

In the future, periodic control examinations of all PVC workers, especially of those engaged in VC polymerization, at short intervals employing sensitive methods should be obligatory unless it should prove feasible to eliminate completely any possible air contamination.

Some of the many scientific questions connected with the problem of vinyl chloride disease may not be answerable until results of further extensive animal experiments^{20,21,101} and of prospective and retrospective large-scale studies²² as well as of continuous monitoring of working areas^{12,100,102,103} are available.

REFERENCES

1. ADAM, Y. G., A. G. HUVOVS & S. I. HAJDU. 1972. Malignant vascular tumors of liver. *Ann. Surg.* 175: 375.
2. ALDRIGHT, I. F. 1967. Vinyl chloride processes. *Chem. Eng.* 74 (March 27): 123.
3. ALDRIGHT, I. F. 1967. Manufacture of vinyl chloride. *Chem. Eng.* 74 (April 10): 219.
4. ALDRIGHT, I. F. 1967. Polymerization of vinyl chloride. *Chem. Eng.* 74 (May 8): 151.
5. ALDRIGHT, I. F. 1967. Vinyl chloride polymerization by suspension processes yields polyvinyl chloride resins. *Chem. Eng.* 74 (June 5): 145.
6. ALDRIGHT, I. F. 1967. Vinyl chloride polymerization by emulsion, bulk and solution processes. *Chem. Eng.* 74 (July 3): 85.
7. ANGHIESCU, FL., M. OTOIU, E. DOBRINESCU, L. HAGI-PARASCHIV-DOSSIOS, GII. DOBRINESCU & V. GANEA. 1969. Consideratii clinico-patogenice asupra fenomenului Raynaud la muncitorii din industria policlorurii de vinil. *Med. Interna* 21: 473.
8. AUSTIN, G. T. 1974. Industrially significant organic chemicals (Part 3). *Chem. Eng.* 81 (March 18): 27.
9. BAADER, E. W. 1960. Klinische Grundlagen der sechszwanzig meldepflichtigen Berufskrankheiten. Urban & Schwarzenberg. München, West Germany.
10. BAADER, E. W., Ed. 1961. Handbuch der gesamten Arbeitsmedizin. Vol. II/1: Berufskrankheiten. Urban & Schwarzenberg. München, West Germany.
11. BAGHIRZADE, M. F., E. U. HERTEL & P. SCHUMACHER. 1971. Hämangioendotheliom (Reticulosarcoma angioplasticum) der Leber und alte Echinokokkus-Infektion. *Acta Hepato-Splenol.* 18: 224.
12. BARETTA, E. D., R. D. STEWART & J. E. MUTCHLER. 1969. Monitoring exposures to vinyl chloride vapor: breath analysis and continuous air sampling. *Am. Ind. Hyg. Assoc. J.* 30: 537.
13. BASALAEV, A. V., A. N. VAZIN & A. G. KOCHKOV. 1972. K patologeniz izmenenii voznikayushchikh pri dlytel'nom vozdeistvii vinilkhlorda. *Gigiena Truda Prof. Zabollevaniya* 16(2): 24.
14. BASU, A. K., J. BOYER, R. BHATTACHARYA, K. C. BASU MALLIK & K. P. SEN GUPTA. 1967. Non-cirrhotic portal fibrosis with portal hypertension: a new syndrome. Part I. Clinical and function studies and results of operations. *Indian J. Med. Res.* 55: 336.
15. BASU MALLIK, K. C., K. P. SEN GUPTA, A. K. BASU, S. K. BISWAS, N. C. PAL & J. BOYER. 1967. Non-cirrhotic portal fibrosis with portal hypertension: a new syndrome. Part II. Histopathological studies. *Indian J. Med. Res.* 55: 351.
16. BECK, K., W. DISCHER, M. HEINZ, B. KINN, K. SCHNEIDER & R. TENNER. 1968. *Atlas der Laparoskopie*. F. K. Schattauer Verlag, Stuttgart, West Germany.
17. BECKER, V. & K. BÜSCHER. 1961. Ueber das Hämangioendotheliom der Leber. *Acta Hepato-Splenol.* 8: 356.
18. BIANCHI, L. 1970. Zum Problem der Leberfibrose. *Schweiz. Med. Wochschr.* 100: 1214.
19. BOYER, J. L., K. P. SEN GUPTA, S. K. BISWAS, N. C. PAL, K. C. BASU MALLIK, F. L. FIERA & A. K. BASU. 1967. Idiopathic portal hypertension. Comparison with the portal hypertension of cirrhosis and extrahepatic portal vein obstruction. *Ann. Internal Med.* 66(1): 41.
20. BRIT. MED. J. 1974. Vinyl chloride and cancer. 1: 590.
21. BROHSENMAYER, S., F. SCHIAFFNER & H. POPPER. 1966. Fat-storing cells (lipocytes) in human liver. *Arch. Pathol.* 82: 447.
22. BROUSSARD, G. 1969. Patologia da resine polivinilice. *Med. Bull.* 52(2): 102.

