10	8	23	2	6	9	8	66
	Both	15	9	27	3	7	11	9	81
	Males	2	1	4	1	1	6	3	18
1972	Females	9	10	13	5	4	11	11	63
	Both	11	11	17	6	5	17	14	81
	Males	4	0	6	1	1	0	0	12
1973	Females	8	9	11	3	5	7	6	49
	Both	12	9	17	4	6	7	6	61
	Males	4	0	8	1	2	2	2	19
1974	Females	6	6	11	3	3	10	9	48
	Both	10	6	19	4	5	12	11	67
	Males	1	0	8	1	1	1	1	13
1975	Females	9	6	13	3	4	5	6	46
	Both	10	6	21	4	5	6	7	59
	Males	5	2	11	3	5	3	1	30
1976	Females	2	1	12	1	4	4	6	30
	Both	7	3	23	4	9	7	7	60

Continuation

1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
	Males	0	2	12	1	3	5	0	23
1977	Females	7	2	18	2	4	5	3	41
	Both	7	4	30	3	7	10	3	64
1978	Males	7	1	21	1	0	1	3	34
	Females	6	4	21	3	6	6	4	50
	Both	13	5	42	4	6	7	7	84
	Males	3	1	5	3	3	2	2	19
1979	Females	12	4	19	6	4	8	6	59
	Both	15	5	24	9	7	10	8	78
	Males	7	2	15	1	1	5	3	34
1980	Females	12	4	30	3	1	8	8	66
	Both	19	6	45	4	2	13	11	100
	Males	10	1	18	2	1	2	3	37
1981	Females	10	0	29	4	5	8	10	66
	Both	20	1	47	6	6	10	13	103
	Males	6	1	24	0	3	2	1	37
1982	Females	20	1	34	4	4	8	5	76
	Both	26	2	58	4	7	10	6	113
	Males	14	0	33	3	7	5	1	63
1983	Females	26	3	53	1	7	18	3	111
	Both	40	3	86	4	14	23	4	174
	Males	21	1	37	7	4	6	5	81
1984	Females	30	2	54	5	4	11	12	118
1704	Both	51	3	91	12	8	17	17	199
	Males	29	1	34	4	12	5	3	88
1985	Females	38	4	62	9	14	11	10	148
	Both	67	5	96	13	26	16	13	236
	Males	8	0	6	1	1	2	1	19
1986	Females	7	3	22	1	9	3	4	49
	Both	15	3	28	2	10	5	5	68
	Males	137	18	262	35	53	59	39	603
Σ	Females	236	89	474	66	120	178	151	1314
	Both	373	107	736	101	173	237	190	1917

Note: * patients born between June, 1967 and December, 1967 were 18,3 – 18,9 years old at the time of Chernobyl accident.

Year of Region Gender Total birth Brest Vitebsk Gomel Grodno Minsk Minsk city Mogilev Males Females Both Males Σ Females Both

Thyroid cancer cases divided by year of birth (group II)

3.4. Analysis of available data of operated thyroid tumors, classification and size

The majority of enrolled cases could be assessed as primary microcarcinomas. Forty per cent of the patients had the tumors equal or less than 1 cm in largest measurement.

Despite two third of cases at therapy had positive lymph nodal involvement. This required extended surgery and could be considered the index of aggressive nature of the disease in young patients.

There was no statistical difference in comparison between two selected groups of thyroid cancer patients. Extrathyroidal growth (T4) was diagnosed in 13.1% of cases in group I and 7.5% in group II. That means that sporadic and radiogenic carcinomas have similar behavior, e.g. invasive and metastatic potential (tabl. 11 and 12).

pTNM		NO	N1a	N1b	Total	(%)
T1a		306	205	59	570	29,7
	M1	1	0	1	2	0,1
T1b		44	26	29	99	5,2
	M1	0	0	1	1	0,1
T2a		265	292	215	772	40,3
	M1	0	1	5	6	0,3
T2b		23	52	87	162	8,5
	M1	1	2	2	5	0,3
T3a		13	5	7	25	1,3
	M1	0	0	0	0	0,0
T3b		0	1	6	7	0,4
	M1	0	0	0	0	0,0
T4a		21	78	81	180	9,4
	M1	0	3	7	10	0,5
T4b		3	14	54	71	3,7
	M1	0	1	6	7	0,4
Total		677	680	560	1917	100,0
(%)		35,3	35,5	29,2	100,0	

TNM UICC extent for patients from the group I

pTNM		N0	N1a	N1b	Total	(%)
T1a		1	4	3	8	20,0
	M1	0	0	0	0	0,0
T1b		0	0	1	1	2,5
	M1	0	0	0	0	0,0
T2a		8	8	8	24	60,0
	M1	0	0	0	0	0,0
T2b		0	0	2	2	5,0
	M1	0	0	0	0	0,0
T3a		1	0	0	1	2,5
	M1	0	0	0	0	0,0
T3b		0	0	0	0	0,0
	M1	0	0	0	0	0,0
T4a		0	0	1	1	2,5
	M1	0	0	1	1	2,5
T4b		0	0	2	2	5,0
	M1	0	0	0	0	0,0
Total		10	12	18	40	100,0
(%)		25,0	30,0	45,0	100,0	

TNM UICC extent for patients from the group II

Table 13

Size (largest measurement) of thyroid carcinomas (groups I and II)

