

Malignant melanoma in children aged 0-12. Review of 289 cases of the literature.

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Summary

The rarity of prepubertal melanoma prevents a statistical evaluation of data and a comparison with the data of melanoma in adults. We tried to fill this gap by reviewing 289 cases published in the relevant literature of the last century. Although taking into account their understandable lacunas, these data allowed us to do some considerations. The distribution of cases per year in the first 12 years is uniform. The female is slightly more frequently -54.7%- affected by malignant melanoma as compared with the male even at this prepubertal age. The site distribution in the two sexes is different as compared with adults. In females the trunk is more frequently affected -41.56%- than in males -30.71%-. Moreover, the lower limb is almost equally affected in females -25.32%- and in males -26.77%-. The head is more significantly -27.76%- affected in the prepubertal age as compared with adults -16.63%-. The most important favoring factor at this age -present in one third of the cases- is congenital melanocytic nevus, especially the giant type. The number of died children is significantly affected by the presence of a giant congenital melanocytic nevus -70.15%-, whereas it is not influenced by the age and the sex -37.40% in males and 39.24% in females-. The number of died children is also influenced by the presence of adenopathy -63.40% versus 6.17% in cases without adenopathy-.

Key words

Melanoma in children, giant melanocytic nevus, site of melanoma in children.

Even a skilled and long-living pediatric dermatologist, after a third of century activity, is usually not able to collect a number of cases of malignant melanoma, which could enable a statistical evaluation and a comparison with the large data available in adults. To try of filling this gap we collected 289 cases of melanoma in children aged 0 to 12 years in the relevant literature.

Although taking into account the diagnostic problems already underlined by all the Authors facing this topic (15) we compared their clinical features with those ones of adults, which are available in many series, often overcoming thousand cases, as that one collected by us in the years 1975-2000 in Bari. The latter is reported on page 143 of this issue.

Material and methods

The material consists of 289 cases of the literature (131 males and 158 females), affected by malignant melanoma, whose age ranged between 0 and 12 years. Five cases transmitted through the placenta were excluded by this series and reported on page 137 of this issue. Also the cases included in more or less large series, but lacking the clinical features of the individual cases were excluded and their comprehensive data were compared with those ones of the actual series. The cases with the relevant clinical features and pathological findings, when available, are listed as follows. At the end of this series are listed 7 cases recently reported in the relevant literature.

289 CASES OF MELANOMA OF THE LITERATURE, AGED 0-12 YEARS.

Author, year	Age (yrs), sex	Site	Predisposing factors	Type	Thickness (mm)	Clark's level	Ulceration	Extension	Follow-up (months)	Treatment	Out-come
Bolgert, 1962	Newborn, M	Trunk	GCN	Nodular	Unknown	Unknown	YES	Local recurrence	12	Removal, radioth.	A
Baader, 1992	Newborn, F	Back, buttocks	GCN	Unknown	Unknown	Unknown	Unknown	Localized	36	Removal	A
Stromberg, 1979	Newborn, M	Scalp	GCN	Multiple foci	Unknown	Unknown	NO	Bone destruction	6	Removal	A
Song, 1990	Newborn, M	Scalp	Unknown	Unknown	Unknown	Unknown	NO	Localized	2 hours	None	D
Hayes, 1984	Newborn, M	Leg	NO	Unknown	>5.0	V	Unknown	Lymph nodes, liver	70	Remov., chemot.	A
Stromberg, 1979	Newborn, M	Scalp	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	216	Removal, limphaden.	A
19), 100), 1987	Newborn, M	Back	GCN	Unknown	Unknown	Unknown	Unknown	Diffuse, placenta	17 hours	None	D
Oldhoff, 1968	Newborn, M	Thigh	Multiple GCN	Unknown	Unknown	Unknown	YES	Local recurrence	120	Amputation	A
Pratt, 1981	Newborn, M	Scalp	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes, bone, abdomen	23	Unknown	D
Prose, 1987	Newborn, F	Abdomen	Unknown	Unknown	9.0	V	YES	Localized	12	Removal	A
32), 1998	19 days, F	Back	GCN	Unknown	Unknown	Unknown	YES	Diffuse metastases	24	Unknown	D
Boddie, 1987	Newborn, F	Hand	None	Nodular	5.0	IV	YES	Lymph nodes, lung	114	Removal, chemot., radioth.	A
Conu, 1971	7 days, F	Foot	Unknown	Unknown	3.5 cm	Unknown	Unknown	Lymph nodes	Unknown	None	Unkn.
Ishii, 1991	Newborn, M	Thigh	None	Unknown	Unknown	Unknown	Unknown	Diffuse metastases	18	Chemotherapy	D
Sweet, 1941	Newborn, M	Genitalia	GCN	Unknown	Unknown	Unknown	Unknown	Encephalic metastas.	17 days	None	D
Pack, 1952	Newborn, F	Back	GCN, adenocr. kid.	Multiple	Unknown	Unknown	NO	Encephalic metastas.	192	Unknown	D
Ahmed, 1979	2 weeks, M	Trunk	GCN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	1	Unknown	D
Koyama, 1996	Newborn, F	Scalp	GCN	Nodular	Unknown	Unknown	Unknown	Localized	Unknown	Rhabdom. diff.	A
Naraysingh 1986	Newborn, M	Back	GCN	Unknown	Unknown	Unknown	Unknown	Liver	1,5	Skin graft, lymph. transf.	D
Lyall, 1967	Newborn, M	Hand	None	Unknown	Unknown	Unknown	Unknown	Lymph nodes	30	Amputation	A
Hendrickson, 1981	2 months, F	Back	GCN	Nodular, multiple	Unknown	Unknown	NO	Localized, minimal deviation	6	Removal	A
Moss, 1986	3 months, F	Forearm	Unknown	Unknown	1.5	IV	Unknown	Unknown	84	Unknown	A
Scalzo, 1997	3 months, M	Scalp	Unknown	Borderline	Unknown	Unknown	Unknown	Unknown	49	Unknown	A
Coe, 1925	3 months, F	Scalp	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	2	Unknown	D
Hendrickson, 1981	3 months, M	Scalp	GCN	Unknown	Unknown	Unknown	Unknown	Localized	18	Unknown	A

Author, year	Age (yrs), sex	Site	Predisposing factors	Type	Thickness (mm)	Clark's level	Ulceration	Extension	Follow-up (months)	Treatment	Outcome
Trozak, 1975	4 mts, M	Cheek	None	Unknown	Unknown	IV	Unknown	Lymph nodes	240	Unknown	A
Workman, '92	4 mts, F	Buttocks	GCN	Nodular	Unknown	Unknown	Unknown	Localized	60	Unknown	A
Wu, 1997	4 mts, M	Trunk	GCN	Unknown	Unknown	Unknown	Unknown	Abdomen metastases, brain	1	Unknown	D
Hendrickson, 1981	7 mts, M	Scalp, cheek	GCN	Unknown	Unknown	Unknown	Unknown	Local recurrence	29	Removal	A
Ruiz-Maldonado, 1992	8 mts, F (p.c.)	Trunk	GCN	Unknown	Unknown	Unknown	Unknown	Diffuse metastases	Unknown	Removal chemotherapy	D
Wu, 1997	9 mts, F	Arm, face, trunk, buttocks	GCN	Unknown	Unknown	Unknown	Unknown	Lymph nodes, lung, pleura, pelvis	12	Removal, chemotherapy	D
Quaba, 1986	10 mts, F	Trunk	GCN	Nodular	Unknown	Unknown	Unknown	Diffuse metastases	12	Unknown	D
Kato, 1989	1, F	Foot	Nail pigmentat. at 6 mts.	In situ	Unknown	Unknown	Unknown	Localized	24	Removal	A
Spatz, 1996	1, M	Scalp	GCN	Unknown	1.8	III	NO	Localized	60	Unknown	A
Spatz, 1996	1, M	Scalp	GCN	Superficial	4.8	III	YES	Localized	78	Unknown	A
Strojan, 2000	15 mts, F	Scalp	GCN	Nodular	27	IV	YES	Lymph nodes, lung	5	Removal	D
Brandt, 1956	14 mts, M	Trunk	GCN	Unknown	Unknown	Unknown	Unknown	Arm metastases, pelvis	8	Removal, radiotherapy	D
Penman, 1971	15 mts, M	Scalp	Multiple CN	Unknown	Unknown	Unknown	Unknown	Lymph nodes, bone	13	Remov., radiot., chemotherapy	D
Mensi, 1966	16 mts, M	Back	GCN	Unknown	Unknown	Unknown	Unknown	Diffuse	20 days	None	D
Brandt, 1956	14 mts, M	Scalp	GCN	Unknown	Unknown	Unknown	Unknown	Lung metastases	6	Removal, radiot.	D
Schultz, 1961	17 mts, F	Back, neck, shoulder, chest	GCN	Unknown	Unknown	Unknown	Unknown	Diffuse metastases	10	Unknown	D
35), '55	18 mts	Back	GCN	Unknown	Unknown	IV	NO	Lymph nodes, metastases	6	Chemotherapy	D
54), 74, 48), 81	F										
Flemming, 1985	21 mts, M	Cheek	Acquired nevus		4.3	V	YES	Localized	24	Removal	A
Chun, 1993	22 mts, M	Foot	CN	Unknown	Unknown	Unknown	Unknown	Localized	72	Removal	A
Bartoli, 1994	2, F	Shoulder	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	62	Remov., lymphaden	A
Bartoli, 1994	2, M	Leg	Unknown	Unknown	Unknown	Unknown	Unknown	Multiple metastases	4	Lymphaden. chemot.	D
Ruiz-Maldonado, 1992	2, F (p.c.)	Scalp	GCN	Unknown	Unknown	Unknown	Unknown	Diffuse metastases	24	Removal, chemotherapy	D
46), '96	2, F	Eyelid	Unknown	Nodular	5.6	Unknown	Unknown	Unknown	10	Removal	A
Spatz, 1996	2, F	Scalp	NO	Unknown	3	IV	YES	Unknown	24	Unknown	A
Barnhill, 1995	2, F	Arm	NO	Unknown	7.85	IV	Unknown	Lymph nodes	36	Unknown	VM
Kato, 1989	2, F	Hand	Nail pigmentat. at 1 yrs.	In situ	Unknown	Unknown	NO	Localized	24	Removal	A
Malec, 1977	2, F	Perineal	GCN trunk	Nodular, buttocks	Unknown	Unknown	NO	Diffuse metastases	14	Removal	D
Saksela, 1968	2, F	Foot	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	120	Remov., radioth. lymphaden.	A
Wu, 1997	2, F	Plantar surfi big toe	NO	Unknown	1.5	Unknown	Unknown	Localized	137	Removal	A

