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ON THE TENDENCY OF EWING'S SARCOMA TO HEAL SPONTANEOUSLY, AND ON THE ALTERATIONS DUE TO IRRADIATION

BY

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This sarcoma derives its name from Ewing, who was the first to describe it, in 1921. It has attracted a good deal of attention, especially on account of its uncertain genesis, its sensitivity to irradiation, and its frequently dramatic course. The regression and disappearance of the tumour after irradiation arouse hopes of a good prognosis, and a recurrence or the appearance of new foci, both of which are so often observed a short time after irradiation, are all the more disappointing.

The clinical course of Ewing's sarcoma after irradiation has been described by several authors; but its histological appearance after irradiation has not received so much attention. As early as 1905 *Kienböck* pointed out that it would be of considerable practical importance to discover whether different sarcomata react differently to irradiation, and what are the histological findings in a sarcoma which will retrogress with irradiation. Since then over 40 years have elapsed, and our knowledge on this subject is still very imperfect. The same is true of our knowledge of Ewing's sarcoma in particular.

The majority of histological examinations of irradiated Ewing's sarcomata have been made a considerable time after treatment, when the tumour has either regressed or disappeared altogether. However, some information on the appearance of a tumour shortly after irradiation is given by *Schinz*

and *Uehlinger* (1931) and *Stewart-Harrison* (1934). The former describe a Ewing's sarcoma of the proximal epiphysis of the tibia. The leg was amputated 12 hours after a single dose of 120 °/₀₀. HED. The nuclear stain had partly disappeared; some of the nuclei were pyknotic, others had disintegrated into intensely coloured irregular chromatin knots. (Fig. 1). In Stewart-Harrison's case half the tumour was irradiated

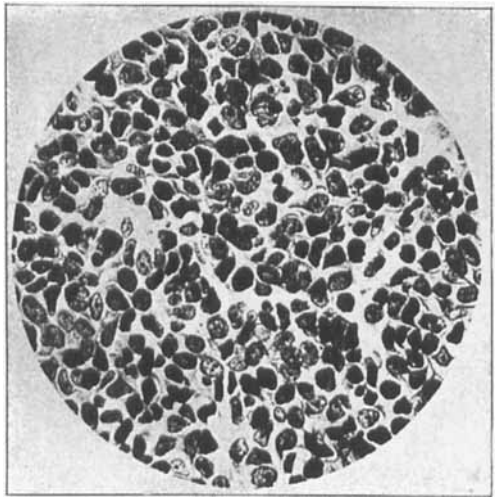


Fig. 1 a.

Microphotograph showing an unirradiated portion of a Ewing's sarcoma localized below the proximal metaphysis of the tibia. Big conglomerations of medium-sized, almost round cells with large either rather compact or rather vesicular nuclei. (Schinz u. Uehlinger: Ergebnisse der medizinischen Strahlenforschung, Band V. Abb. 77. S. 473.)

(750 r) 12 hours before amputation. The histological section resembles that of Schinz and Uehlinger in all essentials.

Zuppinger (1933) also examined a Ewing's sarcoma immediately after irradiation. 180 r were administered 3 times to the front and once to the back of the tumour, which was situated on the humerus, over a period of 4 days. A biopsy was taken the day after the last exposure and showed the condition after irradiation, but the author does not give an illustration or any histological details.

Brav and *Rechtmann* (1938) and *de Santos* (1934) describe cases in which the interval between the irradiation and the biopsy were rather longer. The former administered 180 r 3 times and a biopsy was made some days later; no marked effect of the irradiation could be seen in either of 2 specimens. In Santos' case a biopsy was made 9 days after the ex-

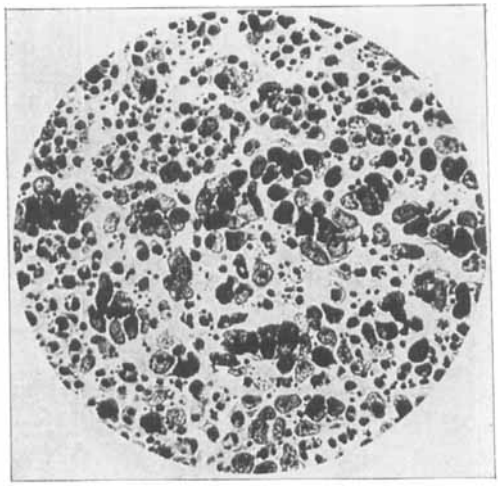


Fig. 1 b.
Microphotograph showing an irradiated portion of a Ewing's sarcoma, taken 12 hours after test-irradiation. Intense signs of disintegration. The nuclear stain has vanished in some places, other nuclei either are strongly pyknotic or disclose disintegration into separate, irregular and intensely staining particles of chromatin. 300 pyknoses to a total of 100 more or less intact cells are seen. (Schinz u. Uehlinger, id.).

posure, and 14 days later the limb was amputated. Sections taken through the tumour were very thoroughly examined both macroscopically and microscopically, and cyst formation, haemorrhages, necroses, areas of fibrosis and of bone formation are mentioned. The author does not discuss the connection between these changes and irradiation, and does not mention any effects of the latter in his description of the surgical specimen.

Table 1.

Case	Primary Growth	Irradiation[1])	Clinical Course	Histological Findings at Primary Tumour Site (Necropsy)
I Female, aged 24 years (76,035)	Left ilium adjacent to sacroiliac articulation. Biopsy: Ewing sarcoma	Irradiation to ant. and post. pelvic ports 1st series: 5,100 r 2nd series: 2,500 r 3rd series: 6,380 r 4th series: 2,100 r Total: 16,080 r at intervals from Feb., 1933, to April, 1934	Died 17 months after initial series, of bronchopneumonia and widespread metastases	Large masses of viable and proliferating tumour cells in bone and adjacent soft parts
II Male, aged 14 years (99,562)	Seventh dorsal vertebra with invasion of adjacent soft parts. Biopsy: Ewing sarcoma	Dosage of 5,000 r to 10×20 cm portal over spine. Irradiation delivered in 34 days	Died 9 Months after treatment. Disseminated metastases	Masses of viable proliferating tumor cells in vertebra and surrounding muscles and ligaments
III Male, aged 19 years	Right scapula adjacent to glenoid. Biopsy: Ewing sarcoma	A total dose of 6,320 r to ant. and post. portals, 20×20 cm, including scapula and shoulder joint. Irradiation given over 29 days	Died twelve and a half months after treatment, of extensive disseminated metastases	Masses of viable tumour cells in bone at primary site, and extending beneath suprascapular muscles

[1]) Dosage expressed in r units measured in air (Wulf ionization chamber)

Clopton and *Womack* found that degeneration had occurred after irradiation. Their patient was a young woman of 24 who had a Ewing's sarcoma in her thigh. After irradiation she was free from pain for 14 days; the effect on the tumour itself is not recorded. After this initial period of 14 days, and in spite of further irradiation, the tumour began to grow again. The limb was amputated 8 weeks after the completion of the course of irradiation. Microscopic examination showed necrotic tissue with scattered accumulations of large, round, deep-staining nuclei and scant cytoplasm. In places the nuclei were quite irregular. The author ascribes these changes to irradiation: this would mean that the cells had been directly affected, but it is unlikely that this would still be visible 8 weeks after irradiation.

Brunschwig (1936) described 3 cases of Ewing's sarcoma which were unaffected by irradiation (see Table 1, which is taken from Brunschwig).

Kolodny (1927), *Phemister* (1931), and *Swensson* (1943), found no tumour cells present in their cases. Kolodny's case was a boy of 6 years who had a Ewing's sarcoma on his right tibia. For 2 years he had been treated for osteomyelitis. When the diagnosis of Ewing's sarcoma was established 2 series of irradiations were given and the tumour regressed. Two months after the last irradiation a large sequestrum was removed together with a considerable quantity of necrotic tissue. No trace of sarcoma could be found on microscopic examination.

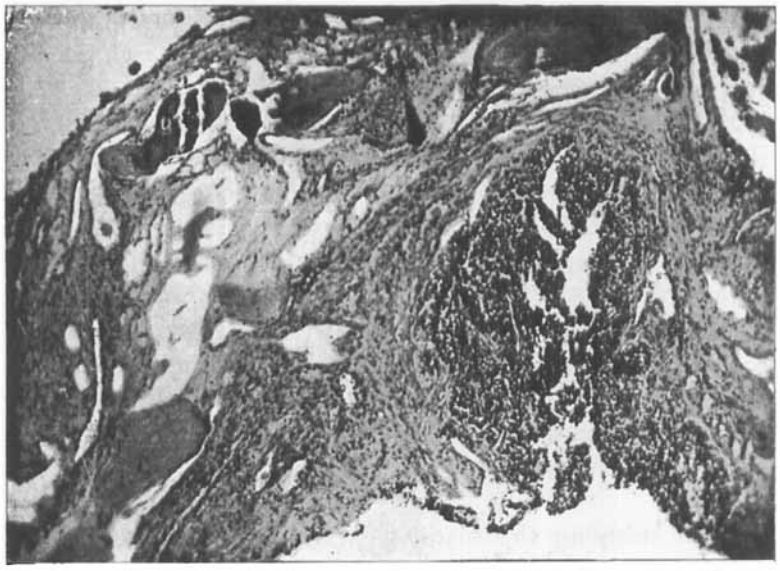
Phemister described a case of a Ewing's sarcoma on the clavicle of a man of 33 years. The author calls it an undifferentiated round-cell sarcoma, but both the histological description and the clinical course seem to point to a Ewing's sarcoma. A biopsy was made and a week later $^5/_7$ HED were administered and followed 2 months later by a further dose of 1 HED. The tumour disappeared. The clavicle was resected 4½ months after the biopsy and histological examination showed no trace of the tumour. Swensson's case was a 76-year-old man who had a Ewing's sarcoma in the humerus. The diagnosis was confirmed on surgical exploration. A

tumour dose of 3,500 r was administered and the limb was amputated. Histological examination showed that all the tumour cells had been destroyed.