23. BRÜHL, W. 1966. Zwischenfälle und Komplikationen bei der Laparoskopie und gezielten Leberpunktion (Ergebnis einer Umfrage). *Deut. Med. Wochschr.* 91: 2297.
24. CANADA, DEPARTMENT OF NATIONAL HEALTH AND WELFARE, INDUSTRIAL HEALTH DIVISION. 1949. A guide to the diagnosis of occupational diseases. King's Printer. Ottawa, Ontario, Canada.
25. CARR, J., R. M. BURGISON, J. F. VITCIA & J. C. KRANTZ, JR. 1949. Anesthesia. XXIV. Chemical constitution of hydrocarbons and cardiac automaticity. *J. Pharmacol. Exptl. Ther.* 97: 1.
26. CHATELAIN, A. & P. MOTILLON. 1967. Un syndrome d'acro-ostéolyse d'origine professionnelle et de constation nouvelle en France. *J. Radiol. Electrol. Med. Nucl.* 48: 277.
27. CHEMICAL ECONOMICS HANDBOOK. September 1973. Vinyl Chloride and Polyvinyl Chloride Resins. Stanford Research Institute. Menlo Park, Calif.
28. CHEMIEWIRTSCHAFT IN ZAHLEN. VERBAND DER CHEMISCHEN INDUSTRIE E.V., Ed. 1973. 15th edit. Econ-Verlag. Düsseldorf, West Germany.
29. CHENOWETH, M. B. & C. L. HAKE. 1962. The smaller halogenated aliphatic hydrocarbons. *Ann. Rev. Pharmacol.* 2: 363.
30. CHIEF INSPECTOR OF FACTORIES. 1953. Annual Report for the Year 1951. Cmd. 8772, H.M.S.O. London, England.
31. COOK, W. A., P. M. GIEVER, B. D. DINMAN & H. J. MAGNUSON. 1971. Occupational acroostecolysis. II. An industrial hygiene study. *Arch. Environ. Health* 22: 74.
32. CORDIER, J. M., C. FIEVEZ, M. J. LÉFÈVRE & A. SEVRIN. 1966. Acro-ostéolyse et lésions cutanées associées chez deux ouvriers affectés au nettoyage d'autoclaves. *Cahiers de Médecine du Travail (Association Professionnelle belge des Médecins du Travail 4 janvier 1966)*.
33. CRECH, J. L., JR. & M. N. JOHNSON. 1974. Angiosarcoma of liver in the manufacture of polyvinyl chloride. *J. Occupational Med.* 16: 150.
34. DALLMANN, W. B. & H. W. GERHARD. 1965. A comment on splenic scanning. *BMHP. Radiology* 84: 497.
35. DALLMANN, W. B. & H. W. GERHARD. 1965. Thorotrast tumours. A review of the literature and report of two cases. *Acta Pathol. Microbiol. Scand.* 53: 147.
36. DALLMANN, W. B. & H. W. GERHARD. 1965. Thorotrast tumours. A review of the literature and report of two cases. *Acta Pathol. Microbiol. Scand.* 53: 147.
37. DANZIGER, H. 1960. Accidental poisoning by vinyl chloride: report of two cases. *Can. Med. Assoc. J.* 82: 828.
38. DEESE, D. E. & R. E. JOYNER. 1969. A study of chronic human exposure. *Am. Ind. Hyg. Assoc. J.* 30: 537.
39. DEUTSCHMANN, W. B. & H. W. GERHARD. 1965. Thorotrast tumours. A review of the literature and report of two cases. *Acta Pathol. Microbiol. Scand.* 53: 147.
40. DEVONEVILLE, DR. & A. M. FLUDES. 1965. Des résines polyvinylques. Servi Vernou, avril 1953. As cited in T.
41. DIMOV, D. & T. BERITIC. 1971. I Toksikol. 22: 53.
42. DINMAN, B. D., W. A. COOK, W. I. CHIECK. 1971. Occupational acroostecolysis. *Arch. Environ. Health* 22: 61.
43. DODSON, V. N., B. D. DINMAN, & H. J. MAGNUSON. 1971. Occupational acroostecolysis. *Arch. Environ. Health* 22: 83.
44. DOMNINGHAUS, H. 1972. Kunststoffsarten-Anwendungen. 2nd edit. VDI-Verlag. Düsseldorf, West Germany.
45. DOMNINGHAUS, H. 1973. Kunststoffformen. 2nd edit. VDI-Verlag. Düsseldorf, West Germany.
46. DUBLIN, L. I. & R. J. VANE. 1941. Occupational hazards and diagnostic signs. U.S. Department of Labor, Bureau of Government Printing Office. Washington, D.C., p. 65. As cited in Danziger, 1960.
47. DUBLIN, L. I. & R. J. VANE. 1941. Occupational hazards and diagnostic signs. U.S. Department of Labor, Division of Labor Standards. Bulletin No. 41 (revised). U.S. Government Printing Office. Washington, D.C., p. 65. As cited in Danziger, 1960.

d lactic de-
l. scandinav.

the human
h. Baet. 80;

of oxidative
ophopyridine

n carcinoma

Cancer Res.

