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EVALUATION OF RADIATION TREATMENT OF PAINFUL CONDITIONS OF THE LOCOMOTOR SYSTEM

A double blind study

by

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Inflammatory and degenerative changes in joints and adjacent structures often cause pain; the exact mechanism by which this is elicited is not completely understood (BONICA 1953). It has been suggested that oedema following the increased capillary permeability in inflammation may exert pressure on nerve endings and result in pain (LINDAHL & REXED 1950, OLSSON 1958, ASBOE-HANSEN 1963, HEIMANN 1964, CABITZA 1965, SICUTERI 1965, BALLABIO 1965). Impairment of venous drainage from subchondral bone as part of the inflammatory reaction may also contribute to pain (HULTH 1969). The alleviation of pain that takes place after the administration of antiphlogistic drugs would to some extent support these opinions.

A relationship may exist between increased hydrogen ion concentration and pain — as evident in inflammatory conditions (MENKIN 1937, ROPES et coll. 1953, CUMMINGS et coll. 1966, GOLDIE et coll. 1969). REVICI et coll. (1949) believed that local changes in damaged tissues may bring about a lowering of the nerve threshold for pain, and that end organs ordinarily concerned with other

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forms of sensations are altered in a way to cause the impulses originated to evoke the sensation of pain.

LINDAHL (1961) has demonstrated the relationship between increased hydrogen ion concentration and severe pain in the skin, whereby the hydrogen ion may be the chemical mediator that triggers the pain stimulus in the nerve endings. Alkalinization alleviated pain.

Painful conditions of the locomotor system — possibly due to the above mechanism — have long been regarded suitable for radiation treatment. Proliferating tissue, such as endothelium in newly formed blood vessels in the subchondral region, and partly the region of the inflammatory reaction in the joint capsule at its junction with the bone cartilage, are sensitive to ionizing radiation. On the other hand, PENDERGRASS et coll. (1941) and ELLINGER (1957) stressed that irradiation transfers an area of passive hyperemia into active hyperemia which among other things decreases oedema and increases in lymphatic flow. White blood cells and particularly the lymphocytes are still more radiosensitive and react to low doses of one or a few hundred rad (TROWELL 1952).

Irradiation may cause slight initial acidosis which however is followed by a longstanding alcalosis (ELLINGER 1957). Another factor that is also influenced by irradiation is the calcium content of tissue. This is increased, which leads to a more marked anti-oedematous effect (ELLINGER 1957, HULTBERG et coll. 1963).

Radiation treatment is supposed to counteract the establishment of certain strongholds for the maintenance of the inflammatory reaction that leads to pain in some common joint and juxta-articular disorders. Suitable doses for treatment of these diseases are considered to be in the region of a few hundred R and not over 1 000 R in one series. A total dose of up to about 2 000 R is considered to produce no disturbing late side effects, such as fibrosis and impairment of the mobility of the joint.

In the treatment of spondylosis deformans of the spine the doses have to be low due to the risk of neoplastic bone marrow disease (GRAHAM 1960).

The conception that pain relief can be attained has been widely accepted but little reported. SANDSTRÖM et coll. (1937) gave details of successful treatment. OCHSNER et coll. (1940) published the results in fifty-two patients with posttraumatic pain. There was relief of pain in thirteen out of twenty-seven postfracture patients, in six out of fourteen posttraumatic patients without fracture, and in five out of eleven patients with joint pain following operation. Relief was therefore obtained in approximately 50 %. HORWITZ et coll. (1944) reported successful treatment in nine patients with hydroarthrosis of the knee joint. STOLL (1957) assessed the relief of pain in sixty-two patients receiving radiation therapy for posttraumatic arthrosis, para-arthrosis and fasciitis. Alleviation was reached in 50 % of patients within 1 to 4 weeks. HULTBERG et coll. (1963), though

Table 1

Distribution according to age and sex in the two groups subjected and not subjected to radiation

	Group given radiation treatment			Group not receiving treatment		
	Men	Women	Total	Men	Women	Total
20—30	4	1	5	3	1	4
31—40	4	7	11	9	6	15
41—50	22	19	41	18	19	37
51—60	27	35	62	19	29	48
61—70	20	28	48	28	29	57
71—80	10	20	30	11	16	27
81—90	3	5	8	1	5	6
			205			194

having carried out no systematic investigation on the results of radiation treatment in joint disorders, were nevertheless of the opinion that it may be of benefit. LEQUESNE (1967) found that radiotherapy had no effect in osteo-arthritis of the hip joint except when there was an associated trochanteric bursitis.