Ewing (1929) points out that: "highly vascular tumours melt down rapidly under radiation from necrosis of capillary endothelium often with interstitial haemorrhage. Or the slow progress of obliterative endartheritis may sooner or later shut off the blood supply and lead to bulky necrosis".

Stewart (1933) "found an unusual circulation consisting of well-defined, thick-walled vessels" in resistant Ewing's sarcomata, and believes that "these circulatory conditions militate against sensitivity". He believes too that "there should be a decided change in the method of irradiation of these tumours. The massive doses should be replaced by divided irradiation".

While studying the histological changes in cases where irradiation had been employed the present author realised that an intimate knowledge of the spontaneous regressive and reactive processes connected with Ewing's sarcoma is essential for a proper understanding of the way in which radiation therapy acts. Clinical observations show that in Ewing's sarcoma characteristic periods of fever occur and that an increase in local temperature is accompanied by much greater congestion and swelling than in other tumours. These effects have been attributed to the reaction of the organism to the tumour in its effort to heal it. Undoubtedly the regressive changes are at least partly due to failure of blood supply and of nutrition: however, they may, to some extent, equally well be supposed to result from the reaction by the organism. The products of the disintegrated tumour cells may give rise to reactive processes and to the formation of connective tissue. However, regressive and reactive changes are so intimately interconnected that it is doubtful whether their cause can be distinguished. Several authors describe regressive and reactive changes. *Kolodny* (1927) states in his comprehensive study of bone tumours that "the gross anatomic appearance in Ewing's sarcoma is mainly a result of the agressiveness of the affected



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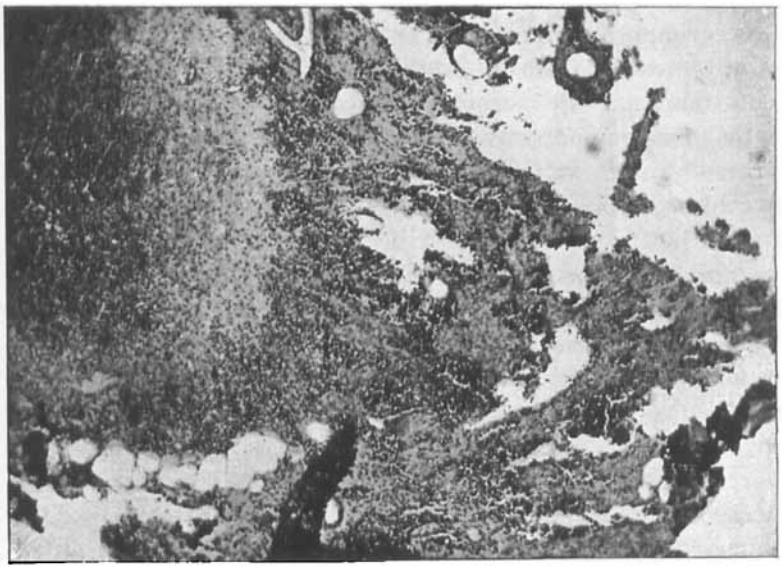


Fig. 2. 65 ×
Jnr. 16193/1943 (see Table II, no. 3 and page 20). Specimen from 1933.

bone and of the regressive changes in the tumour mass". The protracted and intermittent course of Ewing's sarcoma in some cases has also been described in detail. It seems that none of the authorities believes that these regressive and reactive changes and the characteristic course of the disease indicate a tendency towards spontaneous healing.

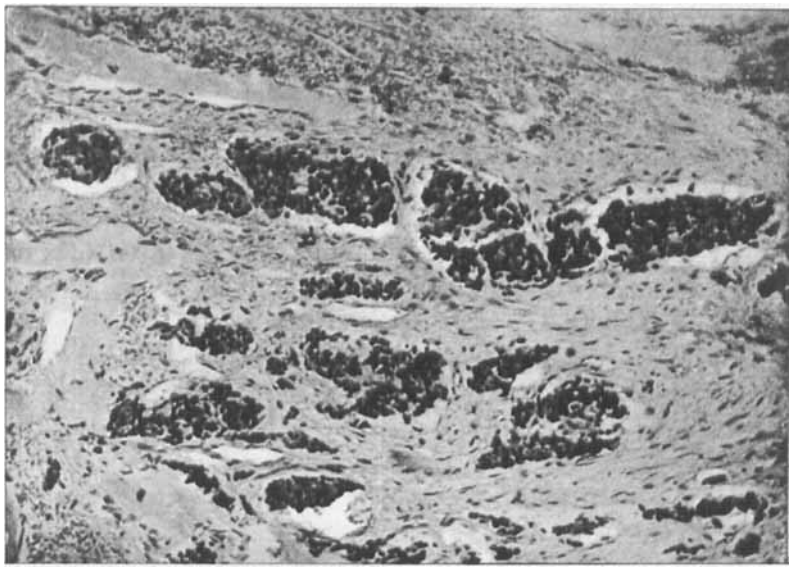


Fig. 3. 160 ×
Jnr. 13716/42. See table II, nr. 5. Specimen from 1942.

Regressive changes such as necroses, cyst formation and haemorrhages, have been described by *Kolodny* (1927), *Krayenbühl* (1929). *Borak* (1932), *Soeur* (1932), *Stewart-Harrison* (1934), *Hellner* (1935) and others. The following authors have studied the histology of regressive changes: *MacGuier* and *Whorter* (1924), and *Porter, Lenorgan* and *Gunn* (1936).

Schinz and *Uehlinger* (1931) and *Beck* (1941) hold that necroses, cysts and haemorrhages appear spontaneously and are the causes of changes in the size of the tumour. *Borak*

(1932), *Lattman* (1934) and *Geschichter* and *Copeland* (1936) suppose that variations in the size of the tumours are caused by the haemorrhages in it and their reabsorption. Borak observed that these changes in the size of the tumour corresponded with the periods of pyrexia.

With regard to the reactive processes the bone lamellae formed by the periosteum (onion skin layers) have been studied especially by the roentgenologists. *Kolodny* (1927) writes: "with the approach of the tumour cells to the outside of the bone the periosteum proceeds to its protective reaction". New bone layers are deposited on the bone mass when it reaches the cortex, and when the tumour penetrates this new bony shell another forms around it, and thus the typical layers of bone come into existence. This new bone formation has been recorded by *Krayenbühl* (1932), *Hellner* (1935), *Foote* and *Andersson* (1941), *Schinz* and *Uehlinger* (1931), *Stewart-Harrison* (1934) and *Swensson* (1943) found no new bone formation in cases which had had no treatment. *Geschichter* and *Copeland* (1936) found that the medullary cavity was often obliterated by new bone and state that "this reaction, we believe, is due to an attempt by the bone to heal in a manner often noted in fractures by a transition to osteoclasts and osteoid tissue".

Beck (1941) observed that the bone-marrow in the vicinity of the tumour became fibrous. *Geschichter* and *Copeland* (1936) pointed out that the tumour is often surrounded by a thin layer of connective tissue. *Kolodny* (1927) speaks of a thin pseudo-capsule confining the tumour but disappearing at a later stage when the tumour is more fully developed. *Geschichter* and *Copeland* (1936) and many other authors have described fibrous septa running radially through the tumour.

A zone of peripheral inflammatory reaction consisting mainly of lymphocytes has been observed by *Kolodny* (1927), *Schinz* and *Uehlinger* (1931), *Hellner* (1935), *Konjetzny* (1933) and *Geschichter* and *Copeland* (1936).

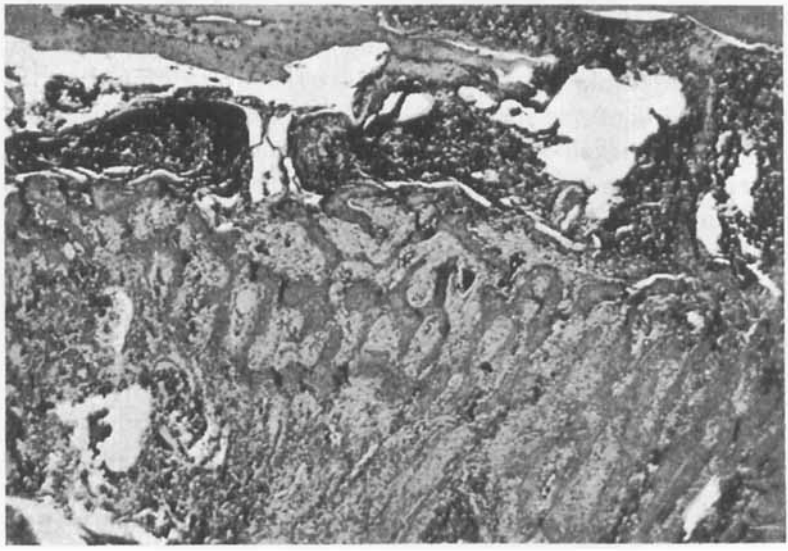
It has already been mentioned that some cases of Ewing's

sarcoma have a particularly protracted course. The reason for this, which is not common among other malignant tumours, may be attributed in part to the fact that for a long time the tumour is confined locally to a very small area and does not show any marked tendency to expand, and further metastases do not occur in this stage. The protracted course of the disease was noted by Geschichter and Copeland (1936) who analysed their cases and found that before 1930 the average time between the appearance of a Ewing's sarcoma as a tumour and its definite diagnosis was 13.5 months; after 1930 the time was 8 months. In 2 cases the patient gave a history of over 4 years (how long the swelling had been noticed was not stated) and in 3 cases of 5, 7, and 10½ years respectively, before a definite diagnosis was made. The case with a history of 7 years had had swelling from the beginning.