DEPARTMENT OF PATHOLOGY, KAROLINSKA INSTITUTET, STOCKHOLM,
SWEDEN. HEAD: AKE WILTON, M.D.

THOROTRAST TUMOURS

A Review of the Literature and Report of two Cases

By

SVEN DAHLGREN

Received 24.iii.61

Although thorotrast was used as a contrast medium to a fairly wide extent in Scandinavia as late as the 1940s, there has been no report from these countries of malignant tumours ascribed to this technique. Since the latency period for malignant "thorotrast" tumours ranges from 10 to 35 years it would seem likely that in the next few years a large number of such cases will be encountered. In recent years a number of such cases have been reported from other countries.

In connection with the description of two new cases, one of a fibrosarcoma at the site of injection and the other cancer of the bile ducts, a detailed study of the literature in the field has been made.

Thorotrast is a colloidal solution of thorium dioxide (ThO_2), containing about 25 per cent of the dioxide with a particle size of between 3 and 10 $\text{m}\mu$, 25 per cent of partly inverted carbohydrates and 50 per cent water, with small amounts of preservatives. Thorium has a half-life period of 1.4×10^{10} years, and 20 ml of thorotrast are equivalent in radioactive effect to about one μg radium.

The radiation emitted by thorium consists of 90 per cent alpha-, 9 per cent beta- and one per cent gamma-rays. (Johansen 1954).

Survey of the Literature

Thorotrast deposited in the tissues can be demonstrated histologically. In sections stained by van Gieson's method particles of thorotrast appear as brownish black granules, and in those stained by the haematoxylin-eosin method they are purple. Although characteristic the histologic picture is not specific for thorotrast. The particles can, however, be recognized by autoradiography and determination of the radiation spectrum (Roberts & Carlson 1956).

Soon after its introduction in 1928, this medium won favour in many different spheres of radiology, including myelography, encephalography, retrograde pyelography, mammography, salpingography, cholangiography and for visualizing fistulas, the sinuses and lacrimal ducts, but it is in angiography that it has been most commonly used, especially in Sweden.

The possibility of radioactive injury from thorotrast, in the first place cancer, and then damage to the vessels, was recognized shortly after its introduction, but in spite of persistent warnings, thorotrast gained in popularity owing to its advantages over media used hitherto, chiefly the absence of vascular reactions and allergic complications. Moreover, it is very homogeneous.

In comparatively few instances have clinical complications been reported (*Thomas et al* 1951, *Backer* 1957, *Johansen* 1960), but indications have been found to form readily at the site of injection. Sporadic cases of anaemia and hepatic disorders have been described, and follow-up examinations have revealed histologic changes in the liver, spleen, bone marrow, skeleton and other organs, chiefly in the form of fibrosis, necrosis and granulomas. (*Rotter* 1951). *Lindgren* (1938) described cerebral damage after arteriography with the medium. In 21 cases out of 35 there was histologic evidence of thorium in the cerebral vessels and in 6 of these there were small haemorrhagic areas and softenings. In several countries, including Sweden, the use of thorotrast was discontinued in the 1940s, but in other countries this was still being recommended as one of the foremost media far into the 1950s (in, for instance, angiography).

Early damage with this substance is slight. Study of long-term effects, especially growth of malignant tumours, requires protracted observation of the patient, and for this reason they have in the past not received due attention. The increasing use of radioactive materials in recent years, however, has attracted focused interest on the subject of thorotrast tumours.

As early as 1935-36 it was demonstrated on laboratory animals that thorotrast injected intravasally, interperitoneally and subcutaneously could give rise to tumours (*Selbie* 1936, *Foulds* 1939, *Guimaraes et al.* 1955 and *Johansen* 1954). The first case of thorotrast tumour in man (endothelial-cell sarcoma of liver) was discovered in 1946 by *MacMahon et al.* (1947) and since then some 60 cases of such tumours have been described.

These may be divided into three groups: according to their mode of origin:

- (A) Tumours appearing at the site of injection (Table 1).
- (B) Tumours due directly to thorotrast deposited in the hollow organs, etc. (Table 2).
- (C) Tumours due to thorotrast injected systemically and deposited in the reticuloendothelial system (Table 3).

For the tumour to be ascribed to thorotrast deposited in the tissues the following conditions should be satisfied: (I) Thorotrast particles should be found in the immediate vicinity of the tumour. (II) The latency period should be sufficiently long, and (III) the radiation dose

TABLE 1
Tumours at Site of Injection.

Author	Tumour	Purpose of Injection	Dose, cc	Lat. per year	Sex	Pl. Age Year
Plenge et al.	Fibrosarcoma	Cerebral angiography	20	6	F	54
1954						

Age at diagnosis or death.