Evaluation of the results in a special treatment of inflammatory and degenerative joint disorders becomes difficult as the course is most variable. Moreover, also the radiation treatment varies both with regard to fractionation and total dose. Some believe in smaller doses at repeated intervals (OCHSNER et coll. 1940, STOLL 1957, HULTBERG et coll. 1963), e.g. 25 to 100 R a day for 3 to 5 days. Others find an initial treatment with up to 400 R daily, with a total of 2 400 R in a week, to be of greater benefit (DE LORIMIER 1937), and HORWITZ et coll. (1944) suggested 250 R a week for 6 or 7 weeks.

Difficulties in the evaluation of results of a therapeutic agent may thus arise when the disease for which a patient is treated causes symptoms that at least for some time subside spontaneously and also when the mode by which the therapeutic agent is applied varies considerably. Controlled series have as yet not been encountered, excepting one reported as a discussion by NEWELL in 1939 and one by PLENK in 1952. In the former series, boils in alternate cases were shielded from the radiation by a lead filter; practically no difference in the clinical course of the whole series was apparent. PLENK reported no difference in the results of a treated and non-treated controlled series of calcifying tendinitis of the shoulder. LINDAHL & BACKLUND (personal communication) in a double blind study recorded no difference in the results of treated and untreated groups with joint disorders.

The aim of the present study was to compare two groups of patients with

Table 2

Diagnoses and number of patients in the two groups which received respectively true and 'false' treatment for different disorders

	Radiation treatment	'False' radiation treatment	Total
Spondylosis			
Cervical	34	47	81
Thoracic	—	1	1
Lumbar	2	4	6
Arthrosis (osteoarthritis)			
Arthrosis def. art. hum. scap. (roentgen evidence of cartilage destruction of hum. head)	3	7	10
Arthrosis def. art. acromioclav.	3	6	9
Arthrosis def. art. cubiti	—	1	1
Arthrosis def. art. carpometacarp.	5	1	6
Arthrosis def. coxae	14	9	23
Arthrosis def. genus	53	39	92
Arthrosis def. art. talocrur.	2	2	4
Arthrosis def. art. metatarsophal.	3	—	3
'*Tendinitis*'			
Peritendinitis hum. scap.	70	71	141 (5 acute cases)
Epichondylitis lat. et med. hum.	11	14	25
Trochanteritis	4	2	6
Tendinitis lig. coll. regio genus	1	—	1
Calcaneodynia (spur and plantar bursitis)	5	4	9
Synovitis			
Genus	2	—	2
Metatarsophal.	1	—	1
Other	10	8	18
			Total 439

ailments of the locomotor system, only one of which received radiation treatment using a double blind technique.

Material and Methods

The series consists of 399 patients referred for disorders of the locomotor system. The age and sex distribution appear in Table 1 and the diagnoses of the

treated locomotor ailments, amounting to 439, are given in Table 2. Roentgen examinations were performed in all the patients prior to the treatment in order to exclude malignant or other disease not suitable for this type of treatment.

All the patients were before the treatment individually interrogated and examined by an orthopaedic surgeon who did not know which patients were to receive treatment. The diagnosis was modified when it did not agree with the initial one. A radiologist selected the area to be treated. The patients in one of the groups were subjected on alternate days to a series of roentgen treatments according to a given procedure. Every second day this procedure was repeated for the other group of patients but then irradiation was prevented by a lead diaphragm. The procedure was repeated for both groups until conclusion of the treatment period. Neither the patient, nor the orthopaedic surgeon, the radiologist or the referring physician, were to know who had received the true radiation treatment.

Six weeks following the conclusion of the treatment procedures, control of the patients was made by the orthopaedic surgeon, who still did not know which patients had received irradiation. The interrogation was thus renewed and included post therapy results and an objective examination. The fee for treatment, as decided by the National Health Insurance representative, was paid by all patients, irrespective of treatment or not. When the follow-up study was terminated, the code for the treated and untreated patients was released and studied by the orthopaedic surgeon and the radiologist.