Of 37 cases published by Hamilton (1938) 2 gave a history of over 4 years, another 2 of 3½ years, one of 3 years, 2 of 2½ years, and 4 of 2 years.

Campbell and Hamilton (1938) describe a patient suffering from "rheumatic pains" for 4 years before the correct diagnosis of Ewing's sarcoma was made. Foote and Andersson (1941) describe a Ewing's sarcoma of the 7th rib of a fifteen-year-old boy who had intermittent pain for 8 years before the disease could be correctly diagnosed. Most authors who have studied Ewing's sarcoma have called attention to the intermittent character of the symptoms.

The present author proposes to discuss both the changes which take place in Ewing's sarcomata after irradiation treatment and the regressive and reactive changes in cases where irradiation treatment has not been given. These last have led him to believe that Ewing's sarcoma tends to heal spontaneously. He has been able to study cases of Ewing's sarcoma which have been examined histologically and treated at the "Radiumhemmet" in Stockholm and at the Radiological Clinic in Lund. The material consists of 17 cases treated with irradiation and 16 untreated cases.



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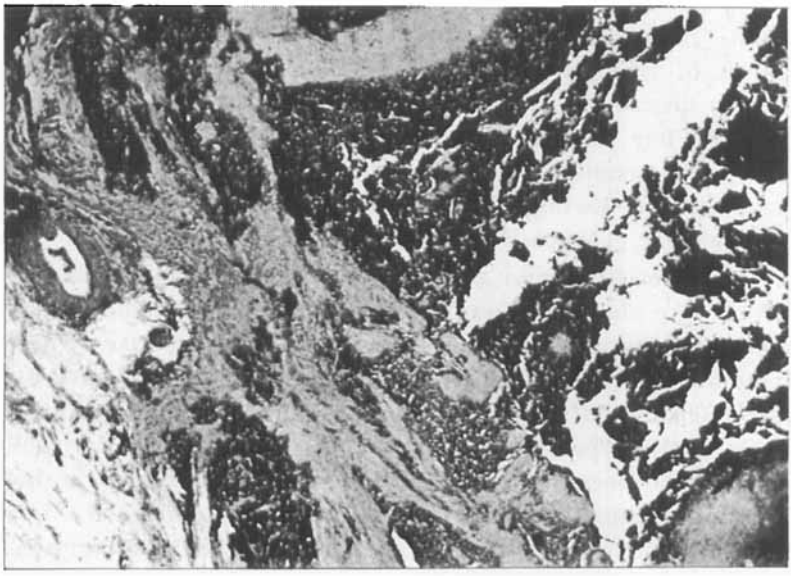

Fig. 4. 25 ×

Jnr. 10279/1940. See Table II, no. 6.

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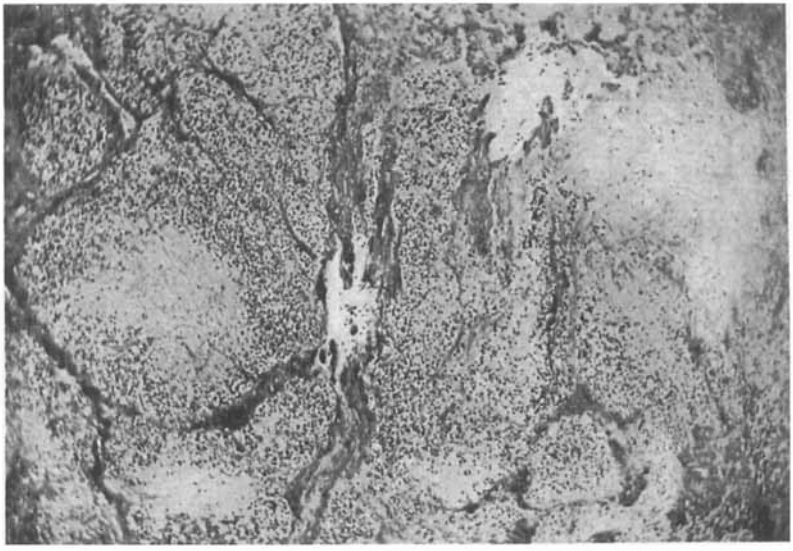


Fig. 5. 85 ×

Jnr. 7898/1937. See Table II, no. 12.

Table

Case No.	Sex Intials Hospital No.	Date of Admission	Age on Admission (Years)	Tumour Site	Past history	Clinical findings	Irradiation	
							Date	Dose of 1 single course
1.	*M.* A. K. M. 6717/37	6.8 1937	22	R. humerus	1 year	Pain and swollen right upper arm. Treated as osteitis.	9.8.— 23.8. 1937	400 r
2.	*M.* B. E. O. 7025/41	10.5. 1943	33	Sternum	4 months	Swelling in sternum. Pain. Lassitude. Loss of weight.	12.5.— 17.6. 1941	300 r 400 r
3.	*F.* B. I. E. 16193/43	1933	6	R. Tibia	3 years	1933 limp. 2 pathological fractures.	—	—
		3.11. 1943	16		12 years	1943. Intermittent swelling, pain and fever.		
4.	*M.* F. L. H. 9892/42	26.6. 1942	19	Os ilium	4 years	Intermittent low-back pain with sciatic radiation. Stiffness and pain in left hip-joint.	2.7.— 20.7. 1942	*Postope-* 300 r
5.	*M.* F. H. 13716/42	14.10. 1942	35	10 th. L. rib.	2 months	Rapidly increasing swelling. No pain.	14.10.— 27.10. 1942	*Postope-* 300 r 400 r

2.

(Skindose) Total Dosage	Field (Area of Exposed Tissue)	Operative Interference: Date of	Operative Interference	Histological findings	Time Lapse without Symptoms	Recurrence after	Result
2,800 r 2,800 r	Medial Lateral		None	Tumour invaded by diffuse fibrosis. Necrosis, newly formed bone. Haemorrhages.	None		Died of metastases in 5 months
2,700 r 2,700 r 500 r 1500 r × 2	Frontal Lateral Posterior Mediastinum		None	Connective tissue abundant partly as pseudocapsule. Haemorrhages, Necrosis, Pyknosis, Karyolysis, Karyorrhexis affecting nuclei.	None		Died of metastases in 1 month
—	—		Excision + insertion of bone graft	1933. Tumour poorly vascularisized. Dense connective-tissue and newly formed bone partly surrounding tumour as a capsule. No degenerative changes. Lymphocytes. (Fig. 2).	9 years	9 years	
		17.11. 1943	Amputatio cruris dexter.	1943. Tumour with large vessels. Haemorrhages. Thromboses. Coagulation necrosis. Karyolysis,. Karyorrhexis, Pyknosis. Little connective-tissue.	6 months		Died of metastases in a year
rative 2,700 r	Frontal aspect	26.2. 1942	Laminectomy	Tumour with thick-walled blood vessels. Large, partly liquefactive necrosis. Normal tumour tissue around blood vessels. Karyolysis. Karyorrhexis. Pyknosis.			
		13.6. 1942	Exposure of tumour	Metastases: poorly vascularized. Rosette-like formations.	None		Died of metastasis in 1 month
rative		1940	Resectio costae	*1940.* Tumour presenting large thin-walled cystic areas. Dense pseudocapsule of connective tissue. A few cells with pyknosis.	2 years	2 years	Alive in good health
2,100 r 2,100 r	Posterior aspect.	1942	Recurrence, reoperated	Cystic areas compressed to form clefts. Connective tissue more abundant. Bone formation. (Fig. 3).	5 years	—	Alive in good health

Table

Case No.	Sex Intials Hospital No.	Date of Admission	Age on Admission (Years)	Tumour Site	Past history	Clinical findings	Irradiation	
							Date	Dose of 1 Single course
6.	*F.* H. E. M. 10279/40	24.10. 1940	20	L. Tibia	6 months	Hydrops, pain. High sedimentation rate. Symptoms appeared in connection with pregnancy.	27.11. 1940— 7.2. 1941	*Postope-* 400 r 300 r
7.	*F.* I. H. M. A. 11248/40	29.11. 1940	24	L. Fibula	(recurrence)	Intermittent swelling and pain.	18.12. 1940— 11.1. 1941	*Postope-* 400 r
8.	*M.* J. G. 3910/27	30.8. 1927	26	R. Femur	3 years	Intermittent pain. Pathological fracture.	May— Nov. 1929	1/4 HED 1/3 HED
9.	*F.* L. I. B. M. 12057/43	22.5. 1943	14	L. inguinal region	3 years	Intermittent pain in left hip-joint. Treated as Tb. coxitis.		
10.	*F.* De L. M. A. 8981/43	2.9. 1940	13	L. sacro-iliac. region	1 month	Backache. Fever. Loss of weight. Palpable masses in skull.	Sept.— Nov. 1940	
11.	*F.* L. S. Lund	4.1. 1941	1	L. Temporal.	14 days	Swelling. Numbness. General decline. Facial paralysis.	3.1.— 12.2. 1941	100 r 200 r

2 (cont.)

