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EFFECTS ON THE CARDIOVASCULAR SYSTEM OF IRRADIATION FOR MALIGNANT LYMPHOMA

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Complications from the cardiovascular system in connection with irradiation of malignant tumours were observed by COUTARD & LAVEDAN (1922) and have since then been repeatedly reported (LEACH 1943, HARTWEG 1960, JONES & WEDGWOOD 1960). The interest has been focused mainly on the heart and arrhythmias, exudative and constrictive pericarditis (COHN et coll. 1967, TENERIELLO et coll. 1970, GREENWOOD et coll. 1974) myocardial fibrosis, abnormalities of the coronary arteries (TRACY et coll. 1974) have been reported. ECG abnormalities have been described by WHITFIELD & KUNKLER (1957) as well as abnormalities observed in the light microscope (cf. JONES & WEDGWOOD) and in the electron microscope (BURCH et coll. 1968). However, the opinions differ regarding the frequency and severity of the injury to the heart caused by radiation therapy of tumours in its neighbourhood (VAETH et coll. 1961) as well as the pathogenesis behind the changes observed. Irradiation may produce tissue injury directly or secondarily to vascular injury, but autoimmune reactions have also been suggested (ELLINGER 1957, GIARD & CRINQUETTE 1970).

At Radiumhemmet a series of patients has been examined regarding complications from the cardiovascular system in connection with irradiation for a variety of malignant tumours. The incidence and type of complaints and ECG abnormalities have

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Table 1

Patient material and radiation treatment given

Irradiated region	No. of patients	Additional treatments during follow-up period*	Total absorbed dose (Gy)	Treatment period (days)
Head, neck, supraclavicular fossa, axilla	5	4	24–50	15–54
Mediastinum	36	11	12–58	16–84
Mantle technique	(27)	11	21.7–46	33–84
Other technique	(9)		12–58	16–55
Abdomen	12	2	12–44	17–63
Inverted Y-field	(10)	2	28–44	32–63
Other technique	(2)		12–43	17–53
Groin	2		24–35	20–35
Total	55			

* The same regions irradiated as in the first column.

been recorded as well as blood pressure changes. Their functional importance was evaluated by exercise tests before and after the treatment. The results in patients with malignant lymphomas are now reported.

Material

The material consisted of 55 patients (30 males and 25 females) irradiated for malignant lymphoma during the years 1969 to 1971. For technical reasons it was not possible to use all types of tests in each patient; in 4 patients only blood pressure and heart rate were recorded.

The irradiated region and the distribution of the patients are given in Table 1, together with the absorbed tumour doses and the total period of treatment. Additional irradiation was given in some cases during the follow-up period. The patients were treated either with a ^{60}Co therapy unit or with roentgen radiation from a 6 MV linear accelerator. In general the patients were irradiated five days a week with a daily tumour dose of 2 Gy (200 rad). The mediastinum was irradiated with the mantle technique in 27 of 36 patients. In 10 of 12 patients with abdominal irradiation the inverted Y-field technique was used.

Methods

ECG was recorded with a Mingograf 61 or 81 (Siemens-Elema, Solna, Sweden). Conventional 12-lead ECG was recorded, with the precordial leads as CR leads.

When the ECG was recorded at rest only, the tracing covered 30 to 40 seconds. When also an exercise test was performed the ECG was recorded continuously during and for at least 4 min after the exercise. During exercise chest-head leads were recorded (HOLMGREN & STRANDELL 1961). All ECG abnormalities were classified according to the Minnesota code (BLACKBURN et coll. 1960) as modified for use with CR leads and exercise testing (ÅSTRAND et coll. 1967). ECG at rest was recorded before the treatment started, at the end of each week and at one and 6 months following termination of treatment. Exercise ECG was recorded before the treatment started and one and 6 months after the end of treatment.