24861003

TABLE 1
Tumours at Site of Injection.

Author		Tumour	Purpose of injection	Dose cc	Lat. per year	Sex	Pt. Age* year
Plenge et al.	1954	Fibroblastsarcoma	Cerebral angiography	20	6	F	54

* Age at diagnosis or death.

TABLE 2
Tumours after Deposition of Thorotrast in Performed Cavities.

Author		Tumour	Purpose of Injection	Dose cc	Lat. per year	Sex	Pt. Age* year
Zollinger	1949	Spindel-cell sarc., kidney	Pyelography	30	16	M	64
Austoni	1950	Carc. breast	Mammography	10	12	M	47
Ruf & Philipp	1950	Carc. eyelid	Dacryocystography	-	35	M	51
Hofer	1952	Carc. maxillary sinus	Maxillary visual.	-	10	F	64
Vögtlin & Minder	1952	Bronchogenic carc.	Bronchography	30	18	M	47
Gros et al.	1955	Carc. maxillary sinus	Maxillary visual.	-	15	M	36
Scheiße	1955	Malign perit. thorotrastoma	Intraperitoneal	24	17	F	60
Boemke	1956	Carc. kidney	Pyelography	-	-	M	75
Budin & Gershon-Cohen	1956	Carc. breast	Mammography	-	17	M	43
Federlin & Scior	1957	Carc. ovary	Salpingography	-	23	F	45
Jacob & Schostok	1957	Carc. kidney	Pyelography	-	25	F	49
Roth	1957	Bronchogenic carc.	Bronchography	-	13	M	38
Nielsen & Kracht	1958	Mixed tumour kidney	-	-	-	F	66
Verhaak	1958	Adenocarc. kidney	Pyelography	-	21	F	43
Verhaak	1958	Carc. in situ, kidney	Pyelography	-	23	F	44
Gelzer & Scheidegger	1959	Carc. seminal vesicle	Urethrovesicography	-	14	M	68
Alken et al.	1960	Carc. kidney	Pyelography	-	23	M	56
Cattell & Kahn	1960	Peritonealcarc.	Salpingography	-	21	F	48
Gros et al.	1960	Carc. maxillary sinus	Maxillary visual.	-	14	F	49
Kligerman et al.	1960	Carc. maxillary sinus	Maxillary visual.	-	18	F	32
Kligerman et al.	1960	Carc. maxillary sinus	Maxillary visual.	-	21	M	39
Kligerman et al.	1960	Carc. maxillary sinus	Maxillary visual.	-	10	M	70
Kligerman et al.	1960	Carc. maxillary sinus	Maxillary visual.	-	15	F	70
Krückemeyer et al.	1960	Carc. kidney	Pyelography	-	23	F	45

* Age at diagnosis or death.

should be sufficiently high. (The measurement of the radiations should preferably be performed on the organ concerned).

In the following compilation only malignant tumours have been included.

In group A there is only one case of malignant tumour. There are, however, cases of benign fibrous tumours belonging to this category (Rotter 1951). These appeared in direct connection with the thorotrast particles deposited extravasally at injection.

Group B is fairly heterogeneous since thorotrast was used in so many different types of radiologic examination. A common feature of all these cases, however, is that the medium was deposited in cysts, fistulas, performed cavities, etc., and after the examination all the contrast medium injected had not been removed.

It should be noted here that the cases attributed to *Ruf & Philipps* were also reported by *Rudolphi* in 1951. Similarly, *Budin & Gershon-Cohen's* patient was published by *Brody & Cullen* (1957), *Scheibe's* case by *Klemm* (1955) and *Federlin & Scior's* by *Schwenzer & Federlin* (1957).

In the group C cases, in which malignant tumours were due to deposit of thorotrast in the reticuloendothelial system after systemic injection, the contrast medium was used chiefly in cerebral angiography and hepatolienography. The tumours were practically all localized in the liver but a few cases are described where they appeared in other organs in contact with the thorotrast foci in the liver, spleen or lymph nodes (Group 3 B). Cases of leukaemia ascribed to thorotrast deposits are borderline ones of this group but are not included in this review. (*Wohlwill* 1942, *Spier et al.* 1947, *Grebe* 1954, *Netóusek* 1957).

Thorotrast is taken up in the reticuloendothelial system and deposited chiefly in the liver, spleen and bone marrow in the ratio 7:5:1. (*Rössle* 1949). A very small amount was also deposited in the lungs and the adrenals. The amount excreted is insignificant. The particles of thorotrast are deposited as large aggregates, which gradually increase in size.

In the spleen the changes do not take the form of tumour growth but of progressive destruction with fibrosis of the parenchyma. The spleen is usually reduced in size and has a firm consistency (*Looney* 1955, *Looney & Colodzin* 1956). Vascular changes in the spleen have also been described (*Levy* 1960).