(Skindose) Total Dosage	Field (Area of Exposed Tissue)	Operative Interference: Date of	Operative Interference	Histological Findings	Time Lapse without Symptoms	Recurrence after	Result
rative 1500 r 2400 r 800 r	Different areas	1.11. 1940	Amput. femor.	Bone destruction. Bone formation. Diffuse fibrosis. Coagulatory and liquefactive necrosis. Connective tissue ingrowing in coagulation necrosis. Spicule formation. Degenerative cells. (Fig. 4).	1 month		Died of metastases after 2 months
rative 2,400 r 2,400 r 2,400 r	 Medial Lateral Inguinal	1935 5.12. 1940	Amp. antecrur. Recurr. Operation repeated	(Recurrence). Tumour with numerous blood vessels presenting rosette-like arrangements. Connective tissue plentiful. Large necrosis. Degenerated cells.	5 years	5 years	Died of metastases in 7 years
× 25 × 8	Various areas of tumour	1927 1930	Scraping out of tumour Amputat. of femur.	1927. Thick-walled enlarged blood vessels. In places liquefactive necrosis with degenerated cells at borders. Thromboses and haemorrhages. Newly formed bone.	2 years	2 years	Died of metastases after 4 years
			None	Necrosis with some liquefaction. Haemorrhage. Degenerated cells. Moderate quantity of connective tissue. Lymphocytes.	None		Died of metastases in 3 mths.
	The whole irradiationtreatmt. consisted of small doses			Diffuse fibrosis throughout entire tumour. Fibrous capsule. Reactive bone formation.	None		Died of metastases after 5 months
1000 r 600 r	On tumour and cervic. lymph nodes			Powerful periosteal reaction with formation of bone and connective-tissue. Small necroses.	5 months	5 months	Died of metastases after 18 months

Table

Case No.	Sex Intials Hospital No.	Date of Admission	Age on Admission (Years)	Tumour Site	Past history	Clinical findings	Irradiation	
							Date	Dose of 1 single course
12.	*M.* O. G. H. 7898 37	13.10. 1937	26	L. Humerus	2 months	Stiffness, swelling and pain in right elbow. Treated as Tb. arthritis.	18.10. —2.11. 1937	400 r
13.	*M.* P. G. F. 4922 29	5.9. 1929	19	L. Scapula	5 months	Paraesthesiae in left arm.	1929 1930	1/4 H. E. D. 1/4 H. E. D.
14.	*M.* P. K. 7169 38	2.8. 1938	69	Vertebra	6 months	Increasing paresis below umbilicus.	2.8.— 6.8. 1938	400 r
15.	*F.* S. A. B. Lund	17.8. 1943	16	L. Ath. Rib.	10 days	Nodule observed. No pain.	17.8. —4.9. 1943	*Postope-* 300 r
16.	*M.* W. A. Lund	27.1. 1940	17	L. Scapula	6 months	Pain in left arm. Node observed. Postoperative. Raised sedimentation rate.	27.1. —28.2. 25.5.— 1.6 1940	*Postope-* 200 r 200 r

CASES WITHOUT IRRADIATION TREATMENT

(see Table 2)

In general the tumours showed the characteristic features of Ewing's sarcoma. In one case, however, large thin-walled cysts filled with blood were seen, and in 2 other cases the tumour had been penetrated by enlarged vessels with markedly thick walls. 2 specimens showed a rosette-like appearance of the tumour cells; one of these was a lung metastasis whose

2 (cont.)

(Skindose) Total Dosage	Field (Area of Exposed Tissue)	Operative Interference Date of		Histological Findings	Time Lapse without Symptoms	Recurrence after	Result
2,600 r 2,600 r	Outside Inside			Large coagulation necroses. Degenerated tumour cells. Dense connective-tissue ingrowing both in tumour and in necroses. Leukocytes and lymphocytes in the necrosed areas. (Fig. 5).	None		Died of metastases after 5 months
× 30 × 30	On tumour in 5 fields			Thick-walled blood vessels. Degenerated cells. No connective tissue.	1 year	1 year	Died of metastases after 18 months
2,000 r	One field on tumour			Moderate fibrosis. Moderate quantity of necroses.	None		Died of metastases and urinary infection after 2 months
ative 2,400 r 2,400 r	2 fields on operation-area	4.8. 1943	Resection of the 4th rib.	Diffuse pyknosis. Degenerated cells. Fibrosis. Newly formed bone.	3 years		Alive, in good health
ative 1,200 r × 5 1,600 r × 2	5 fields on tumour and metastasis	18.1. 1940	Resection L. scapula	Coagulatory and liquefactive necroses, partly disclosing leuko- and lymphocytes. Degenerated cells. Newly formed bone.	4 months		Died of metastases 8 months after operation

primary tumour did not show this appearance; the other was a metastasis in the soft tissues from a primary tumour which was not available for examination.

The following spontaneous changes were seen:

1) Regressive changes in the tumour cells with necroses.

2) Reactive processes, consisting of cellular infiltration, and the formation of connective-tissue and bone.

3) Haemorrhages and thromboses.

Regressive changes affected the nuclei (pyknosis, karyorrhexis, and karyolysis) and the cytoplasm. They were observed in some degree in nearly all cases, most frequently at the boundary between necrotic and normal tissue. Different stages of cell degeneration without actual necrosis have been found elsewhere in tumour tissue, both in solitary cells and in groups of cells. In many cases the final stage of cell degeneration has been a coagulation necrosis, the cell contours remaining intact and without any tendency to liquefaction. Here and there areas of necrosis have been observed where the tumour cells were converted into amorphous masses probably as a preliminary to liquefaction. It is impossible to predict with any certainty from the histological section the final outcome of the necroses, but it would seem that the necrotic material, even that of coagulation necrosis is to a great extent lysed without any appreciable interference from macrophages. A cystic area is formed by the lysis of a large number of necrotic areas.

In coagulation necroses it would be reasonable to expect that connective-tissue would grow in in several places. But there is little evidence of healing with subsequent formation of connective-tissue.

Connective tissue appears both on the periphery of the tumour and inside it. On the periphery it often appears in response to periosteal proliferation as a quite thick layer of dense capsule-like connective tissue, into which the tumour cells penetrate in slender radiation bundles and proliferations. In it cortical bone formation is seen both as a laminated expansion of the bone with parallel "onion-skin" layers of superficial ossification, and as spicules. Within the tumour the connective-tissue is found around the vessels. Large septum-like extensions also occur, dividing the tumour tissue into larger and smaller lobes and a more delicate fibrous meshwork has sometimes been seen. In a few cases the fibrosis was so pronounced that it was the predominating feature, the tumour tissue being divided into very small areas, many of which showed signs of more or less advanced degeneration.

The connective tissue formed from the periosteum is gradually incorporated into the tumour. Bone formation has also been seen in the centre of the tumour.

Haemorrhages were frequently found in the tumour; not all were of recent date, and therefore attributable to the opera-

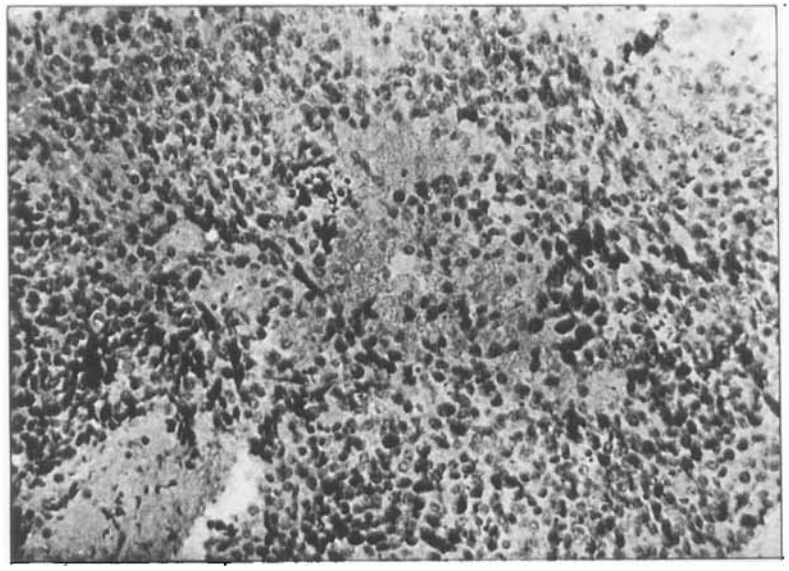


Fig. 6. 120 ×
Jnr. 4212/1939. See Table III, no. 18 and page 31.

tion: some were in fact much older. Blood pigment partly within phagocytes testified to reabsorption of the haemorrhages. Thrombi in various stages have been observed in richly vascular tumours. In one case they were accompanied by very large necroses in the tumour tissue.

A striking feature was the scarcity of inflammatory cells in the centre of the tumours. A few leucocytes, lymphocytes and plasma cells were seen in the necroses at the periphery.