Author, year	Age (yrs), sex	Site	Predisposing factors	Type	Thickness (mm)	Clark's level	Ulceration	Extension	Follow-up (months)	Treatment	Outcome
46), '96	2, M	Cheek	Unknown	Nodular	3.7	Unknown	Unknown	Localized	60	Removal	A
Skov-Jensen, 1966	2, M	Thigh	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	60	Removal, radiotherapy	A
Vennin, 1985	2, M	Trunk	NCG	Unknown	Unknown	Unknown	Unknown	Lymph nodes, pleura	3	Lymphaden., chemotherapy	D
Fish, 1966	2, M	Trunk	NCG	Unknown	Unknown	Unknown	NO	Lymph nodes	2	Remov., lymphad., chemotherapy	D
Padilla, 1988	2, F	Groin	NCG	Unknown	2.5 cm	V	YES	Lymph nodes, liver	13	Remov., chemot., interferon	D
Williams, 1954	2, F	Arm	GCN	Unknown	Unknown	Unknown	Unknown	Metastases	8	Unknown	D
McGovern, '63	2, M	Cheek	Unknown	Unknown	Unknown	Unknown	Unknown	Localized	48	Unknown	A
Pratt, 1981	2, M	Face	Unknown	Unknown	Unknown	Unknown	Unknown	Localized	102	Remov., radioth.	A
Hendrix, 1954	2, M	Lumbo-sacr.	GCN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	3	Removal	D
Yagawa, 1955	2, F	Back	GCN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	7	Unknown	D
Lartigau, 1995	2,3/M	Knee	Unknown	Unknown	0.85	V	Unknown	Lymph nodes	267	Removal	A
Truax, 1953	2,5 M	Scalp	GCN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	12	Removal, lymphaden.	D
46), '96	3, F	Arm	Unknown	CN	7.3	Unknown	Unknown	Unknown	42	Removal	A
46), '96	3, F	Cheek	Unknown	Nodular	7.8	Unknown	Unknown	Lymph nodes	18	Removal	A
46), '96	3, F	Buttock	Non det	Unknown	6.7	Unknown	Unknown	Unknown	48	Removal	A
46), '96	3, F	Cheek	Unknown	Nodular	4.0	Unknown	Unknown	Unknown	18	Removal	A
Barnhill, 1995	3, F	Hand	NO	Unknown	2.5	IV	Unknown	Unknown	Unknown	Unknown	LFU
Lerman, 1970	3, F	Scalp	GCN	Nodular	Unknown	Unknown	YES	Diffuse metastases	15	Removal, lymphaden.	D
McGovern, '63	3, F	Back	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	48	Unknown	A
Lisboa, 1961	3, F	Back	GCN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	36	Unknown	D
Forbus, 1952	3, F	Back, buttock	GCN	Unknown	Unknown	Unknown	YES	Brain metastases	4	Unknown	D
Barnhill, 1995	3, M	Face	XP	Unknown	0.18	II	Unknown	Localized	4	Unknown	A
Vennin, 1985	3, M	Buttock	GCN	Unknown	Unknown	Unknown	Unknown	Groin metastases	6	Chemotherapy	D
Hayes, 1984	3, F	Trunk	GCN	Unknown	Unknown	IV	Unknown	Lymph nodes, bone m.	10	Remov., chemot.	D
Patton, 1963	3, M	Back	GCN	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	A
18), 1965	3, F	Back	GCN	Unknown	Unknown	Unknown	Unknown	Unknown	6	Unknown	D
Keall, 1981	3, F	Scalp	CN	Unknown	Unknown	Unknown	Unknown	Lymph nodes bone marrow, liver	28	Remov. lymphad., chemotherapy	D
Novakovic, '95	3, F	Unknown	Dyspl. nevus	In situ	Unknown	Unknown	Unknown	Localized	104	Unknown	A
Russo, 1947	3, F	Knee	Unknown	Unknown	Unknown	II	YES	Lymph nodes	60	Radiotherapy	A
Kiryu, 1998	3, F	Hand	Unknown	In situ	Unknown	Unknown	Unknown	Unknown	180	Removal	A
Williams, 1954	3,5 F	Trunk, neck, arm	GCN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	20	Unknown	D
Spatz, 1996	4, F	Cheek	XP	Superfic.	0.23	II	NO	Localized	2	Unknown	A
Spatz, 1996	4, F	Scalp	XP	Superfic.	0.2	II	NO	Localized	2	Unknown	A
Barnhill, 1995	4, F	Scalp	NO	Unknown	15.0	V	Unknown	Diffuse metastases	5	Unknown	D