Exercise tests were performed on an electrically braked bicycle ergometer with multiple submaximal 6-min loads increased in a stepwise manner (SJÖSTRAND 1960). The test was interrupted when the patient reached a heart rate of 170 beats per min or earlier if the patient had to stop because of general fatigue or other subjective complaints. Using the linear relation between heart rate and load during exercise, the physical working capacity was determined or calculated by extrapolation as the load the patient could perform in a relatively steady-state at a heart rate of 170 beats per min (PWC_{170}). The reproducibility of PWC_{170} expressed as the standard error of a single determination is 4.9 per cent (HELLSTRÖM & HOLMGREN 1966). Exercise tests were carried out before the treatment period and one month and 6 months after the end of treatment.

The heart volume was determined in the prone position according to LARSSON & KJELLBERG (1948) with a slight modification introduced by KJELLBERG et coll. (1951). The reproducibility expressed as the standard error of a single determination is 4.2 per cent. The heart volume was determined in those subjects who performed exercise tests and on the same occasions.

Arterial blood pressure and heart rate after 10 min rest supine and after 8 min standing were recorded under standardized conditions. The blood pressure was determined with a mercury manometer and the heart rate palpatorily for 30 s. All the measurements were made in the same room, with the same manometer, on the same arm and by the same nurse. To reduce psychologic influences the initial values were not recorded on the day diagnosis or treatment was announced to the patient, neither on the first visit to the treatment department. Blood pressure and heart rate were determined before the irradiation started, at the end of each week during treatment and one and 6 months after the end of treatment.

Statistical calculations. For each patient the difference between the first blood pressure control (week 0) and the one at the end of the first week of treatment (week 1) was tested for statistical significance separately, in order to avoid the influence of a possibly too high initial blood pressure on the evaluation of the blood pressure changes

Table 2

ECG abnormalities before, during and after treatment

ECG abnormality	Before treatment		During treatment	1 month after treatment		6 months after treatment	
	Rest	During or after exercise only	Rest	Rest	During or after exercise only	Rest	During or after exercise only
Atrial arrhythmias	1	4	4	1	1	4	1
Ventricular ectopic beats	1	3	1		4	1	
ST depression, alone or combined with T wave changes in left ventricular leads	6		2	3		2	
T wave changes	3		7	4		4	
QRS abnormalities	3		2	2		2	
Intraventricular conduction abnormalities	2		2	2		2	
Miscellaneous minor abnormalities	4		2	4		3	
No. of patients examined	51		34	41		36	
No. of patients with ECG abnormalities	15		19	13		12	
Fraction of patients with ECG abnormalities (per cent)	29		56	32		33	

during the rest of the treatment. To eliminate the effects of individually differing blood pressure levels and of missing values among the patients, the change during the rest of the treatment periods was calculated by trend analysis. The regression lines for systolic and diastolic blood pressure and for heart rate during the treatment period were calculated for each patient individually. The t-test was applied in the determination of the statistical significance of the mean values of the regression coefficients for the whole group.

Regarding physical working capacity and heart volume the statistical significance of the difference between the first and the second and third examination, respectively, has been calculated as paired differences and the t-test applied.

Symptoms. At the department of radiation therapy the patient was examined by the physician supervising the treatment, and a history was taken with particular reference to previous complaints referring to the cardiovascular system. During the period of treatment the patient was examined and questioned about complaints once a week. Almost all patients were under the care of the same physician.

Table 3

Physical working capacity (PWC_{170}, kpm/min, mean ± SEM) before and after treatment

	Before treatment	1 month after treatment	6 months after treatment
Male	1 004 ± 70 n = 13	931 ± 81 n = 10	1 009 ± 65 n = 11
Female	595 ± 30 n = 15	546 ± 29 n = 14	562 ± 31 n = 15
Mean of difference ($\bar{d}$)		−61*	+10
Probability (p)		< 0.01	n.s.
No. of patients (n)		23	25

* Mantle and mediastinum group: $\bar{d} = -76$, $p < 0.01$, $n = 17$
Other regions: $\bar{d} = -17$, p n.s., $n = 6$