Case No. 3 is of especial interest in the study of spontaneous changes on account of its long and unusual course. The patient

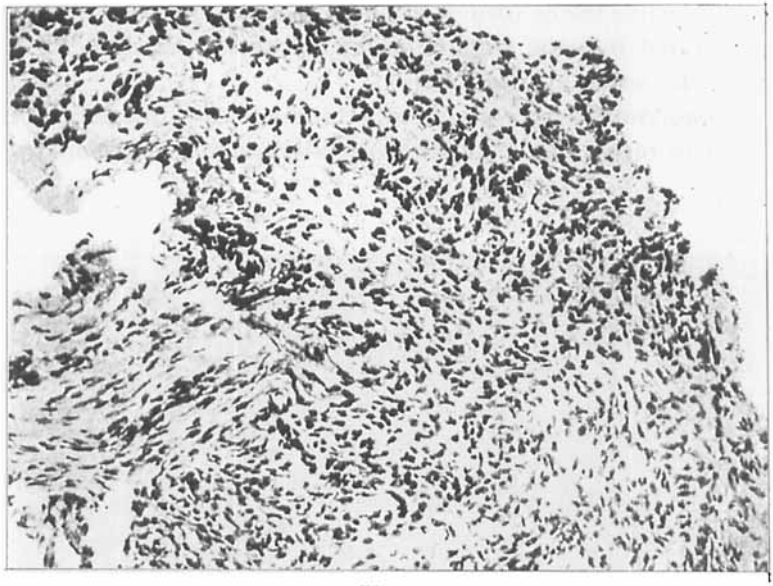


Fig. 7. 120 ×
Jnr. 4996/1936. See Table III, no. 23.

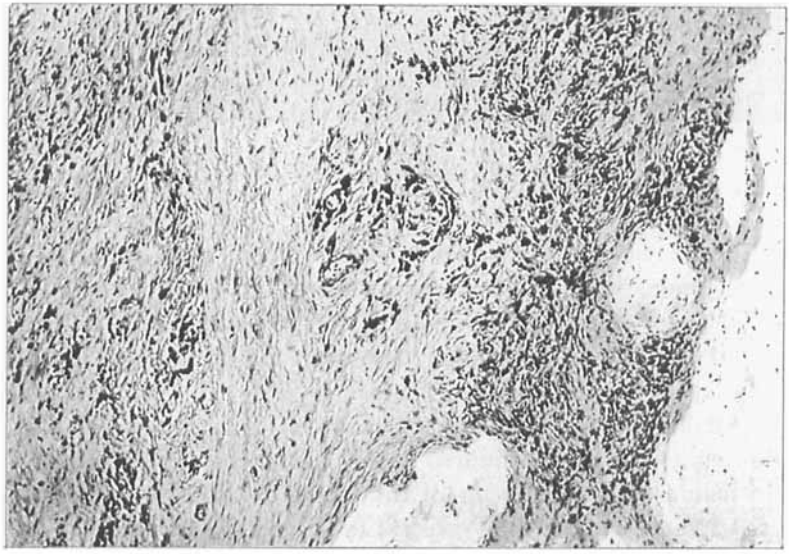


Fig. 8. 85 ×
Jnr. 4996/1936. See Table III, no. 32 and page 33.

was a girl of 7. In 1931 her mother noticed that she dragged her right lower limb and she was examined at St. Göran's Orthopaedic Clinic in Stockholm, with negative results. In 1932 she had a fracture of the upper third of the right leg. Radiography suggested a focus of osteitis fibrosa besides the fracture.

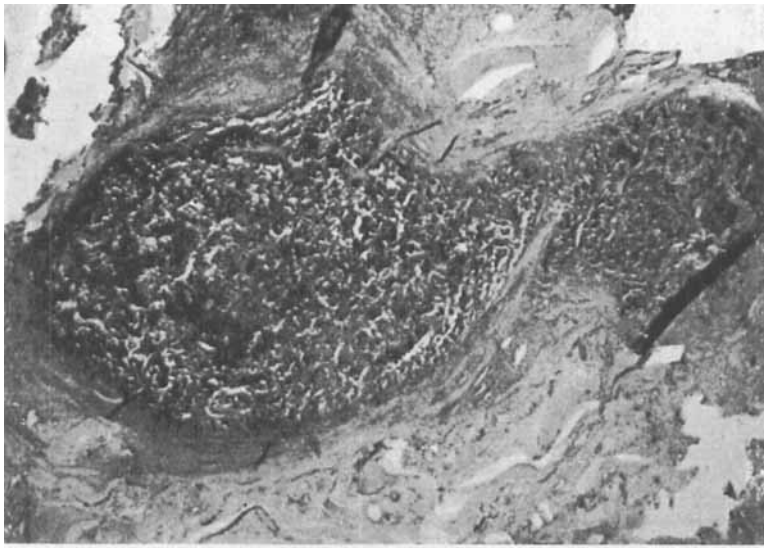


Fig. 9. 20 ×
Jnr. 6163/1938. See Table III, no. 25 and page 32.

Plaster of Paris was applied for 6 weeks and the fracture healed but the roentgenogram showed a persisting plum-sized cyst with a thin cortex. On September 17th, 1933 the patient was readmitted to the Clinic with a refracture. On September 21st os purum was grafted deep to the periosteum of the left tibia (Professor Waldenström). On October 23rd the graft was removed and introduced as os novum deep to the periostum of the right tibia at the level of the cyst and the fracture. At operation the bone in the neighbourhood of the cyst was found distended with a mushroom-like appearance. The bone-marrow was scraped out for a considerable distance below the cyst.

Histological examination of the specimen (Dr. Wahlgren) suggested either a Ewing's sarcoma or a haemangio-endothelioma. The tumour was fairly poor in vessels; there was a considerable quantity of connective-tissue and newly-formed tissue, which had partly encapsulated the tumour, and a fair number of lymphocytes. No signs of degeneration were seen. (See fig. 2).

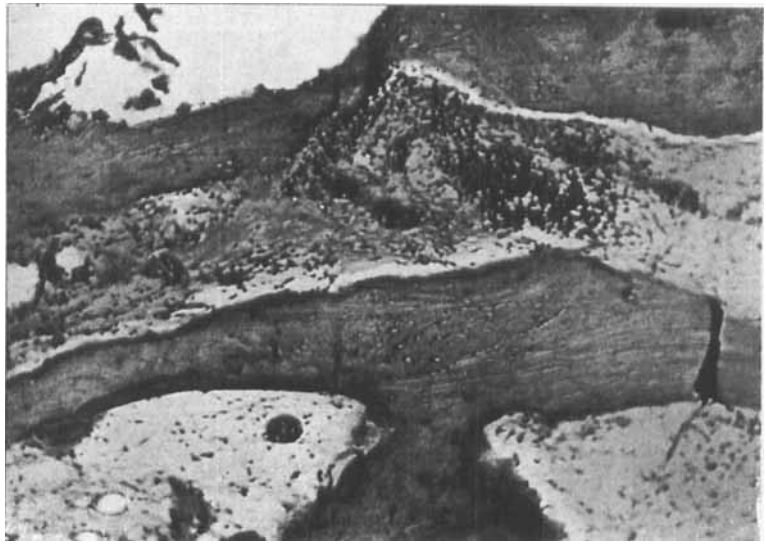
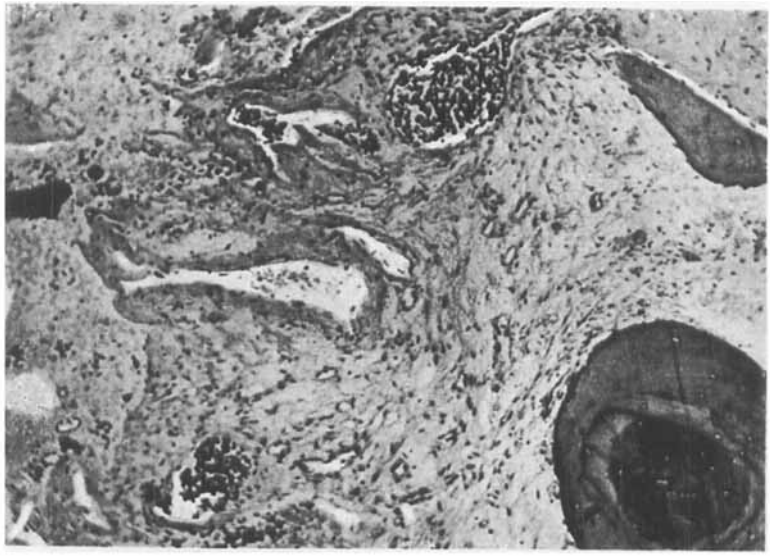


Fig. 10. 85 ×
Jnr. 717/42. See Table III, no. 28 and page 33.