The following factors were applied in the radiation treatments: 170 kV, HVL 1 mm Cu, and usually 40 cm SSD.

The shoulders were irradiated with 10 cm $\times$ 12 cm collimators. Two opposing beams were used, with an exposure of 3 $\times$ 150 R. In acute cases the exposures were lower, i.e. 75 or 100 R. Knees were also irradiated with two opposing fields with the same collimators and 3 $\times$ 200 R. Hips were treated with three treatment fields, one ventral, one lateral and one dorsal, the field size being 9 cm $\times$ 15 cm. The SSD in these treatments was 50 cm and the exposure per field 3 $\times$ 200 R. Trochanteritis was treated with one ventral and one lateral field, applying the same field size and dose.

Patients with spondylosis deformans cervicalis thoracalis et lumbalis were treated with two dorsal fields angled at 25 to 30°. In the cervical spine the collimators measured 4.5 cm $\times$ 12 cm and in the thoracic and lumbar spine the fields were generally 6 cm wide and 10 to 15 cm long. The SSD for the cervical spine was 40 cm and for the thoracic and lumbar spine 50 cm. Every field was exposed to 3 $\times$ 200 R. Epicondylitis was treated with a field measuring 6 cm $\times$ 8 cm and 4 $\times$ 150 R. Patients with calcaneodynia were treated with the same tubes and two opposing fields, one medial and one lateral, the exposure being 3 $\times$ 150 R.

Table 3

Diagnoses and subjective and objective evaluations of the results in the group treated with radiation

	Total	Subjective evaluation		Objective evaluation		
		Improvement	Same or worse	Improvement	Same	Worse
Spondylosis cervicalis cum rhizopathia	34	21	13	14	18	2
Spondylosis thoracalis						
Spondylosis lumbalis	2	1	1	1	1	—
Peritendinitis hum. scap.	70	52	18	31	32	4
Epicondylitis lat. et med. hum.	11	5	6	4	6	1
Arthrosis def. art hum. scap.						
Arthrosis def. acromioclav.	6	5	1	3	3	—
Arthrosis def. art. cubiti	—	—	—	—	—	—
Arthrosis def. art. carpometacarp.	5	4	1	2	3	—
Trochanteritis	4	3	1	2	1	1
Calcaneodynia	5	4	1	3	2	—
Tendinitis regio genus						
Synovitis genus	3	3	—	2	—	—
Synovitis metatarsophal.	1	—	1	—	1	—
Arthrosis def. coxae	14	6	8	4	7	2
Arthrosis def. genus	53	37	16	22	30	1
Arthrosis def. art. talocrur.						
Arthrosis def. art. metatarsophal.	5	4	1	2	2	1
Other	10	7	3	5	1	—
Total	223	152 (68 %)	71 (32 %)	95 (43 %)	107 (48 %)	12 (5 %)

No collimators were used in other regions. The areas around the treatment fields were protected with lead rubber.

Osteoarthrosis of the joints of the hand was irradiated with 3 × 150 R to one volar and one dorsal field. Osteoarthrosis of the joints of the foot was treated in the same way with two opposing fields and 3 × 200 R. Osteoarthrosis of the metatarsophalangeal joints was treated with one dorsal field and 4 × 150 R.

The depth doses calculated in the different treatment regions were approximately between 500 and 1 000 rad.

Table 4

Diagnoses and subjective and objective evaluations of the results in the group not exposed to radiation

	Total	Subjective evaluation		Objective evaluation		
		Improvement	Same or worse	Improvement	Same	Worse
Spondylosis cervicalis cum rhizopathia	47	33	14	20	20	3
Spondylosis thoracalis						
Spondylosis lumbalis	5	1	4	1	4	—
Peritendinitis hum. scap.	71	47	24	38	19	7
Epicondylitis lat. et med. hum.	14	9	5	8	4	1
Arthrosis def. art. hum. scap.						
Arthrosis def. acromioclav.	13	10	3	9	2	—
Arthrosis def. art. cubiti	1	1	—	1	—	—
Arthrosis def. art. carpometacarp.	1	1	—	1	—	—
Trochanteritits	2	1	1	—	1	—
Calcaneodynia	4	3	1	3	1	—
Tendinitits regio genus						
Synovitis genus	—	—	—	—	—	—
Synovitis metatarsophal.	—	—	—	—	—	—
Arthrosis def. coxae	9	5	4	1	6	—
Arthrosis def. genus	39	23	16	9	28	2
Arthrosis def. art. talocrur.						
Arthrosis def. art. metatarsophal.	2	1	1	1	1	—
Other	8	4	4	1	6	1
Total	216	139 (64 %)	77 (36 %)	93 (43 %)	92 (43 %)	14 (6 %)

During all the treatments, true or 'false', a dental roentgen film was placed in the beam as a check. It was of course blackened in all the true treatments and was unexposed in the 'false' ones.