Table 4

Heart volume (ml, mean ± SEM) before and after treatment

	Before treatment	1 month after treatment	6 months after treatment
Male	799 ± 33 n = 13	774 ± 36 n = 12	804 ± 38 n = 11
Female	657 ± 37 n = 17	625 ± 39 n = 15	632 ± 35 n = 16
Mean of difference ($\bar{d}$)		−22	+6
Probability (p)		< 0.05	n.s.
No. of patients (n)		27	27

Results

ECG at rest was recorded in 51 subjects before the treatment started. Abnormalities were noted in 15 of the patients (29 per cent, Table 2). ST depressions, with or without low or inverted T wave, corresponding to the left ventricle were observed in 6 subjects (Modified Minnesota code No. 4.1–4.3, 4.5, 4.7) and isolated T wave changes in another 3 patients (code No. 5.1–5.4). Definite evidence of an old myocardial infarction was noted in one patient and minor QRS abnormalities which possibly indicated minor myocardial infarctions were observed in 2 patients (code No. 1.2.8, 1.3.2, 1.3.4). During the treatment period ECG recording was repeated once a week in 34 of the patients. During this period the frequency of atrial arrhythmia and of T wave changes slightly increased. The latter appeared on an average after 4 weeks of treatment. On the other hand, ST depressions were noted less frequently. In total, ECG abnormalities were encountered in 19 of the 34 patients (56 per cent). At one and 6 months following treatment the frequency of arrhythmias, ST depressions and T wave changes were essentially the same as before treatment.

Atrial arrhythmia or ventricular ectopic beats were observed in some patients during or after exercise only (code No. 8.9, 10.6–10.8 and 10.2, 10.5, respectively). The

Table 5

Blood pressure and heart rate ($\bar{X} \pm SD$)

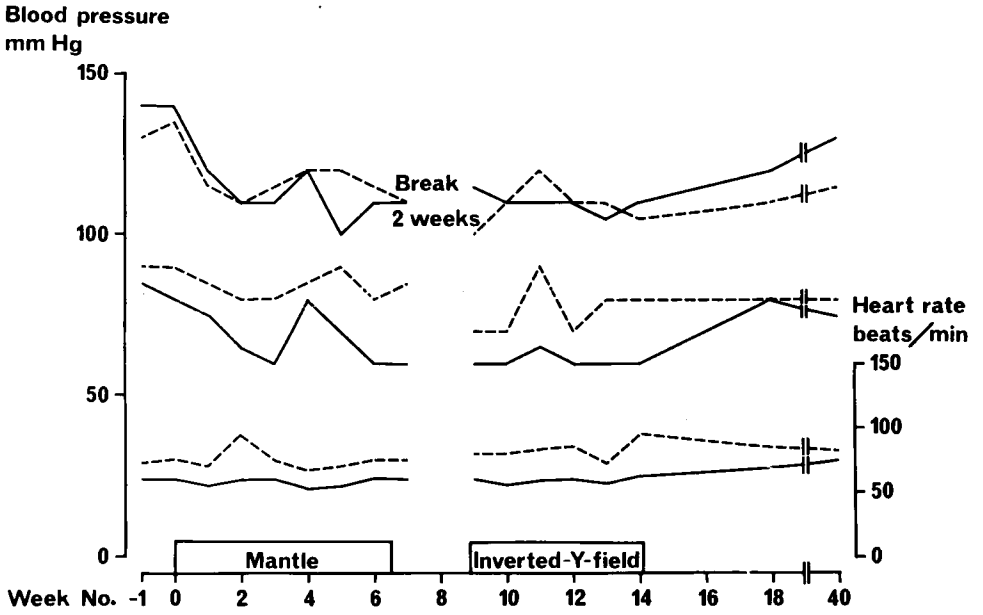
	Blood pressure (mm Hg)		Heart rate (beats/min)	No. of patients
	Systolic	Diastolic		
Supine				
Week 0	129±15	76±12	81±13	36
» 1	123±13	71± 9	80±13	30
» 2	120±13	71±11	77±14	32
» 3	121±14	72±12	78±13	36
» 4	120±13	72±11	76±14	26
» 5	120±13	72±10	80±16	30
» 6	118± 9	70±10	82±15	21
1 month after treatment	121±11	74± 9	80±14	20
6 months after treatment	123±17	80± 9	80±14	11
Standing				
Week 0	126±17	85±11	95±16	33
» 1	117±14	83±10	96±12	27
» 2	119±13	83±10	93±16	30
» 3	120±14	83±12	93±14	33
» 4	120±13	85±11	91±13	24
» 5	118±13	84±11	95±16	27
» 6	119±12	84± 9	92±12	18
1 month after treatment	120±10	87± 9	99±15	23
6 months after treatment	124±16	86±10	96±21	11