Author, year	Age (yrs), sex	Site	Predisposing factors	Type	Thickness (mm)	Clark's level	Ulceration	Extension	Follow-up (months)	Treatment	Outcome
Barnhill, 1995	4, M	Scalp	NO	Unknown	5.4	V	Unknown	Metastases	12	Unknown	D
Barnhill, 1995	4, F	Foot	NO	Unknown	Unknown	I	Unknown	Localized	12	Unknown	A
Barnhill, 1995	4, F	Thigh	NO	Unknown	5.2	V	Unknown	Localized	192	Unknown	A
Barnhill, 1995	4, F	Buttocks	NO	Unknown	5.72	V	Unknown	Localized	1	Unknown	A
Allen, 1953	4, F	Neck	NO	Unknown	Unknown	Unknown	Unknown	Lymph nodes	240	Removal	A
Lerman, 1970											
Roth, 1990	4, F	Thigh	NC	Superficial	0.52	III	NO	Localized	36	Removal	A
Tate, 1993	4, F	Trunk	GCN	Unknown	Unknown	Unknown	Unknown	Brain	4	Removal, chemo-radiother.	D
46), 1996	4, M	Cheek	Unknown	Nodular	3.4	Unknown	Unknown	Unknown	33	Removal	A
46), 1996	4, M	Thigh	Unknown	Nodular	5.4	Unknown	Unknown	Unknown	60	Removal	A
Kato, 1989	4, M	Hand	Nail pigmentat.	In situ	Unknown	Unknown	NO	Localized	24	Removal	A
			at 1 year								
Poore, 1954	4, M	Mouth	CA adreno-cortical	Nodular	Unknown	Unknown	Unknown	Diffuse metastases	34	Remov., radioth., estrogens	D
Lerman, 1970											
Kaplan, 1974	4, M	Scalp	Giant cong. blue nevus	Unknown	Unknown	Unknown	Unknown	Diffuse metastases	72	Removal	D
Silverberg, '71											
Dobson, 1955	4, M	Elbow	Unknown	Unknown	Unknown	Subcutan.	YES	Lymph nodes, local rec.	112	Remov., radioth.	A
Montgomery, 58	4, M	Cheek	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	48	Unknown	D
Wu, 1997	4, M	Trunk, brain	GCN	Unknown	Unknown	Unknown	Unknown	Abdominal metastases	1	Biopsy, laparot.	D
Hayes, 1984	4, F	Face	Unknown	Unknown	Unknown	IV	Unknown	Lymph nodes	14+	Remov., chemoth.	A
Crotty, 1992	4, M	Chest	Displ. nevus	SSM	0.7	IV	Unknown	Localized	17	Unknown	A
Borges, 1984	4, F	Chest	GCN	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	A
Pratt, 1981	4, F	Scalp	Unknown	Unknown	Unknown	Unknown	Unknown	Localized	180	Remov., radioth.	A
Pratt, 1981	4, F	Shoulder	CN	Unknown	Unknown	Unknown	Unknown	Localized	180	Removal, graft	A
Fuste, 1944	4, F	Shoulder	GCN	Unknown	Unknown	Unknown	Unknown	Unknown	72	Unknown	D
McWhorter, '54	4, F	Cheek	None	Nodular	Unknown	Unknown	NO	Localized	252	Diatherm., radium	A
Pontius, 1961	4,5/M	Armpit	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	24	Unknown	D
Derrick, 1958	4,5/M	Perianal	GCN	Unknown	Unknown	Unknown	NO	Visceral	6	Unknown	D
Lartigau, 1995	5, M	Eye lid	Unknown	SSM	1.87	III	Unknown	Unknown	157	Removal	A
Lartigau, 1995	5,1/M	Thigh	Unknown	SSM	2.97	IV	Unknown	Lymph nodes	61	Remov., chemoth.	A
Lartigau, 1995	5,5/M	Trunk	GCN	Nodular	10	V	Unknown	Lymph nodes	135	Remov., chemoth.	A
46), '96	5, F	Arm	Unknown	Nodular	2.6	Unknown	Unknown	Unknown	60	Removal	A
Williams, 1954	5, F	Arm	GCN	Unknown	Unknown	Unknown	Unknown	Brain	12	Unknown	D
Mehregan, '93	5, F	Back	Unknown	Nodular	3	IV	Unknown	Localized	Unknown	Removal	Unkn.
McGovern, '63	5, F	Arm	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	3	Unknown	A
Crotty, 1992	5, F	Thigh	Unknown	MM	1.6	IV	Unknown	Ovary, omentum	146	Remov., lymphad.	D
Hayes, 1984	5, M	Arm	GCN	Unknown	10	V	Unknown	Lymph nodes	12+	Remov., chemoth.	A
Pratt, 1981	5, F	Foot	CN	Unknown	Unknown	Unknown	Unknown	Localized	192	Removal	A
Hendrickson, 81	5, M	Scalp	Giant blue nevus	Unknown	Unknown	Unknown	Unknown	Diffuse metastases	96	Removal	D
Silverberg, '71											
Vennin, 1985	5,5/F	Foot	CN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	9	None	D
Bartoli, 1994	6, M	Chest	Unknown	Unknown	3.4	IV	Unknown	Localized	47	Removal	A
Bartoli, 1994	6, F	Hand	Unknown	Unknown	2.9	IV	Unknown	Unknown	43	Removal	A
Scalzo, 1997	6, M	Arm	Fam. dyspl. n.	SSM	0.1	IV	Unknown	Unknown	60	Unknown	A

Author, year	Age (yrs), sex	Site	Predisposing factors	Type	Thickness (mm)	Clark's level	Ulceration	Extension	Follow-up (months)	Treatment	Outcome
46), 1996	6, F	Cheek	Unknown	Nodular	5.5	Unknown	Unknown	Satellitosis	35	Removal	A
Boddie, 1987	6, F	Calf	None	Unknown	7.2	V	NO	Lymph nodes	24	Remov., chemoth.	A
McGovern, '63	6, F	Cheek	XP	Unknown	Unknown	Unknown	Unknown	Lymph nodes	36	Unknown	D
Zwaveling, '66	6, F	Calf	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	24	Unknown	A
46), '96	6, M	Knee	Unknown	Nodular	4.5	Unknown	Unknown	Lymph nodes	144	Removal	A
46), '96	6, M	Knee	Unknown	Nodular	Unknown	Unknown	Unknown	Unknown	22	Removal	A
46), '96	6, M	Back	Unknown	Nodular	14	Unknown	Unknown	Lymph nodes	14	Remov., chemoth.	D
Spatz, 1996	6, M	Leg	NO	Superficc.	10	V	YES	Localized	2	Unknown	A
Spatz, 1996	6, M	Cheek	XP	CN	1.96	IV	YES	Localized	8	Unknown	D
Lartigau, 1995	6,3/M	Arm	NO	Unknown	Unknown	V	Unknown	Lymph nodes	156	Remov., chemoth.	A
Lartigau, 1995	6,1/F	Trunk	NO	Nodular	5.6	V	Unknown	Lymph nodes	187	Remov., chemoth.	D
Chun, 1993	6, M	Thigh	CN	Unknown	Unknown	I	Unknown	Localized	120	Removal	A
Chun, 1993	6, M	Buttock	NO	Unknown	Unknown	II	Unknown	Localized	120	Removal	A
Novakovic, '95	6, M	Scalp	Dyspl. nevus	In situ	Unknown	Unknown	Unknown	Localized	Unknown	Unknown	A
Quaba, 1986	6, M	Trunk	GCN	Nodular	Unknown	Unknown	Unknown	Diffuse metastases	24	Removal, lymphaden.	D
McDonald, '48	6, M	Knee	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	36	Unknown	A
Crotty, 1992	6, F	Buttock	Unknown	Unknown	2.6	IV	Unknown	Lymph nodes, liver	158	Unknown	D
Hayes, 1984	6, F	Trunk	Unknown	Unknown	2.7	IV	Unknown	Localized	Unknown	Remov., lymphad.	A
Hayes, 1984	6, M	Trunk	GCN	Unknown	2.1	IV	Unknown	Lymph nodes	14	Remov., chemoth.	D
Hayes, 1984	6, F	Trunk	Unknown	Unknown	0.5	II	Unknown	Localized	Unknown	Remov., lymphad.	A
Jablokoff, 1879	6,5/F	Buttock	GCN	Unknown	Unknown	Unknown	Unknown	Brain	6 1/2	Unknown	D
Bartoli, 1994	7, M	Chest	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	194	Remov., lymphad.	A
Lartigau, 1995	7, F	Thigh	Radio-chemoth.	Superficc.	3.4	IV	YES	Localized	136	Unknown	A
Boddie, 1987	7, M	Wrist	None	Unknown	Unknown	Unknown	Unknown	Localized	126	Rem., lymph., chem.	A
Spatz, 1996	7, F	Arm	NO	Superficc.	2	IV	NO	Localized	92	Unknown	A
Barnhill, 1995	7, F	Trunk	NO	Unknown	4.18	V	Unknown	Unknown	Unknown	Unknown	LFU
Lerman, 1970	7, M	Arm	GCN	Nodular	Unknown	Unknown	NO	Lymph nodes, lung	8	Removal, lymphaden.	D
Coffey, 1951	7, F	Sacral	None	Unknown	Unknown	Unknown	Unknown	Lymph nodes	24	Removal, lymphaden.	A
Allen, 1953	7, F	Neck	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	240	Removal	A
Spatz, 1996	7, M	Shoulder	NO	Nodular	4	IV	NO	Localized	84	Unknown	A
Spatz, 1996	7, M	Ear	NO	Nodular	3.34	IV	YES	Localized	36	Unknown	A
Barnhill, 1995	7, M	Ear	NO	Unknown	1.87	IV	Unknown	Lymph nodes	108	Unknown	A
Clarke, 1952	7, M	Foot	Atypical nevus	Unknown	Unknown	Unknown	Unknown	Lymph nodes	240	Removal, lymphaden.	A
Lerman, 1970	7, M	Face	NO	Unknown	2.3	IV	Unknown	Localized	192	Remov., lymphad.	A
Goltz, 1963	7, F	Trunk	GCN	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	A
Bartoli, 1994	8, M	Foot	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	135	Remov., lymphad.	A
Spatz, 1996	8, F	Shoulder	NO	Superficc.	0.9	III	NO	Localized	96	Unknown	A
Spatz, 1996	8, F	Nose	XP	Superficc.	0.39	II	NO	Localized	89	Unknown	A
Spatz, 1996	8, F	Knee	NO	Unknown	11	V	YES	Localized	5	Unknown	A
Webster, 1944	8, F	Shoulder	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes, recurr.	4	Removal	A
Saksela, 1968	8, F	Back	Unknown	Mal. blue n.	Unknown	Unknown	Unknown	Unknown	9	Remov., radioth.	D