Year of therapy	Size (cm)									
	<=1	1.1 – 2	2.1 – 3	3.1 – 4	4.1 – 5	5.1 – 6	>6	Total		
Papillary carcinomas										
1986	1	1	1	0	0	0	0	3		
1987	2	4	4	0	0	0	0	10		
1988	4	1	1	1	0	0	0	7		
1989	1	6	3	0	1	0	0	11		
1990	6	14	8	3	0	0	0	31		
1991	24	24	6	4	0	2	0	60		
1992	24	36	14	5	2	0	2	83		
1993	42	38	17	10	1	0	0	108		
1994	61	45	16	6	5	0	0	133		
1995	50	51	16	7	5	0	0	129		
1996	54	57	20	6	0	3	0	140		
1997	55	66	17	5	1	0	1	145		
1998	55	59	22	5	2	0	0	143		
1999	54	90	30	6	4	3	0	187		
2000	72	67	19	5	0	1	0	164		
2001	83	66	12	11	0	0	1	173		
2002	93	86	24	7	0	0	1	211		
Total	681	711	230	81	21	9	5	1738*		

Year of therapy	Size (cm)									
	<=1	1.1 – 2	2.1 – 3	3.1 – 4	4.1 – 5	5.1 – 6	>6	Total		
Follicular carcinomas										
1988	0	1	2	0	0	0	0	3		
1989	1	1	0	0	0	0	0	2		
1990	3	2	0	0	0	0	0	5		
1991	3	6	0	0	0	0	0	9		
1992	1	1	0	0	0	0	0	2		
1994	3	1	1	0	0	0	0	5		
1995	3	4	0	0	1	0	0	8		
1996	2	3	0	1	0	1	0	7		
1997	1	0	0	0	0	0	0	1		
1998	0	1	1	0	2	0	0	4		
1999	5	2	2	1	0	0	0	10		
2000	1	3	1	0	1	0	0	6		
2001	0	2	1	0	1	0	0	4		
2002	0	2	2	2	0	0	0	6		
Total	23	29	10	4	5	1	0	72**		
			Medul	lary carci	nomas					
1990	0	1	0	0	0	0	0	1		
1996	1	2	1	0	0	0	0	4		
1998	1	2	0	0	0	0	0	3		
1992	0	1	0	0	1	0	0	2		
1999	0	1	1	0	0	0	0	2		
2001	0	1	0	0	0	0	0	1		
2002	0	1	0	1	0	0	0	2		
1993	0	0	0	0	1	0	0	1		
1994	0	0	1	0	0	0	0	1		
Total	2	9	3	1	2	0	0	17		
Anaplastic carcinomas										
1991	0	1	0	0	0	0	0	1		
1994	1	0	0	0	0	0	0	1		
Total	1	1	0	0	0	0	0	2		

Continuation of table 13

Note: * In 81 cases of papillary and ** 7 follicular carcinomas the largest tumor size was not detected. These patients underwent repeated surgery for relapses after primary procedures in regional hospitals.

ANNEX 1

UNIFOCAL CARCINOMAS

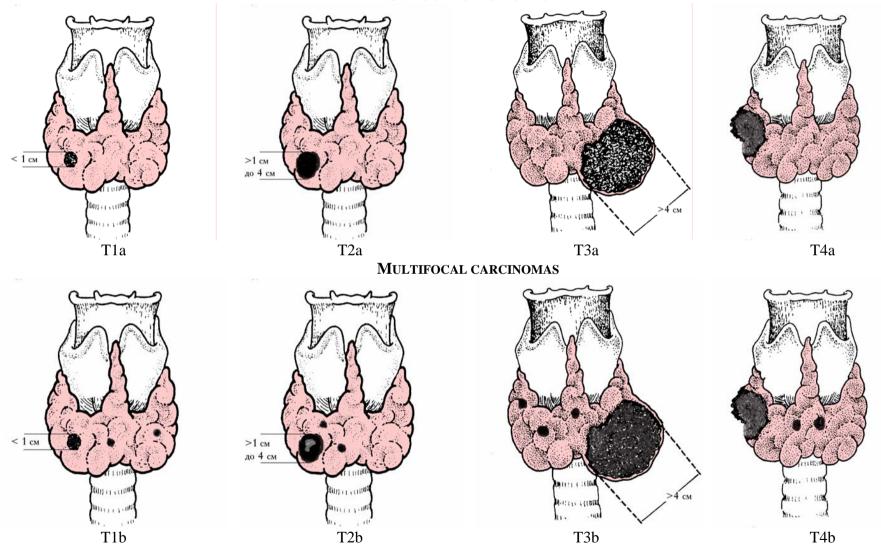
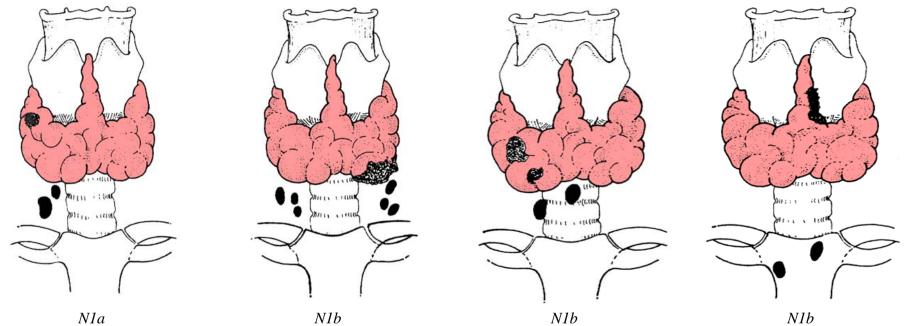


Fig.2 "T" criteria for TNM (UICC)



N1a (ipsilateral positive neck lymph nodes)

N1b (bilateral positive neck lymph nodes)

N1b (positive central lymph nodes)

NIb (positive mediastinal lymph nodes)

Fig.3 "N" criteria for TNM (UICC)

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