On March 2nd the patient had completely recovered. Radiography showed consolidation and sclerosis of the cyst round the bone. Irradiation therapy was not applied and no further operation was done. The patient was examined regularly in the Orthopedic Clinic of the Karolinska Institute, Stockholm. The radiographs showed no change, and the patient remained symptom-free until the spring of 1943, when she noticed a swelling on the inside of the leg at the site of the old fracture. The swelling became alternately larger and smaller, the variations in size corresponding frequently with pyrexia. On November



85 ×

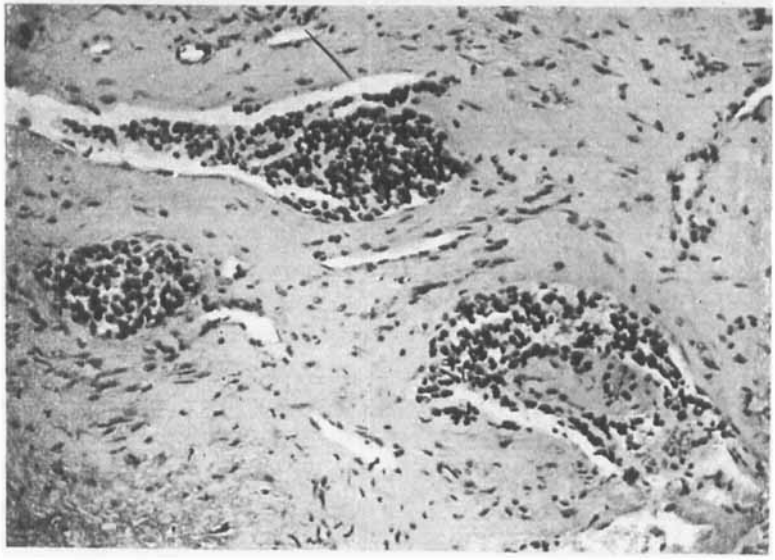


Fig. 11. 160 ×

Jnr. 7308/1942. See Table III, no. 30.

2nd 1943 she was readmitted and was found to have a swelling the size of a plum on the inside of the right leg. Radiography showed that the cystic focus had considerably increased in size and on November 28th the leg was amputated above the knee (Professor Friberg). Histological examination (Professor Reuterwall) showed the characteristic features of a Ewing's

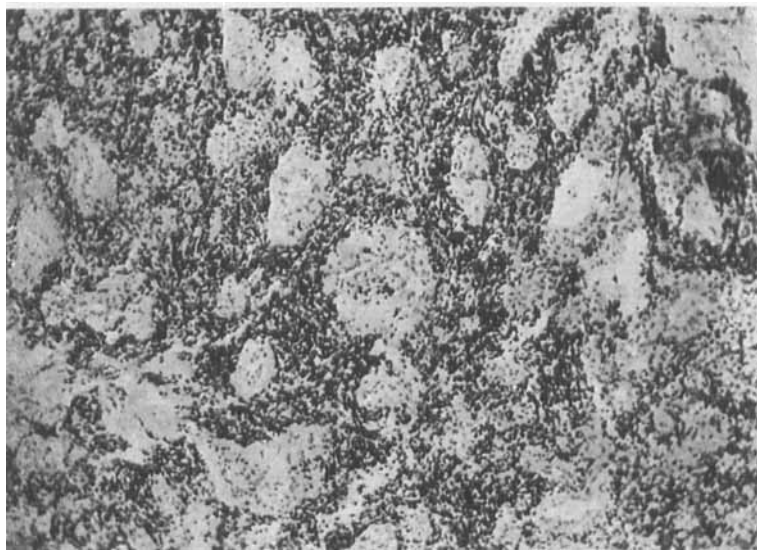


Fig. 12. 85 ×
Jnr. 8606/1937. See Table III, no. 33 and page 34.

sarcoma; there were a fair number of coarse, thick-walled vessels, necroses, haemorrhages, thromboses and degenerated cells; there was, however, little connective tissue present. The appearance was very similar to that of the 1934 specimen which must, therefore have been a Ewing's sarcoma. On September 18th 1944, the patient died of metastases.

In this case the first histological examination, made about 3 years after the onset of symptoms showed tumour tissue rich in connective tissue but with few vessels. After operation when the bone marrow had been removed and the graft inserted healing took place with consolidation and sclerosis

of the bony tissue surrounding the cyst. Recurrence only occurred some 9 years later, when a swelling the size of a plum was observed. At this later stage the histological appearance was different: necroses, haemorrhages, thromboses and degenerated cells were all found and there was less connective tissue.

CASES TREATED WITH IRRADIATION

(see Table 3, where the cases are arranged approximately according to the irradiation dose)

Case 17. This small dose does not seem to have affected the tumour cells.

Case 18. Marked degeneration of nearly all the tumour cells. The nuclei show karyorrhexis, karyolysis, and pyknosis. The cytoplasm shows signs of degeneration with ragged blunt contours. Pseudoclumping is affecting a large number of the tumour cells giving them the appearance of giant cells. Many of the cells have necrosed and formed amorphous masses in which the cell contours cannot be distinguished.

Case 19. There are a fairly large number of necrotic areas due to thrombosis, lying in normal tumour tissue, and in their border zones the nuclei show karyorrhexis, karyolysis and pyknosis and are surrounded by degenerating cytoplasm. Here and there tumour cells have coalesced to form structures resembling giant cells. In one part a barrier of fibrous connective-tissue and new bone is seen between the tumour and the normal tissue. This tumour resembles closely that of Case No. 3. It is not possible to determine with any certainty which of the changes are due to irradiation.

Case 21. There is a large quantity of normal tumour tissue enclosed in a thick, loose capsule of connective-tissue, which also contains many tumour cells, either singly or coalesced to form structures resembling giant cells. These

Tabl

Case No.	Sex Initials Hospital No.	Date of Admission	Age on Admission (Years)	Tumour Site	Past history (Years)	Clinical findings	Irradiation			
							Before pathological diagnosis			Field of Radiation (Area) of exposure
							Date	Dose of 1 course	Total dose	
7.	*F.* B. N. M. 8300/39	8.8. 1939	13	L. 2nd. rib.	5/12	R. pleural exudate with stabbing pain. High sedimentation rate. Treated as Pulmonary T.B.	9.8.— 10.8. 1939	100 r	200 r	Frontal
8.	*M.* E. K. G. 4212/39	17.3. 1939	13	R. 10th. rib.	5/12	Stabbing pleuritic pain. Cough. Loss of weight. A palpable node.	23.3.— 28.3. 1939	100 r	200 r 100 r	Dorsum Lateral
9.	*F.* F. S. Lund	10.7. 1933	13	Skull. Pelvis 4th lumb. verteb.	4/12	Intermittent swelling in inguinal region. Temperature. Backache. Headache.	17.7. 1933	1/4 HED ca. 250 r	1/4 HED ca. 250 r	On 4th lumbar-vertebra
0.	*M.* N. A. S. 6005/34	18.8. 1934	25	Pelvis Sacro-iliac. Toint	11/12	Low-back pain. Loss of weight. Treated as T.B. Fever.	18.8.— 28.8. 1934	1/4 HED 1/8 HED	1/4 HED 1/8 HED	Dorsum
1	*M.* O. T. S. 6449/35	9.9. 1935	10	L. 6th. rib.	1/12	Palpable tumour. Mild pain.	10.9.— 14.9. 1935	1/6 HED	1/6 HED ×3 c. 525 r	Dorsum
2	*M.* F. G. B. 6601/38	4.9. 1938	20	R. os pubis	6/12	Intermittent pain located to right hip-joint. Increasing swelling.	6.7.— 9.7. 1938	300 r 400 r	700 r 700 r	Dorsum Anterior aspect.
3	*F.* J. B. G. 4996/36	29.5. 1936	20	L. 7th. rib.	9/12	Intermittent periods of stabbing pleuritic pain.	27.5.— 8.6. 1936	250 r	500 r 500 r 750 r	Anterior posterior superior surfaces

Skindose) Total Exposure to Rays	Reaction to Radiation	No. of days between last exposure and path. examination	Operations		Histological findings	Period without Morbid Signs (Years)	Recurrence (after) (Years)	Result
			Date					
1450×3 1000×3 2100×3 1800	++	1		None	Tumour cells of normal appearance. Isolated lymphocytes.	2,5	2,5	Death from metastas after 3, years
1200×3 1300×3	++	3		None	Almost all cells show degenerating amorphous necroses. Some cells show tendency to melt together. (Fig. 6).	2/12	No	Death from metastas after 2 months
1/4 HED ×3 1/6 HED ×3	+	20		None	Mainly normal tumour cells. Degenerative cells. Necroses. Connective tissue and newly formed bone in shape of capsule.	None	No	Death from metastas after 1 mont
do.	++	1		None	Normal tumour cells. Small areas undergoing necroses.	6/12	6/12	Death from metastas after 8 months
do.	+++	34	18.10. 1935	Resection 5th—8th L. ribs	Partly massive decomposition of cells, partly entirely normal tumour cells in areas confined by pseudocapsule of connective tissue.	8	No	Death from metastas after 8, years
1500 r ×2	++	1		None	Chiefly normal tumour cells, some show mild degenerative changes.—Necroses.	None	—	Death from metastas after 3 months
2600 r ×3 2250 r 1500 r 2000 r	+++	1		None	Cells with pyknosis in most parts. Moderate quantity of lymphocytes. (Fig. 7).	cf. Case No. 32		

Tabl

ase No.	Sex Initials Hospital No.	Date of Admission	Age on Admission	Tumour Site	Past. history (Years)	Clinical findings	Irradiation			
							Before pathological diagnosis			Field of Radiation (Area of exposure)
							Date	Dose of 1 course	Total dose	
4.	*M.* M. G. 1773/4	3.2. 1943	29	R. Tibia	1/12	Swelling and pain of intermittent type and tenderness of right leg.	8.2.— 11.2. 1943	200 r 300 r	500 r 500 r	Lateral Medial
5.	*M.* L. K. G. 6163/38	15.6. 1938	15	L. Radius	2	Intermittent swelling and pain in left arm. Fever. Increased sedimentation rate.	16.6.— 26.6. 1936	300 r	600 r 600 r	Frontal Posterior
6.	*M.* B. J. Lund	17.8. 1940	12	L. Fibula	3	Intermittent swelling and pain. Stiffness in ankle-joint.	17.8.— 30.8. 1940	200 r	1200 r 1200 r	Lateral Medial
7.	*F.* A. U. B. 1501/37	8.2. 1937	13	2nd. R. rib.	1/12	Observed a growth. No discomfort.	22.2.— 16.4. 1937	200 r 250 r	2500 r	Frontal
8.	*M.* F. T. G. 717/42	10.1. 1942	9	L. Clavicle	1/12	Fracture of clavicle. 6 months later: tumour at site of fracture.	10.1.— 24.1. 1942	300 r	3000 r	Frontal
9.	*M.* J. M. Lund	15.12. 1931	30	10th. L. rib.	4/12	Trauma. Pain and fever of intermittent type.—Tumour.	18.6.— 26.6. 1935 9.3.— 27.3. 1936	235 r	1310 r ×4	4 fields c metastasi in left pleural dome
0.	*M.* R. S. T. F. 7308/42	28.4. 1942	25	L. Ilio-sacral region	3/12	Pain of intermittent type in left hip. Fever. Neurological alterations.	28.4.— 22.5. 1942	400 r	2800 r 2400 r 2400 r	Frontal posterior lateral

3 (cont.)