Author, year	Age (yrs), sex	Site	Predisposing factors	Type	Thickness (mm)	Clark's level	Ulceration	Extension	Follow-up (months)	Treatment	Outcome
Vennin, 1985	8, F	Shoulder	GCN	Unknown	Unknown	IV	Unknown	Lymph nodes	42	Remov., chemoth. lymphaden.	D
Loretan, 1967	8, F	Trunk	GCN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	15	Unknown	D
Lartigau, 1995	8, M	Leg	NO	Nodular	3	IV	NO	Localized	6	Unknown	A
Lartigau, 1995	8, 1/F	Thigh	NO	Unknown	2.52	IV	Unknown	Unknown	160	Unknown	A
Spatz, 1996	8, M	Thigh	NO	Nodular	4.71	V	NO	Lymph nodes	117	Unknown	A
McGovern, '63	8, M	Leg	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	14	Unknown	D
McWhorter, 1954	8, M	Cheek, ear	GCN	Unknown	Unknown	Unknown	NO	Thorax metastases	12	Unknown	D
Wu, 1997	8, M	Cheek	NO	Unknown	Unknown	Unknown	Unknown	Lymph nodes, lung	9	Removal, lymphaden.	D
Kaplan, 1974	8, M	Trunk	Neural GCN	Unknown	Unknown	Unknown	NO	Spermatic funicle	120	Unknown	A
Crotty, 1992	8, F	Arm	Unknown	Unknown	2.1		Unknown	Lymph nodes	114	Unknown	A
Crotty, 1992	8, F	Face	Unknown	Unknown	0.5	V	Unknown	Lymph nodes, skin metast.	11	Unknown	D
Pratt, 1981	8, F	Buttock	NO	Unknown	Unknown	Unknown	Unknown	Brain	23	Removal	D
Moss, 1986	8, M	Scalp	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	66	Unknown	A
Couperus, 1961	8, F	Hand	GCN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	Unknown	Unknown	A
Cordonnier, '66	8, 6/F	Scalp	CN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	8	Remov., radioth.	D
Bartoli, 1994	9, M	Foot	Unknown	Unknown	3.0	III	Unknown	Localized	22	Removal	D
Bartoli, 1994	9, M	Foot	Unknown	Unknown	3.5	IV	Unknown	Localized	6	Removal	A
Scalzo, 1997	9, M	Wrist	Fam. dyspl. n.	Unknown	4.9	IV	Unknown	Unknown	18	Unknown	A
46), '96	9, F	Back	Unknown	Superfic.	1.2	Unknown	Unknown	Unknown	34	Removal	A
46), '96	9, F	Trunk	Unknown	Nodular	1	Unknown	Unknown	Unknown	24	Removal	A
Spatz, 1996	9, F	Thigh	Nevus	Superfic.	1.84	IV	YES	Localized	16	Unknown	A
Barnhill, 1995	9, F	Back	Dyspl nevus	Unknown	Unknown	I	Unknown	Localized	4	Unknown	A
Mehregan, '93	9, F	Back	NO	Unknown	Unknown	Unknown	NO	Diffuse metastases	24	Removal	D
Sander, 1999	9, F	Leg	NO	Superfic.	0.6	II	NO	Unknown	Unknown	Unknown	A
Goldes, 1984	9, M	Face	Leukemia, chemotherapy	Nodular	Unknown	Unknown	Unknown	Diffuse metastases	26	Remov., radioth., chemoth., immunoth.	D
Amagai, 1993	9, F	Leg	Small CN	Nodular	3.8	IV	YES	Unknown	22	Removal	A
Stromberg, '79	9, F	Ear	NO	Unknown	Unknown	Unknown	Unknown	Lymph nodes	72	Removal, lymphaden.	A
Truax, 1953	9, F	Knee	CN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	72	Removal, lymphaden.	
Spitz, 1948											
McWhorter, 1954	9, F	Ear	CN	Unknown	Unknown	Unknown	NO	Lymph nodes	12	Removal, radiotherapy	D
Myhre, 1963	9, F	Back	CN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	30	Unknown	D
Lartigau, 1995	9, M	Knee	NO	Superfic.	2.6	IV	NO	Localized	2	Unknown	A
Spatz, 1996	9, M	Foot	NO	Unknown	2.6	IV	YES	Unknown	0	Unknown	LFU
Spatz, 1996	9, M	Scalp	NO	Unknown	4	IV	YES	Lymph nodes	120	Unknown	A
Lerman, 1970	9, M	Hand	NO	Unknown	Unknown	Unknown	NO	Lymph nodes	66	Diatherm., lymphad	A
Temple, 1991	9, M	Leg	Unknown	Unknown	3.1	III	YES	Unknown	10	Removal	A
Pratt, 1981	9, F	Chest	Blue nevus	Unknown	Unknown	Unknown	Unknown	Localized	132	Removal	A
Ozturkan, 1994	9, F	Leg	CN	Unknown	2	III	NO	Localized	Unknown	Removal	A
Bartoli, 1994	10, F	Chest	Unknown	Unknown	Unknown	Unknown	Unknown	Localized	71	Unknown	D

Author, year	Age (yrs), sex	Site	Predisposing factors	Type	Thickness (mm)	Clark's level	Ulceration	Extension	Follow-up (months)	Treatment	Outcome
Scalzo, 1997	10, F	Scalp	Unknown	SSM	2	IV	Unknown	Unknown	77	Unknown	A
46), '96	10, F	Thigh	Unknown	Nodular	3.6	Unknown	Unknown	Unknown	41	Unknown	A
Spatz, 1996	10, F	Eyelid	XP	Unknown	0.98	III	Unknown	Unknown	0	Unknown	LFU
Melnik, 1986	10, F	Cheek	XP	Nodular	Unknown	Unknown	YES	Diffuse metastases	156	Remov., radioth.	D
Temple, 1991	10, F	Trunk	Unknown	Unknown	0.68	0	NO	Diffuse metastases	6	Removal	D
Fuste, 1944	10, F	Back	GCN	Unknown	Unknown	IV	Unknown	Visceral	5	Radiotherapy	D
Myhre, 1963	10, F	Back	CN	Unknown	Unknown	Unknown	Unknown	Unknown	8	Removal	A
Horgan, 1987	10, F	Calf	Melanocytic nevus	Unknown	2	IV	YES	Lymph nodes	12	Remov., lymphad.	A
46), '96	10, M	Knee	Unknown	Superficial	2.5	Unknown	Unknown	Unknown	2	Removal	A
46), '96	10, M	Foot	Unknown	Nodular	2	Unknown	Unknown	Unknown	19	Removal	A
Lartigau, 1995	10, M	Heel	NO	Aeal lentigin.	2.3	IV	Unknown	Lymph nodes	7	Unknown	A
Spatz, 1996	10, F	Back	Nevus	Unknown	1.57	IV	NO	Localized	131	Unknown	A
Boddie, 1987	10, M	Leg	None	Unknown	Unknown	Unknown	YES	Lymph nodes	72	Remov., chemoth.	A
Navakovic, '95	10, M	2 melanomas back, shoulder	Dyspl. nevus	SSM	0.78	III	Unknown	Localized	Unknown	Unknown	A
Hoagland, 1960	10, M	Chest	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	24	Unknown	A
Duteille, 2000	10, M	Leg	Unknown	SSM	1.3	IV	Unknown	Localized	168	Remov., BCG	A
Masters, 1963	10, M	Neck	Acquired nevo nevocel.	Unknown	Unknown	Unknown	Unknown	Diffuse metastases	15	Removal, lymphaden.	D
Greeley, 1965	10, M	Trunk	GCN	Unknown	Unknown	Unknown	Unknown	Diffuse	Unknown	Unknown	D
Greeley, 1965	10, M	Scalp, buttocks, back	GCN	Unknown	Unknown	Unknown	Unknown	Diffuse	Unknown	Unknown	D
Wu, 1997	10, M	Unknown	GCN	Unknown	Unknown	Unknown	Unknown	Brain	3	Removal	D
Crotty, 1992	10, F	Shoulder	Unknown	SSM	0.6	IV	Unknown	Unknown	63	Unknown	A
Crotty, 1992	10, F	Shoulder	Unknown	SSM	0.5	II	Unknown	Local recurrence	84	Unknown	A
McWhorter, 1954	10, M	Cheek	CN	Unknown	Unknown	Unknown	YES	Femur metastases, brain	72	Unknown	D
Hayes, 1984	10, M	Trunk	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes, bone marrow, liver, kidney	84	Remov., lymphad. chemotherapy	D
De Raeve, '93	10, F	Leg	CN	Unknown	1.3	III	Unknown	Unknown	12	Removal	A
Pratt, 1981	10, F	Leg	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes, brain	22	Remov., lymphad.	D
Lartigau, 1995	10,4/F	Thigh	Unknown	Superficial	0.64	III	Unknown	Unknown	65	Unknown	A
Barnhill, 1995	11, M	Thigh	Unknown	Unknown	5.88	IV	Unknown	Unknown	12	Unknown	A
Spatz, 1996	11, F	Leg	NO	Superficial	1.5	IV	NO	Localized	74	Unknown	A
Spatz, 1996	11, F	Chest	NO	Unknown	5.1	V	NO	Skin metastases	7	Unknown	A
Spitz, 1948	11, F	Foot	Unknown	Nodular	Unknown	Unknown	Unknown	Lymph nodes, lung	6	Radiotherapy	D
Lerman, 1970	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Diffuse metastases	7	Remov., radioth.	D
McGovern, '63	11, F	Leg	CN	Unknown	Unknown	Unknown	Unknown	Lymph nodes	42	Unknown	D
46), '96	11, M	Heel	Unknown	Nodular	2.9	Unknown	Unknown	Unknown	82	Removal	A
Spatz, 1996	11, M	Cheek	NO	Superficial	2.75	IV	YES	Lymph nodes, lung	39	Unknown	D
Novakovic, '95	11, M	Back	Dyspl. nevus	SSM	0.41	III	Non det	Localized	Unknown	Unknown	A
McWhorter, '54	11, M	site not found	Unknown	Unknown	Unknown	Unknown	Non det	Diffuse metastases	6	Unknown	D
Hall, 1952	Unknown	armpit metast	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	D
Hayes, 1984	11, M	Trunk	GCN	Unknown	2.5	IV	Non det	Lymph nodes, pleura	21	Rem., lymph., chem	LFU