Twenty-six cases of different forms of malignant tumours originating in the liver or bile ducts after use of thorotrast have been reported.

An increasing number of cases of liver tumours following application of thorotrast have been reported in recent years, and more can be expected in the immediate future.

If *Silva Horta's* first case (1953) is omitted on the grounds of the short latency period of 3 years 2 months, the average period for the 28 cases published is about 18 years. In 1951 *Thomas et al.* described a case of liver tumour that had appeared 9 years after hepatolienography

idia. As should

curs have been

tour. There are,
to this category
in the thorotrast

used in so many
a feature of all
in cysts, fistulas,
all the contrast

Ruf & Philipps
din & Gershon-
957), Scheibe's
nzer & Federlin

were due to de-
after systemic
ral angiography
all localized in
peared in other
spleen or lymph
rotrast deposits
in 's review.
k 1, 2, 3).

m and deposited
7: 5: 1. (Rösle
lungs and the
rticles of thoro-
increase in size.
our growth but
ma. The spleen
(Looney 1955,
spleen have also

curs originating
been reported.
ing application
d more can be

grounds of the
period for the 28
al. described a
atolienography

TABLE 3 A
After Systemic Infection: Malignant Liver and Bile-Duct Tumours.

Age* Year	Sex	Post Year	Dose cc	Purpose of Infection	Tumour	Author	Age at diagnosis or death.
12	F	12	10	Hepatolienography	Endothelial-cell sarc.	MacMahon et al.	1947
63	F	14	75	Cerebral angiography	Endothelial-cell sarc.	Lüdin	1953
—	F	3.2	20	Cerebral angiography	Endothelial-cell sarc.	Silva Horta	1953
39	M	20	—	Hepatolienography	Carc. common duct	Heitman	1954
54	F	21	80	Hepatolienography	Bile-duct, carc.	Mathes	1954
49	M	12	—	Arteriography	Endothelial-cell sarc.	Frühling	1955
54	M	14	—	Cerebral angiography	Hemangioendothelioma	Tesluk & Nordin	1955
54	M	24	—	Arteriography	Hemangioendothelioma	Caroli et al.	1956
58	M	24	—	Arteriography	Adenocarcinoma	Grossiord et al.	1956
53	F	21	80	Arteriography	Hepato-cellular carc.	Mathes	1956
52	F	23	70	Hepatolienography	Cholangio-cellular carc.	Mathes	1956
45	F	17	—	Arteriography	Hepatic duct, carc.	Roberts & Carlson	1956
46	M	22	—	Arteriography	Endothelial-cell sarc.	Silva Horta	1956
58	M	12	—	Arteriography	Primary carc.	Batzenschlager & Wilhelms	1957
37	M	13	—	Cerebral angiography	Primary carc.	Federlin & Seier	1957
40	F	11	—	—	Carc. common duct	Okimaka et al.	1957
61	M	24	75	Hepatolienography	Hemangioendothelioma	Grampa & Degen	1958
49	M	15	—	Arteriography	Hemangioendothelioma	Hieronymi	1958
16	M	16	—	Arteriography	Bile-duct carc.	Hieronymi	1958
48	F	24	—	Hepatolienography	Primary carc.	Morgan et al.	1958
47	F	22	—	Cerebral angiography	Carc. left hepatic duct	Gardner & Ogilvie	1959
13	M	13	80	Arteriography	Hemangioendothelioma	Koschenbaum	1959
57	M	20	—	Arteriography	Carc. liver and lung	Wertheimann	1959
37	M	14	—	Liveryst. visual.	Bile-duct carc.	Baserga et al.	1960
49	M	12	—	Arteriography	Endothelio-angiosarcoma	Gros et al.	1960
61	M	24	75	Hepatolienography	Cholangiogenous carc.	Kohoutek & Novak	1960
58	M	20	—	Arteriography	Adenocarcinoma	Stemmermann	1960

TABLE 3 B
After Systemic Injection: Malignant Tumours, other Sites than Liver and Bile-Ducts.

Author		Tumour	Purpose of Injection	Dose cc	Lat. per year	Sex	Pt. Age* year
Budin & Gershon-Cohen	1956	Carc. colon	Hepatolienography	-	-	F	65
Hackenthal	1956	Bronchogenic carc.	Arteriography	-	16	M	75
Wuketich & Mark	1957	Carc. paner. and kidney	Arteriography	-	13	M	70
Nielsen & Kracht	1958	Adenocarc. lung	Hepatolienography	-	24	M	43
Gardner & Ogilvie	1959	Giant follic. lymph. spleen	Cerebral angiography	15	15	F	65
Friedrich	1960	Carc. kidney.	Cerebral angiography	-	20	F	55

* Age at diagnosis or death.

Case 1. S

with thorot
tion becaus
Doubt att
had an ass
Many cc
by Abrah
lienograph
carcinoma
be ascribe
present re
ally in vic
colon. The
about 18

Case 1.