(Skindose) Total Exposure to Rays	Reaction to Radiation	No. of days between last exposure and path. examination	Operations: Date	Operations	Histological findings	Period without Morbid Signs (Years)	Recurrence (after) (Years)	Result
500 r ×2 25 r ×10	++	4	15.2. 1943	Amputation R. femur	Almost whole tumour necrotic. No normal tumour cells. Scanty connective tissue.	4	No.	Alive, in good health
600 r×2 2000 r ×2		22	18.7. 1936	Resection L. radius	Necrosis involving most parts of tumour. Entirely normal tumour cells in fibrous, collagenous pseudocapsule. (Fig. 9).	10	—	Alive in good
12 do.		11	10.8. 1940	Amputation antecrur. sin.	Necrosis affecting most portions of tumour. Normal tumour cells found in connective tissue.	2,5	—	Death from metastases after 3 years
do.		7	23.4. 1937	Resection of 2nd. R. rib.	Normal tumour cells found in connective-tissue. Necrosis involving most portions of tumour.	10	No.	Alive, in good health
do.	+++	38	4.3. 1942	Resection of L. Clavicle	Normal tumour cells within a restricted area. No trace of tumour cells elsewhere. (Fig. 10).	4/12	—	Death from metastases after 6 months
On tumour 1/5 HED ×10 in 3 courses	+++	34		None	(Specimen of the metastasis of the left lung): Normal tumour cells in abundant connective tissue.	3,5	—	Death from metastases after 4,5 years
do.		1		None	Small patches consisting of normal tumour cells in massive connective tissue. Small necroses; also degenerating cells. (Fig. 11).	None	—	Death from metastases after 1 month

Table

Case No.	Sex Initials Hospital No.	Date of Admittsion	Age on Admission	Tumour Site	Past. history (Years)	Clinical findings	Irradiation			
							Before pathological diagnosis			Field of Radiation (Area of exposure
							Date	Dose of 1 course	Total dose	
31	*F.* O. A. Lund	7.2. 1940	20	12th. Thoracic Vertebra	6/12	Backache. Weariness. Fever. Treated as Tb spondylitis.	Febr. 1940 Jan. 1941	200 r	3400 r 1600 r 800 r 800 r	Posterior Anterior Left side Right side
32	*M.* J. B. G. 4996/36	29.5. 1926	20	L. 7th Rib.	9/12	Cf. case 23.	27.5.—8.7. 1936	250 r 350 r	2600 r 2250 r 2500 r 2000 r	Frontal Posterior Dorsum upward Front upwards
32	*F.* E. M. 8606/37	17.11. 1937	16	R. femur	2,5/12	Pain and decreased range of movement in right hip-joint. Fever. Loss of weight.	18.7.—11.10. 1938	400 r	2000 r ×2 2700 r ×2 (Ra)	Several fields on metastasis in supraclav. region

tumour cells show all stages of degeneration down to necrosis. Here and there in the connective-tissue are empty spaces containing necrotic tumour remains. Macrophages are also found. It is worth noting that the tumour mass which is within the connective-tissue capsule has remained quite unaffected. From a clinical and roentgenological point of view this tumour had responded very well to treatment, and one may therefore attribute the cell destribution to the irradiation.

Case 22. The tumour has a varied structure. In some areas there are many vessels and in others vessels are scarce. No changes in the tumour cells could be detected in the former but there were degenerative changes in the tumour cells of the latter: karyorrhexis, karyolysis and pyknosis. It is not

3 (cont.)

(Skin dose) Total Exposure to Rays	Reaction to Radiation	No. of days between last exposure and path. examination	Operations		Histological findings	Period without Morbid Signs (Years)	Recurrence (after) (Years)	Result
			Date					
Same dosage and high doses on metastasis	++	60		None	Normal tumour cells in abundant connective tissue. Radio-influence on tissue shown.	2/12	2/12	Death from metastasis after 3 months
Same dosage and high doses on metastasis	+++	64	12.9. 1936	Resect. L. rib.	Disintegrated tumour cells in fibrosed connective tissue. No evidence of normal tumour cells. (Fig. 8).	1,5	—	Death from metastasis after 2 years
Same dosage and high doses directed to right hip.	+	47		None	(Metastases in supraclavicular region). Normal tumour cells in abundant fibrous connective tissue. Tissue shows obvious evidence of radioinfluence. (Fig. 12).	None	—	Death from metastasis after 2 months

possible to determine how far these changes are due to the irradiation

Case 24. In this tumour all stages of cell disintegration are seen; none of the tumour cells appear normal. A fine network of connective-tissue has grown into the large areas of coagulation necrosis from the surrounding tissue, though the connective-tissue proliferation is slight. Large numbers of lymphocytes are present. Both clinically and radiologically the tumour had reacted very favourably to irradiation.

Case 25. A radial section was examined. Most of the tumour has undergone coagulation necrosis and is invaded by lymphocytes, phagocytes and connective-tissue trabeculations. As

three weeks elapsed between the irradiation and the operation the necroses can be ascribed to the effects of the irradiation. In a small section which is surrounded by a thick capsule there are tumour cells of normal appearance.

Case 27. This case demonstrates three ways in which necroses in the tumour are affected: 1) Calcification. 2) Ingrowth of connective-tissue into coagulation necroses. 3) Resorption of liquefied areas. Within the masses of connective-tissue where fibrous matter is particularly plentiful areas of normal tumour are found. Calcification of a necrotic area was not seen in any other case.

Case 28. In the control preparation which was taken before irradiation the tumour cells were arranged in rosettes. Careful examination of the clavicle resected after irradiation shows a small area of tumour cells of normal appearance enclosed in fibrous connective-tissue, and otherwise no remains of either necrotic or living tumour cells. The entire bone-marrow is invaded by fribous proliferations, and has been infiltrated by large numbers of lymphocytes and plasmocytes.

Case 31. The tumour is well preserved in spite of a prolonged course of irradiation with large doses. It has been taken from the twelfth thoracic vertebra and the os ilium. It is noteworthy that the tumour of the ilium contains large thin-walled lacunae filled with blood, while the tumour from the vertebra has the typical appearance of a Ewing's sarcoma.

Case 32 is No. 23 after completion of the irradiation treatment. When this tumour had been treated with small doses there was already considerable regression of the tumour; now it seems to have withered completely under the supplementary doses. Large numbers of disintegrated darkly-staining fragments of tumour cells mottle the fibrous connective-tissue.

Case 33. In spite of strong irradiation the tumour has not shown much response clinically, and this is supported by the pathological examination. The tumour is penetrated by coarse thick-walled blood vessels, and corresponds to the type of Ewing's sarcoma which Stewart described and found to be only slightly sensitive to radiation therapy.

DISCUSSION

Cases where no irradiation had been used showed some spontaneous degeneration and destruction of the tumour cells with necroses and haemorrhages.

In the necrotic areas the structure of the tumour cells is preserved to about the same extent as in rapid coagulation necrosis; but sometimes formations resembling colliquative necroses with rapid lysis of the cells was seen. But even in necroses in which the tumour structure is relatively well preserved, lysis soon follows. As a rule there is no marked reactive cell infiltration. Macrophagocytes are absent. The ingrowth of connective-tissue is comparatively rare, though it is seen occasionally.

The periosteum on the periphery of the tumour seems to be able, by its reaction, to form for a considerable time a barrier against the tumour's penetration into the soft parts. In the present author's case the cellular reaction round the tumour was not enough for it to be attributed to osteomyelitis.

Frequent haemorrhages in the tumours are probably one of the factors causing rapid variation in their size. Probably these haemorrhages both directly and indirectly cause atrophy of the tumour cells, and the thromboses which are sometimes seen have the same effect. Necroses play a bigger part in the spontaneous regression of the tumours than has been described hitherto.

This destruction of tumour tissue, whether due to necrosis or to haemorrhage and its secondary effects is an important factor in the tendency of the tumours to spontaneous healing.