Author, year	Age (yrs), sex	Site	Predisposing factors	Type	Thickness (mm)	Clark's level	Ulceration	Extension	Follow-up (months)	Treatment	Outcome
Hayes, 1984	11, M	Trunk	Unknown	Unknown	3.1	IV	Unknown	Localized	60	Removal	A
Wu, 1997	11, M	Scalp	NO	Unknown	Unknown	Unknown	Unknown	Lymph nodes	8	Removal	D
Laugier, 1961	11, F	Foot	Unknown	Unknown	Unknown	Unknown	YES	Unknown	12	Remov., radioth.	A
Pratt, 1981	11, F	Scalp	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	29	Remov., lymphad.	A
Pratt, 1981	11, F	Cheek	Acquired nevus	Unknown	Unknown	Unknown	Unknown	Lymph nodes, brain	21	Remov., lymphad.	D
Strojan, 2000	11, F	Perianal	Unknown	Polypoid	11	Unknown	Unknown	Lymph nodes, liver	6	Remov., lymphad.	D
Bartoli, 1994	12, F	Chest	Unknown	Unknown	Unknown	Unknown	Unknown	Diffuse metastases	3	Unknown	D
Scalzo, 1997	12, F	Arm	Fam. acquir. n.	SSM	1.95	IV	Unknown	Localized	76	Unknown	A
Scalzo, 1997	12, F	Scalp	Junctional nevus	SSM	Unknown	Unknown	Unknown	Metastases	74	Unknown	D
Scalzo, 1997	12, F	Back	CN	Nodular	1.9	IV	Unknown	Localized	48	Unknown	A
Scalzo, 1997	12, M	Back	Nevus	SSM	1.6	III	Unknown	Unknown	Unknown	214	A
Baas, 1989	12, F	Calf	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	168	Remov., chemoth.	A
Barnhill, 1995	12, M	Scalp	CN	Unknown	7.5	V	Unknown	Lymph nodes	6	Unknown	D
Barnhill, 1995	12, F	Scalp	NO	Unknown	2.8	III	Unknown	Metastases	36	Unknown	D
Chun, 1993	12, F	Cheek	CN	Unknown	0.7	II	Unknown	Localized	24	Removal	A
Roth, 1990	12, F	Back	Dyspl. nevus	In situ	Unknown	Unknown	NO	Localized	Unknown	Removal	A
Sander, 1999	12, F	Trunk	NO	Nodular	1.8	IV	NO	Unknown	17	Unknown	D
Sander, 1999	12, F	Head, neck	NO	Nodular	1.6	III	Unknown	Unknown	Unknown	Unknown	A
Skov-Jensen, 66	12, F	Perineal	NO	Unknown	Unknown	Unknown	Unknown	Diffuse metastases	21	Remov., diathermo.	D
Tate, 1993	12, F	Thigh	NO	Superf. c.	0.92	III	Unknown	Lymph nodes, lung, bone	180	Remov., radioth. chemoth., immunot.	D
Temple, 1991	12, F	Trunk	Unknown	Unknown	2.2	V	NO	Unknown	1	Removal	A
Spitz, 1948	12, F	Foot	Nevus	Unknown	Unknown	Unknown	Unknown	Lymph nodes	5	Removal	D
McGovern, '63	12, F	Thigh	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes	6	Unknown	D
46), '96	12, M	Arm	Unknown	Nodular	3.4	Unknown	Unknown	Unknown	38	Removal	A
Spatz, 1996	12, M	Arm	NO	Unknown	10	V	YES	Unknown	19	Chemotherapy	D
Spatz, 1996	12, M	Back	NO	Superf. c.	1.6	III	NO	Localized	120	Unknown	A
Spatz, 1996	12, F	Thigh	NO	Superf. c.	4	III	NO	Lymph nodes	144	Unknown	A
Spatz, 1996	12, M	Chest	Nevus	Nodular	2.16	IV	NO	Localized	7	Unknown	A
Novakovic, '95	12, M	2 melanomas face	Nevus	Unknown	0.88	II	Unknown	Localized	Unknown	Unknown	A
Sander, 1999	12, M	Trunk	NO	In situ	Unknown	Unknown	Unknown	Unknown	25	Unknown	D
Stromberg, '79	12, M	Back	NO	Nodular	3.1	IV	YES	Unknown	72	Remov., lymphad.	A
McGovern, '63	12, F	Back	Unknown	Unknown	Unknown	Unknown	Unknown	Lymph nodes, local recurr.	12	Unknown	A
Crotty, 1992	12, M	Ear	Unknown	SSM	1.3	III	Unknown	Localized	40	Unknown	A
Crotty, 1992	12, M	Thigh	Unknown	SSM	0.5	II	Unknown	Unknown	44	Unknown	A
Crotty, 1992	12, F	Heel	Unknown	Acral lentigin.	3.1	IV	Unknown	Local recurrence	36	Unknown	D
Crotty, 1992	12, M	Chest	Unknown	Bordeline	0.8	IV	Unknown	Local recurrence	72	Unknown	A
Moss, 1986	12, F	Leg	Unknown	Unknown	0.96	III	Unknown	Unknown	7	Unknown	A
Hayes, 1984	12, M	Foot	Unknown	Unknown	0.36	III	Unknown	Localized	81	Remov., chemoth.	A
Pratt, 1981	12, F	Scalp	Unknown	Unknown	Unknown	Unknown	Unknown	Local recurrence lung, bone	28	Removal, radioth., chemoth.	D
Pratt, 1981	12, F	Thumb	Unknown	Unknown	Unknown	Unknown	Unknown	Recurrence	216	Removal	A
Strojan, 2000	12, M	Back	Familial melanoma	Unknown	Unknown	Unknown	YES	Lymph nodes, liver	53	Removal, lymphad., chemot.	D

Author, year	Age (yrs), sex	Site	Predisposing factors	Type	Thickness (mm)	Clark's level	Ulceration	Extension	Follow-up (months)	Treatment	Outcome
Lartigau, 1995	12,1/F	Knee	Unknown	SSM	3.5	IV	Unknown	Unknown	198	BCG	A
Wu, 1997	12,5 F	Back	NO	Unknown	3.5	III	Unknown	Lymph nodes, brain	16	Remov., lymphad, craniotomy	D
Cheah, 1969	12, M	1° site not found	Unknown	Unknown	Unknown	Unknown	Unknown	Diffuse metastases	4	Unknown	D

LEGENDA:

The number followed by the brackets, in the column Author/year, is the number of the author in the references (pages 173-5).