All the patients were directed not to take any antiphlogistic or other drugs, nor physiotherapy, for their ailments during the treatment period or during the subsequent follow-up period.

Results and Discussion

A total of 395, out of the 399 patients, were controlled. One patient had died and three could not be traced. The overall results, with analyses of the diagnoses, are presented in Tables 3 and 4.

Table 5

Time for improvement following termination of treatment

	During treatment	Immediately after treatment	Weeks after treatment				
			1	2	3	4	5
Exposed to radiation	5	7	29	29	47	15	7
Not exposed to radiation	10	7	16	28	35	13	8

Table 6

Increased pain or other local reaction during treatment in relation to result of irradiation

	Pain during treatment	Subjective result after treatment	
		Improvement	Worse
Exposed to radiation	12	7	5
Not exposed to radiation	11	6	5

The discrepancy in the respective numbers of patients with subjective and objective evaluations is due to the failure of some patients to come to interrogation. The treatment, according to the patients' opinions, was satisfactory in 148 of those who had received radiation treatment and in 135 of those who had not been exposed to radiation, whereas dissatisfaction was recorded for 75 of the patients who had received radiation treatment and 81 of those who had not been exposed to radiation.

The time for improvement following the termination of the series of treatments is recorded in Table 5. A number of patients had some difficulty in giving accurate information and others stated that the pain had subsided gradually. Pain and local discomfort during the treatment period were also registered and related to the end results with a view to find out if these could have been influenced by the reactions (Table 6).

No true differences in the follow-up results, with the doses used in this investigation, could be established between the group exposed and the group not exposed to radiation treatment.

Certain differences in the subjective and objective registrations (Tables 3 and

4) may be noted, however. In Table 3, the subjective improvement is 68 % and the objective improvement 43 %. In Table 4, the subjective improvement is 64 % and the objective improvement 43 %. The difference between the subjective evaluations in the two groups may to some extent depend on the failure of some patients to come to the interrogation and on the difficulty of obtaining a satisfactory after-history. However, the recorded evaluations of subjective improvements are about the same for both groups of patients, exposed or not exposed to the radiation treatment and there is no difference between the two groups in the evaluations of objective improvements.

Our observations are further substantiated by the general individual opinions about the treatments. A strict correlation could be established between 'satisfied' and 'subjective improvement', as mentioned in Tables 3 and 4. In the group exposed to radiation, 66 % 'satisfied' correspond to 68 % 'subjective improvements' in Table 3. In the group not exposed to radiation, 63 % 'satisfied' correspond to 64 % 'subjective improvements' in Table 4. The results obtained correspond well with what is generally accepted by radiotherapists. HOWARD (1957) reported that 70 % of the patients with spondylarthrosis improved after radiation treatment.

A question commonly discussed is the time from final treatment to improvement. In this study, improvement appeared to occur after 2 to 3 weeks both in the exposed and the unexposed groups (Table 5).

The tendency in the whole series as such was thus improvement after a few weeks whether radiation treatment was given or not. Further analysis of the three largest groups, humeroscapular peritendinitis, osteoarthrosis of the knee, and cervical spondylosis, revealed that they together comprised 75 % of the total material, or 157 patients in each of the exposed and unexposed groups. As for the subjective estimation of improvement in the exposed group it was observed in 74 % of humeroscapular peritendinitis, in 70 % of osteoarthrosis of the knee and in 62 % of cervical spondylosis. With 68 % improvement in the total exposed group there is thus good correlation between the subgroups and the whole of the exposed group.

Corresponding observations were made as regards the objective evaluation: 44 % of humeroscapular peritendinitis, 42 % of osteoarthrosis of the knee, and 41 % of cervical spondylosis, or 43 % of the total exposed group, were improved.