The origin of the necroses in Ewing's sarcoma is not known and is difficult to determine; but one is justified in assuming that they result mainly from nutritive disturbances due to insufficient blood supply to the rapidly and irregularly growing masses of tumour cells. In addition to the significance in this connection of thromboses and necroses which have already been mentioned, one may perhaps also envisage an anti-tumour reaction on the basis of immunological reactions, related to a general reaction which is shown by fever.

Cases which had had irradiation therapy showed disintegration of the tumour cells closely related to the irradiation. *Schinz* and *Uehlinger* (1931) and *Stewart-Harrison* (1934) described this as resembling a cytolytic reaction, but it may be pointed out that a similar picture, though to a lesser degree is seen even in cases, which have not been irradiated.

Of the author's cases, 7 have been examined in close relation to irradiation. Only one of them (no. 18) showed such a generalised effect on the cells.

The remaining cases were not examined until a later stage, after the immediate effects of the irradiation had subsided, when the disintegrated cells either remained as necrotic areas which did not stain or had been reabsorbed, and the histological findings resembled those seen in tumours which had not been irradiated.

Thus there is no definite qualitative difference between the later effects of irradiation and the spontaneous changes in a tumour. Quantitatively, however, there is a difference. The necroses which occur in irradiated cases are bigger and may in some cases involve the entire tumour; in addition, irradiated cases almost always show coagulation necroses, connective-tissue is formed more frequently and there is a marked tendency to form capsules, and inflammatory cells which are usually very rare are more numerous in cases which have been irradiated. Some tumours which have had large doses of irradiation have shown changes in the blood-vessels, which appear to be due to the treatment, though it has been difficult to demonstrate a relation between these changes and

specially marked destruction of the tumour cells. Haemorrhages seem to be rather less in the irradiated cases.

Thus we may conclude that the effect of irradiation on Ewing's sarcoma is to intensify the changes which take place spontaneously. It is certain that complete healing of the primary focus can occur, and in this respect Case 3 is of special interest; the tumour showed a definite tendency to spontaneous healing, and histologically connective-tissue was particularly abundant.

It has frequently been observed that Ewing's sarcoma first responds to irradiation, but later seems to become insensitive to the treatment. Pathological examinations suggest that this change in sensitivity is due to the increasing fibrosis. It has frequently been found that tumour tissue enclosed in a fibrous connective-tissue shows no sign of degeneration in spite of powerful irradiation; on the other hand specimens in which there is little fibrosis may also show well-preserved tumour cells, so that it appears that the tumour cells of a Ewing's sarcoma may themselves resist irradiation. The type of Ewing's sarcoma which has coarse blood-vessels appears to be resistant to irradiation from the beginning. This type has been described above, and has been observed previously by *Stewart*.

It appears that fibrosis may not only be the body's protection against the tumour, but also the tumour's protection against the irradiation treatment. Many of the cases showed groups of apparently viable tumour cells in the midst of massive connective-tissue. Are they about to disintegrate or are they enclosed in capsules in order later to revive and cause a recurrence or metastases? The frequency of recurrences in these cases ought to answer this question; but the cases in which a complete histological examination has been possible have also had an amputation or resection and the possibility of a recurrence at the primary focus had therefore been removed, and it is naturally not possible to determine whether a metastasis has arisen from these foci. However, it is clear that in spite of apparently satisfactory clinical regression of

the tumour there is still grave danger that viable tumour cells, resistant to irrradiation, still remain.

Since both spontaneous healing and irradiation produce changes which are similar in all essentials, and it is certain that healing does take place in some cases, it is reasonable to ask whether any cases of spontaneous healing have been observed. No such case has been found in the literature of the subject. However, it is interesting to compare the spontaneous healing of a retinoblastoma, a tumour which *Colville* and *Willis* (1933) and *Willis* (1940) consider to be closely related to Ewing's sarcoma. *Rönström* (1936) collected 7 reports of 7 cases in which spontaneous healing occured. *Kneeper* (1911), *de Klein* (1912) and *Lindenfeld* (1913) each described a case of double retinoblastoma where the eye was enucleated and the diagnosis was confirmed histologically. In all cases the other eye atrophied. Histological examination of the atrophic eye showed a healed retinoblastoma. *Siegrist* (1912), *Putscher* (1915), *Meller* (1916), *Salzmann* (1926) and *Hippel* (1928) describe cases of double retinoblastoma where one eye was enucleated and the other healed with a fair functional result.

Retinoblastoma is usually detected early; at any rate the retinoblastomata which healed were at very early stages of development, while a Ewing's sarcoma is rarely examined at such an early stage. It is justifiable to ask whether on the basis of this comparison with another tumour which appears to be closely related, a Ewing's sarcoma taken at a very early stage might not also heal spontaneously.

CONCLUSION

(1) Ewing's sarcoma shows a tendency to heal spontaneously. This can be demonstrated both clinically and histologically.

(2) The effect of irradiation on a Ewing's sarcoma may be divided into three different phases:

(a) the cytolytic phase, which is seen soon after a short period of irradiation.
(b) the necrotic phase which follows immediately after the cytolytic.
(c) the fibrous phase, which is first seen after a long period of irradiation.

(3) The histology of the fibrous and necrotic phases corresponds in all essentials with the findings of spontaneous reactive and regressive changes.
(4) A Ewing's sarcoma with numerous coarse blood-vessels is intrinsically less sensitive to irradiation after the first response. The insensitivity depends on fibrosis and probably also on changes in the internal constitution of the tumour cells.
(5) The fact that normal tumour cells may still be found in tumours that have been powerfully irradiated and have shown clinical regression of the tumour indicates that radiation treatment should be supported by surgery.
(6) There is no report of spontaneous healing of a Ewing's sarcoma in the literature, but its theoretical possibility is confirmed by comparison with retinoblastomata which are closed related to Ewing's sarcomata: several cases of retinoblastoma have been shown to heal spontaneously.

SUMMARY

A pathological study has been made of 33 Ewing's sarcomata. 17 had had various doses of irradiation before examination, and 16 had had no treatment. A short clinical description is given of all the cases. The changes of cytolysis and fibrosis which were observed in the cases which had been irradiated, were also observed, though to a lesser extent, in the untreated cases. This is interpreted as a tendency of Ewing's sarcoma to spontaneous healing. One case which was without symptoms 9 years after only conservative surgery seems to support this interpretation. Ewing's sarcoma is compared with the closely related retinoblastoma of the eye, of

which a number have been reported to have healed spontaneously.

Biopsy material from cases which have healed clinically after irradiation have shown large and small groups of apparently viable tumour cells. This observation suggests that irradiation should always be combined with radical surgery.

The presence of coarse vessels suggests resistance to irradiation.

RESUME

Il a été procédé à une enquête anatomo-pathologique de 33 cas de sarcome d'Ewing. 17 de ces cas avaient cependant été soumis à un traitement par rayons à différentes doses, avant l'examen. 16 cas n'avaient été soumis à aucun traitement. Il est donné une description clinique sommaire de tous les cas. Les modifications sous forme de cytolyse et de fibrose, observées dans les cas traités par rayons, ont été constatées également, quoique dans une moins grande étendue, dans les cas qui n'avaient pas été traités par rayons. Ceci est considéré comme la tendance qu'a le sarcome d'Ewing à la guérison spontanée. Un cas chez lequel aucun symptôme ne s'était manifesté pendant 9 ans, quoique soumis seulement au traitement chirurgical conservateur, semble appuyer cette opinion. Il est procédé à une comparaison avec le rétinoblastome de l'oeil, étroitement apparenté au sarcome d'Ewing, qui est indiqué dans plusieurs cas comme spontanément guéri.

Les préparations de résections de sarcomes d'Ewing provenant de cas guéris cliniquement par le traitement aux rayons ont montré des groupes plus ou moins étendus de cellules tuméreuses paraissant viables. Cette constatation semble montrer que le traitement par rayons doit toujours être combiné à un traitement chirurgical radical.

Il est donné une description de cas résistants au traitement par rayons et qui se caractérisent par de gros vaisseaux.

ZUSAMMENFASSUNG

Bei 33 Fällen von Ewing'schem Sarkom wurde eine pathologisch-anatomische Untersuchung vorgenommen. 17 von diesen Fällen waren vor der Untersuchung mit Bestrahlung von verschiedener Dosierung behandelt worden. 16 Fälle waren unbehandelt. Es wird eine kurze klinische Beschreibung aller Fälle gegeben. Die Veränderungen in Form von Cytolyse und Fibrosis, die bei den bestrahlten Fällen beobachtet wurden, fanden sich auch, wenn auch in geringerem Umfange, in den nicht bestrahlten Fällen. Dies wurde in dem Sinne aufgefasst, dass beim Ewing'schen Sarkom eine Tendenz zur Spontanheilung bestehe. Ein Fall mit 9jähriger Symptomfreiheit trotz nur konservativer chirurgischer Behandlung scheint diese Auffassung zu stützen. Es wird ein Vergleich angestellt mit dem Retinoblastom des Auges, das dem Ewing'schen Sarkom nahe verwandt ist, und von dem mehrere Fälle von Spontanheilung mitgeteilt worden sind.

Resektionspräparate von durch Bestrahlung klinisch geheilten Fällen von Ewingsarkom zeigten grössere oder kleinere Gruppen von anscheinend lebensfähigen Tumorzellen. Diese Beobachtung spricht dafür, dass die Bestrahlungsbehandlung stets mit einer chirurgischen Radikalbehandlung kombiniert werden sollte.

Bestrahlungsresistente Fälle, die durch grobe Gefässe gekennzeichnet waren, werden beschrieben.

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