M = male; **F** = female; **GCN** - giant congenital nevus; **SSM** = superficial spreading melanoma; **MM** = malignant melanoma; **CN** = congenital nevus

XP = xeroderma pigmentosum; **A** = alive; **D** = died; **mts.** = months; **yrs** = years; **p.c.** = personal communication; **LFU** = lost at the follow-up;

Dyspl. nevus = dysplastic nevus; **Bone m.** = bone marrow; **Diatherm.** = diathermocogulation; **Remov.** = removal; **Chemot.** = chemotherapy;

Subcutan. = subcutaneous; **Lymphaden.** = lymphadenectomy; **Unkn.** = unknown; **Laparot.** = laparotomy; **Local rec.** = local recurrence; **Recurr.** = recurrence;

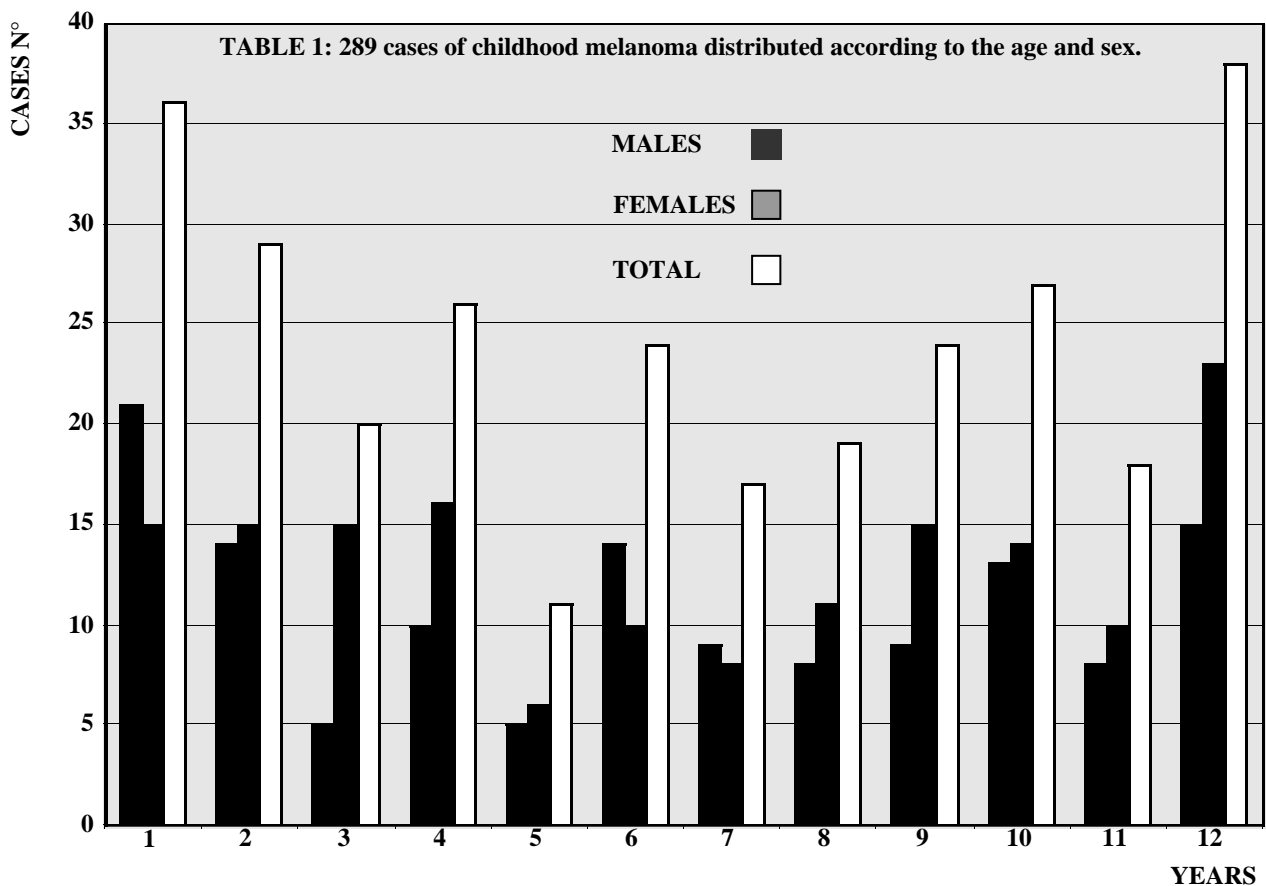
Rhabdom. diff. = rhabdomyosarcoma differentiation; **Radioth.** = radiotherapy; **Lymph. transf.** = lymphocyte transfusion; **Surf.** = surface;

Mal. blue n. = malignant blue nevus; **Adenocr. kid.** = adenocarcinoma kidney; **Metastas.** = metastases; **Superf. n.** = superficial;

Fam. dyspl. n. = familial dysplastic nevus; **Immunoth.** = immunotherapy.

7 cases of childhood melanoma collected after writing the manuscript.

Siegler, 1997	7 mts., M	Forehead	GCN	Unknown	Unknown	Unknown	Unknown	Localized	54	Removal	A
Richardson, 2002	7 mts., F	Scalp	GCN	Unknown	Unknown	Unknown	Unknown	Lymph nodes, liver	20	Remov., chemoth., partial liver removal	A
99), 2002	2, F	Foot	CN	SSM	0.8	Unknown	Unknown	Localized	19	Removal	A
99), 2002	5, M	Arm	NO	Unknown		In situ	Unknown	Localized	144	Removal	A
99), 2002	6, F	Arm	Unknown	Nodular	0.9	Unknown	Unknown	Unknown	266	Removal	A
99), 2002	11, M	Trunk	Unknown	Unknown	0.8	Unknown	Unknown	Localized	1	Unknown	A
Yesudian, 02	11,2, F	Leg	NO	Unknown	Unknown	Unknown	Unknown	Localized	18	Removal	A



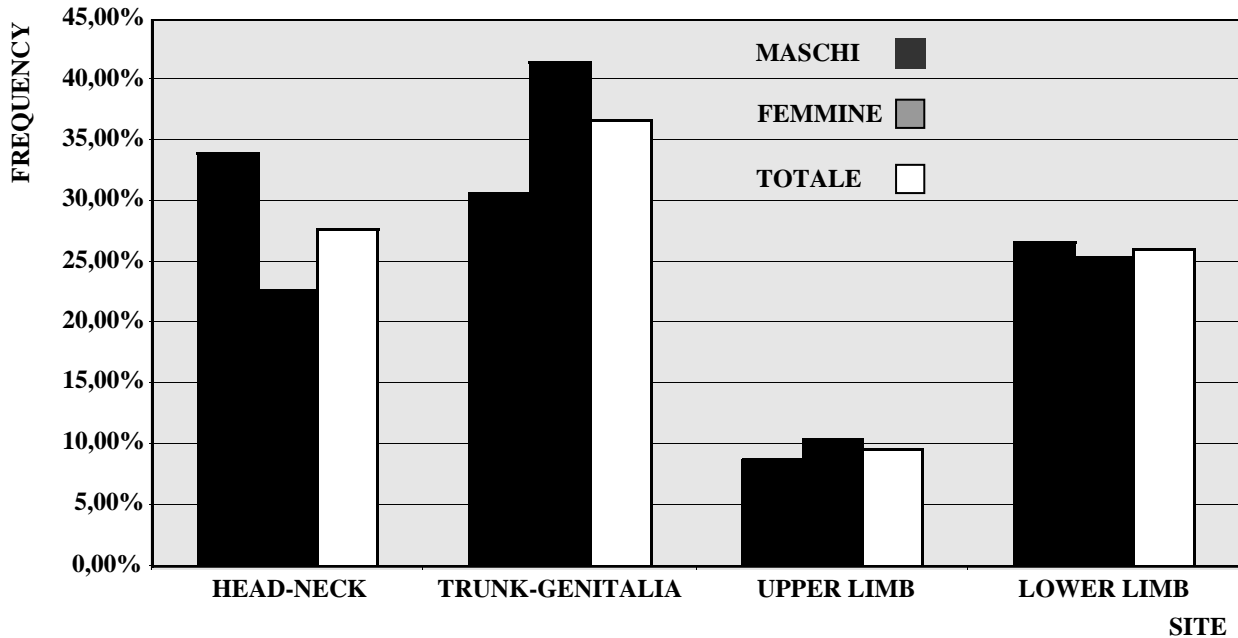
AGE	MALES	FEMALES	TOTAL
1	21	15	36
2	14	15	29
3	5	15	20
4	10	16	26
5	5	6	11
6	14	10	24
7	9	8	17
8	8	11	19
9	9	15	24
10	13	14	27
11	8	10	18
12	15	23	38
TOTAL	131	158	289

Results and comment

In table 1 is reported the distribution of 289 cases -131 males, 158 females- according to the year of age and sex. The distribution is rather uniform in the first 12 years of age. Due to the lack of “a priori” information regarding the distribution of the total number of cases per year of age, we tried to evaluate a 95% confidence interval for the average, using a bootstrap type procedure. Particularly, we extracted 10,000 “bootstrap samples” from the data and obtained the results as follows: 0.025 corrected percentile = 20.083 and 0.975 corrected percentile = 28.583. Therefore the data regarding the first, fifth and twelfth year of age seem to stand aside from the confidence interval. However, the observed variation, although significant from a statistical point of view, is not enough to falsify the hypothesis of a biological uniformity of the prepubertal age with regard to the frequency of malignant melanoma.