frequency of such arrhythmias was unchanged or had decreased one and 6 months following treatment.

Intraventricular conduction abnormalities were observed in 2 patients (code No. 7.2, 7.5) and miscellaneous minor abnormalities in 4 (code No. 2.3, 8.7, 8.8, 9.3).

Appearance of ECG changes during or after treatment was almost the same in patients where the mediastinum had been irradiated compared to patients where other regions had been treated (12/34 and 5/17, respectively). No relation was found between the patient's age or the findings in the first ECG and the subsequent appearance of ECG changes.

Physical working capacity. Exercise test was performed in 34 patients. The mean value of the physical working capacity was normal before the treatment in the 28 patients where PWC_{170} could be calculated (Table 3). The remaining 6 patients discontinued the test because of general fatigue, breathlessness or fatigue in the legs before enough data had been collected to calculate PWC_{170}. Three of these patients had an ordinary heart rate in relation to the load while 3 had a high heart rate in relation to the load indicating a low physical working capacity. At the first reexa-



Blood pressure and heart rate supine (——) and standing (---) in a 34-year-old female with Hodgkin's disease treated with mantle technique and inverted Y-fields for malignant lymphoma.

mination one month following treatment, the average physical working capacity of the whole group had decreased slightly but statistically significantly. This decrease occurred also in patients who were irradiated to the mediastinum but not in those with other regions irradiated (Table 3). No relation existed between reduction in physical working capacity and ECG abnormalities, change in blood pressure or age of the patient. At the examination 6 months following treatment the physical working capacity had returned to pretreatment level in all groups.

Heart volume. The average heart volume was normal before treatment (Table 4). The individual values were within the normal range in all cases except two, who had heart volumes of 508 and 534 ml/m^2, respectively. One month following treatment a slight reduction was found which was probably statistically significant both in the whole group and in the subgroup irradiated for mediastinal tumour. Six months following treatment the heart volume had returned to pretreatment level. In one patient the heart volume increased 125 ml while a decrease of 105 ml was found in another patient. Otherwise all changes were less than 100 ml.

Arterial blood pressure. The mean value of the blood pressure at rest supine and standing was normal before treatment. During the irradiation period a slight continuous decrease in blood pressure was found both in the supine and standing posi-

Table 6

Statistical significance of the changes in blood pressure and heart rate

	Week 0 to week 1			Week 1 to end of treatment		
	Mean difference	No. of patients	Probability	Mean regression coefficient	No. of patients	Probability
Supine						
Blood pressure						
Systolic	−4	30	<0.05	−1.52	36	<0.001
Diastolic	−4		<0.05	−0.64		<0.05
Heart rate	−2		n.s.	−0.00		n.s.
Standing						
Blood pressure						
Systolic	−6	28	<0.001	−1.13	34	<0.05
Diastolic	−1		n.s.	−0.23		n.s.
Heart rate	0		n.s.	0.16		n.s.