A man at
to a hospi
Encephal
vexity. Art
of medium
logic exam
In 1959
neck. Test
made to r
sisting of

24861007



Fig. 1.
Case 1. Neurofibrosarcomatous tumour with small deposits of thorotrast.
(van Gieson) $\times 167$.

with thorotrast. This case has not been included in the above compilation because it seems not to have been sufficiently thoroughly described. Doubt attaches to *Stenmermann's* second case (1960) as this patient had an associated cystadenocarcinoma of the ovary.

Many compilations of thorotrast tumours include a case described by *Abrahamson et al.*, a 63-year-old woman who, 16 years after hepato-lyenography with thorotrast (75 ml), died in bilateral alveolar lung carcinoma. Since no thorotrast was found in the lungs this case cannot be ascribed to the thorotrast and has therefore not been included in the present review. Doubt attaches also to *Budin's* (1956) case, especially in view of the fairly high spontaneous incidence of cancer of the colon. The mean latency time in this heterogeneous group (III B) was about 18 years.

REPORT OF TWO CASES

Case 1.

A man aged 41. Head injury in 1932; epileptic fits began in 1933. He was admitted to a hospital in 1941 for neurologic examination.

Encephalogrammes suggested a brain tumor, situated on the left side of the convexity. Arteriography with thorotrast via the left common carotid artery (amount of medium is not reported) showed arteriovenous aneurysm; confirmed by histologic examination.

In 1959 the patient discovered a nodule in the soft tissues on the left side of the neck. Test excision showed neurofibroma of a benign type, and an attempt was made to remove the tumour. Histologic examination showed neurofibroma consisting of tumour tissue with regions poor in cells and rich in collagen alternating



Case 1. Deposits of thorostrast situated in macrophages and surrounded by neurofibrosarcomatous tumour. (van Gieson) $\times 448$.

with regions rich in cells and poor in collagen. There was no evident palisade disposition. Cellular polymorphism was fairly slight. There were sporadic mitoses. Small deposits of thorostrast were observed.

Radiologic examination. In 1960 tomography of the soft tissues of the neck suggested "thorostrastoma". There were no definite metastases. The spleen was greatly enlarged and the parenchyma contained miliary densifications, which could have been due to thorostrast. Similar densifications were observed around the porta hepatis, which may have been due to thorostrast accumulations in the lymphatic nodes.

15th February, 1960: Sternal puncture showed numerous particles in the marrow with a reduced fat content and increased cellular activity. The bone marrow was markedly hyperplastic. The sections showed a dense cell agglomeration of cells that contained thorostrast.

18th February, and 12th December, 1960: Further attempts were made to remove the tumour since it had increased in size and was considered to be locally malignant.

Histologic examination (performed at the Institute of Radiopathology, Stockholm) showed a partially encapsulated tumour resembling a neurofibroma, and parts of which diffusely merged with connective tissue and fat tissue, suggestive of an infiltrative tendency. In places there were regions fairly dense in cells with some polymorphous nuclei and mitosis. The cells, in both density and disposition, suggested a highly differentiated fibrosarcoma (neurofibrosarcoma). In and around the tumour tissue there were numerous deposits of thorostrast, some of them situated in macrophages (Figs. 1, 2).

To summarize, the patient was a 41 year-old man on whom at the age of 21 cerebral angiography had been performed with thorostrast; since 1959 he had had recurrent neurofibrosarcomatous tumours in the neck at the site of injection of the medium.

Case 2.

A man, aged 41, with headache and tinnitus. Bilateral arterio-venous thorostrast, disc medial cerebral for left pleural then showed a hospital, with was noted, with 20,000. The liver suspected to be

The condition 1959 (with a 1

Autopsy at 1 External ex: mal. No jaund

Circulatory no malformat

A thrombus, i

Respiratory tumour. Lung

surfaces of th

of rice grains

of metastases

pleural surfa

of the palm

The thyr

section was

of malignant

Abdominal

with blood. C

with the app

white in col

drawn up to

The stom:

evidence of

The liver

On the surf:

stages. The

diameter, so

At the hilu

6 cm in dia

to originate

normal, and

of greyish-

para-aortal

Urinary

Spinal co

definite sig

Femur:

Cranium

from a 1.5

cerebral ar

near the f

Microsec

of the hif

tumour w

parts whi

of the tun

ular ther

The tun

fibrous ti

21861009

Case 2.

A man, aged 64, who in 1938 underwent cerebral angiography for examination of headache and epileptic fits from which he had been suffering for some 8 years. Bilateral arteriography via the internal carotid artery, performed with 4×8.5 ml. thorotrast, disclosed an aneurysmal widening of part of the uppermost branch of the medial cerebral artery on the right side. In 1958 the patient was admitted to hospital for left pleural pneumonia and cardiosclerosis, and arthrosis deformans. Radiology then showed a radiopaque thorotrast spleen. In 1959 the man was re-admitted to hospital, with diffuse aching throughout the body, and high temperature. Anaemia was noted, with Hb 55-60 per cent; erythrocytes 3.5 million; white cells 15,600-20,000. The liver was enlarged. Needle biopsy from the liver showed cells that were suspected to be malignant.