As for the group not exposed to radiation treatment similar trends in the subjective estimation were registered. The improvement for humeroscapular peritendinitis was 66 %, for osteoarthrosis of the knee 59 %, and for cervical spondylosis 70 %, or 64 % in the total series.

The objective evaluation revealed better results in humeroscapular peritendinitis, where improvement occurred in 52 %, as compared to 43 % of the total un-

exposed group. Osteoarthrosis of the knee was somewhat worse with only 23 % improvement, but cervical spondylosis with an improvement of 42 % corresponded well to the figure for the total group. It has not been possible to find any obvious reason for this.

There was no statistical difference with the χ^2 test in a comparison of the results in the exposed and the corresponding unexposed groups.

The results of this investigation suggest that no difference exists in the end-results of exposed or unexposed groups of patients to the generally adopted doses of radiation treatment in painful inflammatory and degenerative conditions of the locomotor system.

Addendum in proofs

A questionnaire was sent out to 368 patients seven to eight months after the 6-week control. Fifteen patients could not be traced owing to change of address or death. The patients were asked if there had been any change in their condition since the last control and whether they had received any further treatment. Of the 353 patients who received the questionnaire, 325 replied.

Further treatment had been given to seventeen patients in the treated improved group; they had received physio- and short-wave therapy but no irradiation. Fifteen of the patients in the treated not improved group had had further treatment, excluding irradiation. In the untreated improved group, sixteen patients had received further treatment, excluding irradiation, and in the untreated not improved group eighteen patients had received further treatment, but not irradiation.

The results still indicated that no differences existed as regards the degree of improvement between the treated and untreated groups and that the results had not materially altered since the 6-week control. In the treated group, 104 patients of the 111 improved at the 6-week control were still improved at the 8-month control; of the 47 not improved at the 6-week control, 21 had improved at the 8-month control. In the untreated group, 95 of 108 remained 'improved' and 19 of the 59 changed their statement from 'not improved' to 'improved'.

SUMMARY

A series of 399 patients, suitably controlled and representing 439 painful locomotor ailments, was studied. The conclusion was reached that no difference existed in the end-results of patients exposed and those not exposed to radiation treatment for the conditions.

ZUSAMMENFASSUNG

Ein Material von 399 Patienten, die an 439 schmerzhaften Erkrankungen des locomotorischen Systems litten, wurde kritisch überprüft. Es ergab sich, dass die Strahlenbehandlung das Endresultat nicht beeinflusst.

RÉSUMÉ

Les auteurs ont étudié une série de 399 malades correctement contrôlés et représentant 439 atteintes douloureuses de l'appareil locomoteur. Ils sont arrivés à la conclusion que le résultat final est le même chez les malades traités par radiothérapie pour ces affections et chez les malades qui n'ont pas subi ce traitement.

REFERENCES

ASBOE-HANSEN G.: Connective tissue. Ann. Rev. Physiol. 25 (1963), 41.

BALLABIO C. B.: Clinical properties of Indomethacin. Int. Symp. Non-steroidal Antiinflammatory Drugs, p. 342. Excerpta Med., Amsterdam 1965.

BONICA J. J.: The management of pain. Lea & Febiger, Philadelphia 1953.

BUHTZ H.: Beiträge zur pathologischen Physiologie der Entzündung. 10. Über die Beeinflussung der traumatischen Entzündung durch Röntgenstrahlen. Frankfurt. Z. Path. 44 (1932), 57.

CABITZA A.: Benzindamine in orthopaedics. Int. Symp. Non-Steroidal Antiinflammatory Drugs, p. 434. Excerpta Med., Amsterdam 1965.

CUMMINGS N. A. and NORDBY G. L.: Measurements of synovial fluid pH in normal and arthritic knees. Arthr. and Rheum. 9 (1966), 47.

DE LORIMIER A. A.: Roentgen therapy in acute paraarthritis. Amer. J. Roentgenol. 38 (1937), 178.

ELLINGER F.: Medical radiation biology, p. 448. Charles C. Thomas, Springfield, Illinois 1957.

FEIGENBERG S., POPPE E. och ROMANUS R.: Strålterapi, pp 103, 158. (In Swedish.) Almqvist & Wiksell, Stockholm 1963.