tions, but the heart rate was essentially unchanged (Table 5). Statistically significant reduction in both systolic and diastolic blood pressure supine and in systolic blood pressure standing occurred during the treatment period (Table 6). The initial values were partially restituted after the treatment period. No relation was found between reduction in blood pressure and ECG abnormalities, change in physical working capacity or the anatomic region irradiated. The decrease of the mean value was small; in about half of the patients the systolic blood pressure decreased with 0 to 10 mm Hg only and a similar decrease of the diastolic blood pressure occurred in about two thirds of the cases. A considerable fall in blood pressure (more than 20 mm Hg systolic or diastolic) occurred in about one of 5 patients. This may be illustrated by a case report (Figure).

Case report. A 34-year-old woman with a malignant lymphoma and without previous cardiovascular symptoms. She was treated according to the mantle technique and subsequently with an inverted Y-field technique. During the latter part of the first treatment period she experienced vertigo on change of position, often with accompanying nausea. The blood pressure fell from 140/80 to 100/70 during this period, but the heart rate was unchanged between 52 and 60 beats/min. Physical examination of the heart revealed nothing abnormal. ECG before treatment showed the cardiac rhythm to be initiated at rest by an ectopic atrial focus, while she had normal sinus rhythm during and after exercise. The ectopic atrial rhythm persisted during the first and second week of irradiation and then disappeared. Her physical working capacity (685 kpm/min) and heart volume (410 ml/m^2) were normal. During the second treatment period her fatigue and impaired general fitness persisted as well as vertigo and nausea, especially on change of position from supine. The blood pressure stabilized around 105–110/60–65 mm Hg. Six months after the end of the

Table 6 (*cont.*)

End of treatment to 1 month after treatment			End of treatment to 6 months after treatment		
Mean difference	No. of patients	Probability	Mean difference	No. of patients	Probability
+5	20	<0.05	+2	11	n.s.
+2		n.s.	+7		<0.05
+4		<0.05	+2		n.s.
+4	20	<0.05	+7	11	n.s.
+3		n.s.	+4		n.s.
+3		n.s.	+1		n.s.

first treatment period the diesease had progressed. Splenectomy was performed and chemotherapy instituted. The symptoms were essentially unchanged. On physical examination the general condition was good and nothing abnormal was observed on the heart. The blood pressure was 120/80 mm Hg. Her physical working capacity had decreased to 650 kpm/min at the second examination and to 624 kpm/min at the third one. The heart volume was unchanged (390 and 410 ml/m^2, respectively).

Discussion

The present material consisted of about 25 per cent of all patients treated for malignant lymphoma during the years 1969 to 1971. It represents a random selection as the capacity to handle the examinations and tests was the only factor that influenced whether a patient was included in the material or not.

The incidence of ECG changes before treatment in this group is comparable to what has been found in health surveys in large groups of the general population of comparable age (FRISK et coll. 1957). The increased frequency of arrhythmias found during treatment could possibly be explained by the fact that each patient was examined several times and hence the chance to find occasional ectopic beats increased. However, this factor cannot explain the increased frequency of T wave changes observed during treatment. The increased frequency of ectopic beats and of T wave changes was not related to the irradiation of the heart, as it appeared both in patients irradiated for thoracic tumours and in those with tumours in other parts of the body. The disappearance after treatment is in accordance with the experience of HARTWEG and of WHITFIELD & KUNKLER.

The physical working capacity was on an average normal in relation to what has been found in groups of the general population of comparable age and tested in the same way (FRISK et coll. 1957). The reduction in physical working capacity after treatment was generally slight, but it was more evident in patients irradiated for thoracic tumours indicating a more marked functional impairment.

The slight average reduction in heart volume found one month after treatment could be related to a decrease in or displacement of the blood volume as suggested by PIERCE et coll. (1969). No clinical, radiographic or electrocardiographic evidence of pericardial effusion or myocardial insufficiency was encountered. However, the number of subjects is too small to permit any definite conclusion about the incidence of pericarditis in relation to what has been reported by COHN et coll. and up till now no long-term follow-up has been made.