The significance level $\alpha = 0.05$ was chosen for all the tests used in the statistical evaluation of the results.

TABLE 2: 281 cases of childhood melanoma distributed according to the site and sex.



SITE	MALES	FEMALES	TOTAL
HEAD-NECK	43 (33.86%)	35 (23.00%)	78 (27.76%)
TRUNK-GENITALIA	39 (30.71%)	64 (41.56%)	103 (36.65%)
UPPER LIMB	11 (8.66%)	16 (10.39%)	27 (9.61%)
LOWER LIMB	34 (26.77%)	39 (25.32%)	73 (25.98%)
TOTAL	127	154	281

With regard to the distribution of malignant melanoma in the two sexes, the actual series confirms even at the prepubertal age the slight prevalence of females (54.7%). The latter was reported in numerous adult series, included our adult series (15) and also in childhood series (10, 26, 99). The same prevalence of females in the prepubertal age and even after 60 years of age (15), favors the role of genetic factors as compared with hormonal factors in determining this difference, although some Authors (112) underline the role of estrogens.

In table 2 the number and percentage distribution of 289 cases of childhood melanoma is reported (8 cases were excluded due to the involvement of more than one site).

The distribution of melanoma according to the site (table 2) is characterized by a more frequent involvement of the head -27.76%- as compared with the prevalence in adults -238/1431,

namely 16.63%- of our series (15). The null hypothesis that the percentage involvement of the head in children is equal to that one in adults is rejected. As a matter of fact, in the 2-sample test for equality of proportions χ -square = 18.5865, d.o.f. (degrees of freedom) = 1, p value = 0.

When correcting the surface according to the rule of nine, the head, which follows the trunk in the not corrected distribution, largely becomes the most frequent site involved, followed by the trunk, lower and upper limbs. At this age the involvement of the head prevails in males - 33.86% versus 22.73% in females-, although the difference does not reach a statistical significance. As a matter of fact, the null hypothesis that the percentage involvement of the head is not influenced by sex is accepted. However, the extent of p value is slightly more than 0.05 - χ -square = 3.7632, d.o.f. = 1, p value = 0.0524.

Smaller series of patients aged less than 21 years seem to confirm the main involvement of the head at this age (88) and the prevailing of male sex (124).

As we will later see when talking about the predisposing factors, giant congenital melanocytic nevus is probably the factor responsible for the greater involvement of the head in the first 12 years of age. Taking into account that 10% of these melanomas are present at birth and more than 20% of cases arise in the first 2 years of life, the role played by sun radiations, which is today considered by most Authors as one of the most important factors in the pathogenesis of melanoma in adults, is not significant at this age.

The distribution of sites involved in the two sexes is different from adults. Females present a more frequent involvement of the trunk - 41.56% - as compared with the male sex - 30.71% -. Moreover, the involvement of the lower limb is superimposable in males -26.77% - and in females -25.32% -. The greater involvement of the site trunk-genitalia in females does not reach a statistical significance because the null hypothesis that the percentage involvement of the trunk and genitalia is not influenced by sex is accepted - χ -square = 3.0769, d.o.f. = 1, p value = 0.0794. Also the null hypothesis that the percentage involvement of the lower limb does not depend on the sex is accepted - χ -square = 0.0192, d.o.f. = 1, p value = 0.8898.

According to Whiteman (118) the role played by sex in influencing the site involved is not significant till 14 years. Other Authors (7) report a greater involvement of the head and trunk in males, whereas in females prevails the involvement of the limbs. However, in this series only 25 subjects out of 179 are aged 9 or less and 40 subjects are aged 10-14 years.

Predisposing factors are present in 125 cases out of 289 (table 3). In spite of its rarity, being present in less than 2% of newborns (41) congenital melanocytic nevus is the most frequent predisposing factor of childhood melanoma. The latter arises on a congenital nevus in more than 31% of cases. When including also the two cases of congenital blue nevus, about a third of cases of childhood melanoma arises on congenital nevi. Among the latter, the most rare, namely giant congenital melanocytic nevus is the most frequent predisposing factor of childhood melanoma, being present in 23.18 of cases. The role played by giant congenital melanocytic nevus at this age is underlined by most Authors (31, 92, 94). However, physicians should take into account that giant nevi reported in the relevant literature are usually described because of their association with melanoma. On the other hand, when considering the prevalence of melanoma on giant nevi within a relevant register, its prevalence goes down to 4-6% (31). About 8% of childhood melanomas arise on an acquired

TABLE 3: predisposing factors in 125 out of 289 cases of prepubertal melanoma.

PREDISPOSING FACTORS	MALES	FEMALES	TOTAL
GIANT CONGENITAL NEVUS	34 (25.95%)	33 (20.89%)	67 (23.18%)
CONGENITAL NEVUS	7 (5.34%)	17 (10.76%)	24 (8.30%)
ACQUIRED NEVUS	5 (3.82%)	6 (3.80%)	11 (3.81%)
XERODERMA PIGMENTOSUM	2 (1.53%)	6 (3.80%)	8 (2.77%)
DYSPLASTIC NEVUS	5 (3.82%)	3 (1.90%)	8 (2.77%)
OTHER MALIGNANCIES	2 (1.53%)	0 (0.00%)	2 (0.69%)
BLUE NEVUS	2 (1.53%)	1 (0.63%)	3 (1.04%)
FAMILIAL DYSPLASTIC NEVUS	1 (0.76%)	0 (0.00%)	1 (0.35%)
RADIOTHERAPY	0 (0.00%)	1 (0.63%)	1 (0.35%)
FAMILIAL MELANOMA	1 (0.76%)	1 (0.63%)	2 (0.69%)

TABLE 4: percentage of died children per year of age (histograms).

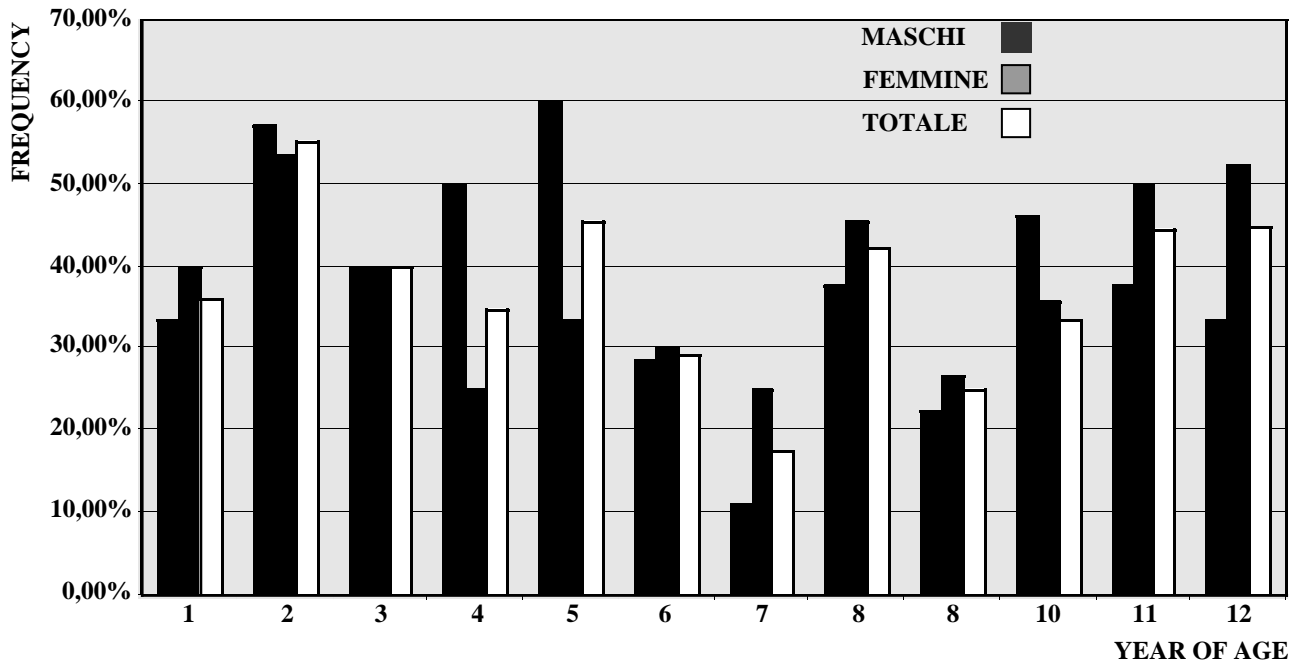


TABLE 4: number and percentage of died children per year of age.