The condition of the patient deteriorated rapidly and he died in the autumn of 1959 (with a picture of cachexia).

Autopsy at the Karolinska sjukhuset.

External examination: Left leg oedematous and bluish in colour. Otherwise normal. No jaundice.

Circulatory system: The heart was normal in size and configuration. There were no malformations. Coronary vessels, the aorta and pulmonary arteries were normal. A thrombus, attached to the wall of the left femoral vein, occluded the lumen.

Respiratory organs: The respiratory tract was unobstructed. No evidence of tumour. Lungs heavier than normal; right 850 g, left 750 g. On the basal pleural surfaces of the inferior lobes there were several slightly elevated formations, the size of rice grains and brownish-red in colour. Extensive pulmonary oedema. No evidence of metastases. Bilaterally in the pars diaphragmatica the parietal leaves of the pleural surfaces showed greyish white deposits, two millimetre thick, and the size of the palm of the hand.

The thyroid gland was fairly much enlarged, and weighed 160 g. The surface of section was homogeneous, smooth and a light greyish-brown colour. No evidence of malignancy.

Abdominal organs: The abdominal cavity contained 750 ml fluid, slightly tinged with blood. On the inferior aspect of the right diaphragm there were two formations with the appearance of metastases, 2×2 cm, consisting of small nodules and greyish white in colour. The peritoneal surfaces were otherwise smooth. The omentum was drawn up towards and partly adherent to the spleen.

The stomach and intestinal tract showed no definite pathologic changes. No evidence of tumour.

The liver weighed 1850 g and extended down below the right border of the ribs. On the surface of the liver were several round greyish-white foci typical of metastases. The surface of section showed numerous metastatic foci up to 3 cm in diameter, some of which contained small quantities of a greyish opalescent mucous. At the hilus there was a diffusely demarcated firm greyish-white tumour, about 6 cm in diameter and growing down towards the head of the pancreas. It appeared to originate in the bile ducts of the hilus region. Around the pancreas, which was normal, and at the greater and lesser curvatures of the stomach there were a number of greyish-white firm lymph nodes with tumorous tissue. Metastases were found para-aortally in the lymph nodes. Porta hepatis normal.

Urinary tract organs. No special features. Prostate normal.

Spinal column: The bone marrow was slightly paler than usual. There were no definite signs of metastases.

Femur: The bone marrow was active, with no metastases.

Cranium and meninges: Normal. Cerebrum: Basal cerebral vessels normal apart from a 1.5×1.5 cm round, calcified focus adjacent to the right branch of the middle cerebral artery, 2 cm from its origin in the circle of Willis. The cerebral parenchyma near the focus showed small older softenings with areas of cystic degeneration.

Microscopic examination: Sections from the large tumour infiltrate in the region of the hilus showed pictures of a moderately differentiated adenocarcinoma. The tumour was composed of large amounts of fibrous tissue well developed glandular parts which contained fairly with cubic and cylindrical epithelium. Large regions of the tumour showed a low stage of differentiation and near these regions in particular there were large areas of necrosis.

The tumour involved both blood and lymph vessels and nerve sheaths. Areas of fibrous tissue contained large quantities of thorotrast particles, some of them

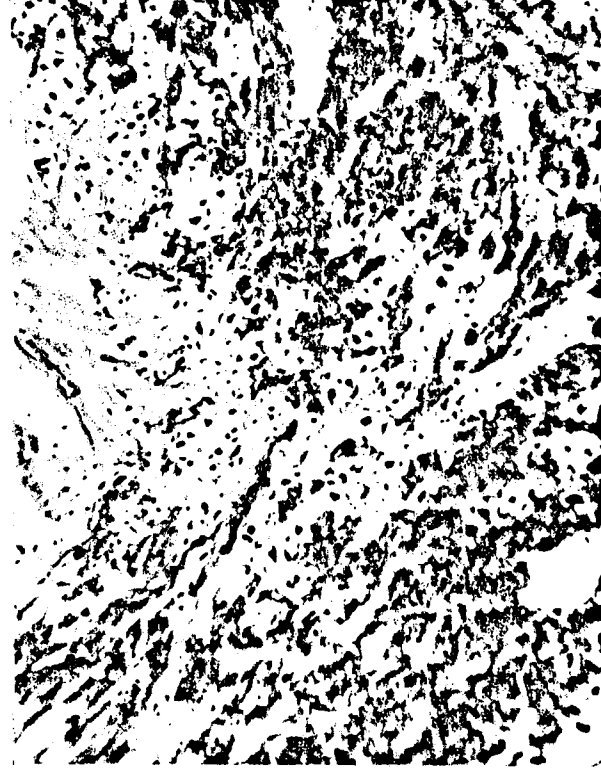


Fig. 3.
Case 2. Adenocarcinoma in the liver containing large deposits of thorotrast. Dense masses in the lower portion represent the thorotrast. (van Gieson) $\times 167$.