During the treatment the blood pressure decreased slightly but statistically significantly at rest supine as well as in the standing position. In the majority of the patients the blood pressure changed very little but fell in some cases considerably, as reported previously by LEACH. The mechanism behind this is not clear, but is further discussed in another report (LARSSON et coll. 1976).

Except in 3 patients with ECG signs of myocardial infarction before beginning of the treatment, no ECG reactions or symptoms at rest or during exercise tests indicating ischaemic heart disease appeared in connection with the irradiation. Hence, the occurrence of angina pectoris or myocardial infarction reported after radiation therapy by TRACY et coll. was not confirmed.

In conclusion, slight transitory ECG abnormalities in connection with the radiation therapy and a slight, transitory, functional impairment of the cardiovascular system shortly after the treatment were found. Most important seems to be the marked fall in blood pressure appearing in some cases which may give the patient considerable discomfort. In patients on antihypertensive drugs it was found necessary to withdraw the drugs in a few cases and gradually resume the antihypertensive treatment as the blood pressure increased again after the end of the irradiation.

SUMMARY

In 55 patients irradiated for malignant lymphoma the complaints were recorded as well as ECG, blood pressure, exercise test and heart volume before, during and one and 6 months following treatment. ECG abnormalities and fall in blood pressure occurred during treatment. Reduced physical working capacity was found one month after treatment. After 6 months all parameters had returned to pretreatment levels. Attention should be paid to the considerable reduction in blood pressure that does occur in some cases during treatment.

ZUSAMMENFASSUNG

Bei 55 Patienten, die wegen eines malignen Lymphoms bestrahlt worden waren, wurden die Beschwerden, das EKG, der Blutdruck, der Arbeitstest und das Herzvolumen vor,

während und 1 und 6 Monate nach der Behandlung bestimmt. Es traten EKG-Abnormalitäten und ein Blutdrucksfall während der Behandlung auf. Eine herabgesetzte physische Arbeitskapazität wurde 1 Monat nach der Behandlung gefunden. Nach 6 Monaten waren alle Parameter auf die Werte vor der Behandlung zurückgegangen. Es sollte auf den wesentlichen Blutdrucksfall, der in einigen Fällen während der Behandlung auftritt, geachtet werden.

RÉSUMÉ

Chez 55 malades irradiés pour lymphome malin, les auteurs ont étudié les signes fonctionnels, l'électrocardiogramme, la tension artérielle, le test d'exercice et le volume cardiaque avant, pendant, un mois après et 6 mois après le traitement. Ils ont observé des anomalies de l'électrocardiogramme et une baisse de la tension artérielle pendant le traitement. Ils ont constaté une diminution de la capacité de travail physique un mois après le traitement. Six mois après, tous les paramètres étaient revenus au niveau antérieur au traitement. On doit tenir compte de la considérable réduction de la pression artérielle qui se produit dans certains cas au cours du traitement.

REFERENCES

ÅSTRAND I., ARESKOG N.-H., BLOMQVIST G., BJERKELUND C., CARLSTEN A., FURBERG C., GREWIN K.-E., HANSEN F., KAIJSER L., KALLIO V., MALMSTRÖM G., NORDGREN L., PUNSAR S., PYÖRÄLÄ K. and THULESIUS O.: The "Minnesota Code" for ECG classification. Adaptation to CR leads and modification of the code for ECGs recorded during and after exercise. Acta med. scand. (1967) Suppl. No. 481.

BLACKBURN H., KEYS A., SIMONSON E., RAUTAHARJU P. and PUNSAR S.: The electrocardiogram in population studies. A classification system. Circulation 21 (1960), 1160.

BURCH G. E., SOHAL R. S., SUN S.-C., MILLER G. C. and COLCOLOUGH H. L.: Effects of radiation on the human heart. Arch. intern. Med. 121 (1968), 230.