YEAR OF AGE	MALES	FEMALES	TOTAL
1	7 (33.33%)	6 (40.00%)	13 (36.11%)
2	8 (57.14%)	8 (53.33%)	16 (55.17%)
3	2 (40.00%)	6 (40.00%)	8 (40.00%)
4	5 (50.00%)	4 (25.00%)	9 (34.61%)
5	3 (60.00%)	2 (33.33%)	5 (45.45%)
6	4 (28.57%)	3 (30.00%)	7 (29.17%)
7	1 (11.11%)	2 (25.00%)	3 (17.65%)
8	3 (37.50%)	5 (45.45%)	8 (42.10%)
9	2 (22.22%)	4 (26.66%)	6 (25.00%)
10	6 (46.15%)	5 (35.71%)	11 (40.74%)
11	3 (37.50%)	5 (50.00%)	8 (44.44%)
12	5 (33.33%)	12 (52.17%)	17 (44.74%)
TOTAL	49	62	111

nevus, in half cases of dysplastic type. Much less frequent are other factors such as xeroderma pigmentosum, immunosuppression due to other malignancies or radiotherapy and finally familial dysplastic nevus and melanoma.

The prognosis of childhood melanoma can be theoretically influenced by several factors. We studied the distribution of the lethal cases according to the age, sex, presence of predisposing

factors, ulceration, regional adenopathy, Clark's level and thickness of the lesions, when these data were available.

During the follow up period, which comprehensively lasted 50 months on average -26 months for the lethal cases and 65 months for the survivors on average- 111 out of 289 children died, namely 38.41% of cases, 49/131 males -37.40%- and 62/158 females -39.24%-.

TABLE 5: Influence of predisposing factors on the lethality (D = died).

	<i>PERCENTAGE OF DIED CHILDREN</i>
IN CASES WITH PREDISPOSING FACTORS	54.40% (68 D/125 cases with predisposing factors)
IN CASES WITH GCN	70.15% (47 D/67 cases with GCN)
IN CASES "DE NOVO"	26.67% (16 D/60 cases "de novo")
IN CASES WITH ULCERATION	36.36% (12 D/33 cases with ulceration)
IN CASES WITHOUT ULCERATION	31.71% (13 D/41 cases without ulceration)
IN CASES WITH LYMPHADENOPATHY	63.40% (97 D/153 cases with lymphadenopathy)
IN CASES WITHOUT LYMPHADENOPATHY	6.17% (5 D/81 cases without lymphadenopathy)
IN CASES WITH THICKNESS <1mm	8.33% (2 D/24 cases <1mm)
IN CASES WITH THICKNESS >1mm	20.00% (21 D/105 cases >1mm)
IN CASES WITH CLARK'S I LEVEL	20% (1 D/5 cases with I level)
IN CASES WITH CLARK'S II LEVEL	0% (0 D/10 cases with II level)
IN CASES WITH CLARK'S III LEVEL	22% (4 D/18 cases with III level)
IN CASES WITH CLARK'S IV LEVEL	24% (13 D/54 cases with IV level)
IN CASES WITH CLARK'S V LEVEL	36.36% (8 D/22 cases with V level)

The distribution of the lethal cases per year seems uniform. In order to verify this hypothesis, we generated 10,000 "bootstrap" samples on the percentage data of table 4 obtaining the figures as follows: corrected 0.025 percentile = 31.655 and corrected 0.975 percentile = 42.801. The hypothesis of uniformity is thus substantially confirmed, when excluding the significantly abnormal datum of the second year -55.17%- and of the seventh year -17.65%-. The null hypothesis that the prognosis "quoad vitam" is not influenced by the sex is accepted. As a matter of fact, in the 2-sample test for equality of proportions $-\chi^2$ -square = 0.0392, d.o.f. = 1, p value = 0.8431-.

Besides age and sex, which do not play a significant role on the lethality, we should now considering the other factors.

Among the children with predisposing factors, 68 out of 125 -54.40%- died as compared with the comprehensive lethality of 38.41%. The lethality in cases of melanoma arisen on giant congenital melanocytic nevi was particularly high, namely 47/67 -70.15%. The null hypothesis that the giant nevus influences the prognosis as well as non giant nevus is rejected $-\chi^2$ -square = 20.9321, d.o.f. = 1, p value = 0. We do not know exactly the percentage of malignant transformation of giant congenital nevus, although a

figure of 4-6% is probable (31). However, giant congenital nevus is the most frequent predisposing factor and the worst prognostic factor for prepubertal malignant melanoma (table 5). Its role as predisposing factor is confirmed by all the Authors (31, 94). It play also a role in the pathogenesis of adult melanoma (54).

In the 60 "de novo" cases there were 16 died children, with 26.67% percentage of lethality, confirming the minor severity of this type of melanoma. As a matter of fact, when comparing the lethality due to melanoma "de novo" with that one of the whole population, the null hypothesis of equality is accepted $-\chi^2$ -square = 2.4737, d.o.f. = 1, p value = 0.1158-.

In 74 cases (table 5) the presence or not of ulceration on the surface of melanoma was reported. The lethality in cases with ulceration -12/33, namely 36.36%-, was higher as compared with cases without ulceration -13/41, namely 31.71%-. However the difference is not statistically significant, because the null hypothesis of equality of the prognosis is accepted $-\chi^2$ -square = 20.0302, d.o.f. = 1, p value = 0.8621-.

In 234 cases (table 5) the presence or not of metastatic adenopathy at the moment of diagnosis was established. The lethality in cases with regional lymphadenopathy -97/153, namely 63.40%- was significantly higher than in cases

TABLE 6: Clark's level in 114 casi.

CLARK'S LEVEL	N° OF CASES (%)
I	5 (4.38)
II	11 (9.65)
III	21 (18.42)
IV	55 (48.24)
V	22 (19.29)

without lymphadenopathy -5/81, namely 6.17%. The p value = 0 - χ -square = 68.2266, d.o.f. = 1- leads to clearly reject the null hypothesis of equality between presence and lack of lymphadenopathy. The latter is therefore a negative prognostic factor for the survival. On the other hand, according to Ceballos et Al. (20), the prognosis of childhood melanoma is not always related to the presence of lymphadenopathy.

We then evaluated the influence of Clark's level and thickness of malignant melanoma on the lethality (table 5). With regard to the Clark's level, the latter was established in 110 cases (table 6). Even though the cases with I, II and III level are scarce, the difference with the lethality of IV level does not seem significant (table 5), whereas the lethality is higher in cases with V level. With regard to the statistical significance of Clark's level, the I and II levels were not evaluated due to the scarce number of cases. We wondered whether the Clark's III level -4/18 children died- has a better prognosis as compared with the Clark's IV level -13/54 died children-. As the χ -square test was not applicable, we performed the Fisher's exact test, which led to p value 1, namely accepting the null hypothesis of equality. In order to establish whether the prognosis associated with the Clark's IV level is better than that one associated with the Clark's V level (8/22 died children) the 2-sample test for equality of proportions was carried out. Its result - χ -square = 0.646, d.o.f. = 1, p value = 0.4215- led to accept the null prognosis of equality between the two levels. Therefore the difference of prognosis showed by the clinical feature is not characterized by statistical significance. With regard to the histological thickness of melano-

TABLE 7: thickness of melanoma in 129 cases (average thickness: 3,96 mm).

THICKNESS	N° OF CASES		
	MALES	FEMALES	TOTAL
< 1 mm	9	15	24
> 1 mm	48	57	105

ma, the latter was evaluated in 129 cases (table 7).

In the 24 cases with thickness less than 1 millimeter 2 children died -8.33%-, whereas in the 105 cases with thickness more than 1 millimeter 21 children died -20.00%-. As the χ -square test was not applicable, we performed the Fisher's exact test, which led to p value 0.2432, namely accepting the null hypothesis of equality of prognosis.

In conclusion, in spite of the limits of the actual series, especially the diversity of the data, mainly with regard to the follow up, the review of the literature confirmed the rarity of childhood melanoma -296 cases in about a century-, the lack of progressive increase of frequency in contrast with the adult, which was also observed by other Authors (10), the different sites involved, with more significant involvement of the head in children as compared with adults and, finally, the same distribution in males and females with regard to the localization on the trunk and lower limb. Finally, the role played by giant congenital melanocytic nevus in the pathogenesis and prognosis of childhood melanoma was confirmed.

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