FREUND F.: Experimentelle Grundlagen der Röntgentherapie entzündlicher Prozesse. Strahlentherapie 40 (1931), 333.

GOLDIE I. and NACHEMSON A.: Synovial pH in rheumatoid knee-joints. I. The effect of synovectomy. Acta orthop. scand. 40 (1969), 634.

— — Synovial pH in rheumatoid knee-joints. II. The effect of local steroid treatment. To be published in Acta orthop. scand.

GRAHAM D. C.: Leukaemia following X-ray therapy for ankylosing spondylitis. Arch. intern. Med. 105 (1960), 51.

HEIMANN P.: Oxyfenbutazon i kirurgien. (In Swedish.) Nord. Med. 71 (1964), 363.

HORWITZ T. and DILLMAN M. A.: The effect of roentgen rays on the joint effusions in certain nonspecific articular lesions in humans and on the normal joints of dogs: A preliminary report. Amer. J. Roentgenol. 51 (1944), 186.

HOWARD N.: The value of irradiation in ankylosing spondylitis. Brit. J. Radiol. 30 (1957), 371.

HULTBERG S., LÖVGREN O. and ROMANUS R.: Inflammatoriska och degenerativa sjukdomar i mjukdelar och leder. (In Swedish.) *In*: Strålterapi, p. 158. Almqvist & Wiksell, Stockholm 1963.

HULTH A.: Osteoarthritis. The ageing of connective tissue. Thule Int. Symp. October 1968. Nordiska Bokhandelns Förlag, Stockholm 1969.

LEQUESNE M.: Disease of the hip in adult life. Folia Rheumatol. Documenta Geigy (1967).

LINDAHL O.: Experimental skin pain. Acta phys. scand. 51 (1961) Suppl. No. 179.

— Personal communication (1969).

— and REXED B.: Histologic changes in spinal roots of operated cases of sciatica. Acta orthop. scand. 20 (1950), 215.

MENKIN V. and WARNER C. R.: Studies on inflammation. XIII. Carbohydrate metabolism, local acidosis and the cytological picture in inflammation. Amer. J. Pathol. 13 (1937), 25.

NEWELL R.: Discussion. Radiology 32 (1939), 314.

OCHSNER H. C. and MUNFORD E. B.: Roentgen therapy for painful conditions of the bones and joints. Radiology 34 (1940), 444.

OLSSON S. E.: The dynamic factor in spinal cord compression. A study on dogs with special reference to cervical disc protrusions. J. Neurosurg. 15 (1958), 308.

PENDERGRASS E. P. and HODES O. J.: Roentgen irradiation in the treatment of inflammation. Amer. J. Roentgenol. 45 (1941), 74.

PLENK H. P.: Calcifying tendinitis of the shoulder. A critical study of the value of X-ray therapy. Radiology 59 (1952), 384.

REINHOLD H. und SAUERBREY R.: Die Röntgentherapie des Schulter-Arm-Syndroms, Epikondyliten an Schulter und Ellenbogen. Dtsch. med. Wschr. 86 (1961), 165.

REVICI E., STOOPEN R., FRENK E. and REVICH R. A.: The painful focus. II. Bull. Inst. appl. Biol. 1 (1949), 21.

ROPES M. and BAUER W.: Synovial fluid changes in joint disease. Harvard University Press, Cambridge 1953.

RUBIN P. and CASARETT G.: Clinical radiation pathology, p. 38. W. B. Saunders Co, Philadelphia 1968.

SANDSTRÖM C. und WAHLGREN F.: Beitrag zur Kenntnis der Peritendinitis calcarea (sogen. Bursitis calculosa) speziell vom patologisch-histologischen Gesichtspunkt. Acta radiol. 18 (1937), 263.

SICUTERI F.: Indomethacin as a new vasoconstrictor and therapeutic agent in migraine. Int. Symp. Non-Steroidal Antiinflammatory Drugs, p. 335. Excerpta Med. Amsterdam 1965.

STOLL B. A.: X-ray therapy in post-traumatic arthritis, paraarthritis, and fascitis. Med. J. Austr. 22 (1957), 868.

TROWELL O. A.: The sensitivity of lymphocytes to ionizing radiation. J. Path. Bact. 64 (1952), 687.