COHN K. E., STEWART J. R., FAJARDO L. F. and HANCOCK E. W.: Heart disease following radiation. Medicine 46 (1967), 281.

COUTARD H. et LAVEDAN J.: Troubles cardio-vasculaires déterminés par les rayons X au cours du traitement des néoplasmes. C. R. Soc. Biol. (Paris) 86 (1922), 666.

ELLINGER F.: Medical radiation biology. pp. 41, 310, 355. Charles C. Thomas, Springfield 1957.

FRISK R. A., HOLMGREN A., STRÖM G. and WERKÖ L.: Stockholms stads hälsoundersökning 1954. III. Viloekg, arbetsekg och fysisk arbetsförmåga. (In Swedish.) Nord. Med. 58 (1957), 1437.

GIARD P. et CRINQUETTE J.: Cardiomyopathie radiothérapique. Mécanisme pathogénique par auto-anticorps. Sem. Hôp. (Paris) 46 (1970), 923.

GREENWOOD R. D., ROSENTHAL A., CASSADY R., JAFFE N. and NADAS A. S.: Constrictive pericarditis in childhood due to mediastinal irradiation. Circulation 50 (1974), 1033.

HARTWEG H.: Über Komplikationen von seiten des Herzens und des Kreislaufs bei Bestrahlungen des Thorax. *In:* Strahlenforschung und Strahlenbehandlung. 2. Band. Urban und Schwarzenberg, München, Berlin 1960.

HELLSTRÖM R. and HOLMGREN A.: On the repeatability of submaximal work tests and the influence of body position on heart rate during exercise at submaximal work loads. Scand. J. clin. Lab. Invest. 18 (1966), 479.

HOLMGREN A. and STRANDELL T.: On the use of chest-head leads for recording of electrocardiogram during exercise. Acta med. scand. 169 (1961), 57.

JONES A. and WEDGWOOD J.: Effects of radiations on the heart. Brit. J. Radiol. 33 (1960), 138.

KJELLBERG S. R., LÖNROTH H. and RUDHE U.: The effect of various factors on the roentgenological determination of the cardiac volume. Acta radiol. 35 (1951), 413.

LARSSON H. and KJELLBERG S. R.: Roentgenological heart volume determination with special regard to pulse rate and the position of the body. Acta radiol. 29 (1948), 159.

LARSSON L.-E., LINDAHL J. and UNSGAARD B.: Fall in blood pressure during radiation therapy. Acta radiol. Ther. Phys. Biol. 15 (1976), 241.

LEACH J. E.: Effect of roentgen therapy on the heart. Arch. intern. Med. 72 (1943), 715.

PIERCE R. H., HAFERMANN M. D. and KAGAN A. R.: Changes in the transverse cardiac diameter following mediastinal irradiation for Hodgkin's disease. Radiology 93 (1969), 619.

SJÖSTRAND T.: Functional capacity and exercise tolerance in patients with impaired cardiovascular function. *In:* Clinical cardiopulmonary physiology, p. 201. Grune & Stratton, New York 1960.

TENERIELLO F., DUREAU G., CHASSIGNOLLE J., RASSAT J.-P., LOIRE R., DU GRÈS B. et MICHAUD P.: Pericardite constrictive et myocardiopathie post-radiothérapique. Ann. Chir. thorac. cardio-vasc. 9 (1970), 423.

TRACY G. P., BROWN D. E., JOHNSON L. W. and GOTTLIEB A. J.: Radiation-induced coronary artery disease. J. Amer. med. Ass. 228 (1974), 1660.

VAETH J. M., FEIGENBAUM L. Z. and MERRILL M. D.: Effects of intensive radiation on the human heart. Radiology 76 (1961), 755.

WHITFIELD A. G. W. and KUNKLER P. B.: Radiation reactions in the heart. Brit. Heart J. 19 (1957), 53.