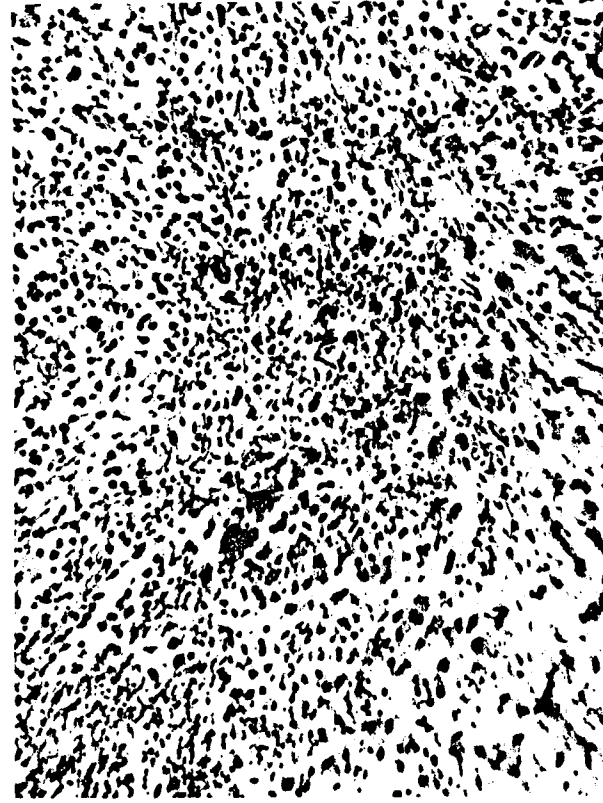


Fig. 4.
Case 2. Metastases in the liver showing intermixture of carcinoma and thorotrast. (van Gieson) $\times 167$.

deposited in macrophages. tions of the same type of pi found in the metastases. difficult to assess the unir thorotrast deposits, especia mild stasis and fatty degenera Pancreas: The tumour t pancreas, which, however, t of thorotrast deposits.

Spleen: The picture is doi situated perivascularly in s atheromatous and arteriose lymphoid tissue largely rep spleen. There was an appri contained numerous deposit small focus with growth of

Bone marrow from vertel tions showed, however, fai cellular and some in large Bone marrow from the fe poetic activity. No tumour.

the time of the injection of t poetically active but consist the occasion of the injection the femur marrow was acti blood vessels at this later o

Lungs: Signs of stasis a pneumonia infiltrates. No deposits. Round the vessels. thracotic deposits. The subpl The small reddish-brown fo granulation tissue rich in showed marked fibrous thic

Lymph nodes: In sections para-aortally and showing n of tumour similar to that f however, was strikingly nec thorotrast particles were see

Kidneys: Moderate arteri deposits.

Thyroid gland: Acini enla increased cell activity. No c

"Radiologic measurement Radiophysical Institute, Stoc spleen and bone marrow.

In brief, a man of 64 y of thorotrast in connec thorotrast deposits were lymph nodes. In connect of the liver, a moderate; from the intrahepatic bil in the regional lymph no

24861011

In both cases the thor tion from thorium part latter case, where there v

deposited in macrophages. The metastases in the liver contained numerous vegetations of the same type of primary foci. Different degrees of differentiation were also found in the metastases. Owing to fairly extensive postmortem changes it was difficult to assess the uninvolved liver parenchyma, but there were fairly many thorotrast deposits, especially round the centrilobular vessels. There were signs of mild stasis and fatty degeneration. No cirrhosis (Figs. 3-4).

Pancreas: The tumour tissue at the hilus of the liver grew down towards the pancreas, which, however, appeared to be intact and its structure normal. No signs of thorotrast deposits.

Spleen: The picture is dominated by the numerous deposits of thorotrast particles situated perivascularly in small and large foci. The vessels were in places strongly atheromatous and arteriosclerotic. The parenchyma contained much blood and the lymphoid tissue largely replaced. No evidence of tumours in the parenchyma of the spleen. There was an appreciable thickening of the capsule and the deepest parts contained numerous deposits of thorotrast. At one place in the capsule there was a small focus with growth of the same cancer described in the liver.

Bone marrow from vertebrae: Largely normal structure. No metastases. The sections showed, however, fairly numerous thorotrast particles, some of them extracellular and some in large macrophages.

Bone marrow from the femur: The sections showed signs of increased haemopoietic activity. No tumour. No thorotrast deposits, possibly due to the fact that at the time of the injection of thorotrast the femur marrow was probably not haemopoietically active but consisted of fat. When the bone marrow, originally active on the occasion of the injection, was subsequently damaged by the thorotrast radiation, the femur marrow was activated. Since, however, no thorotrast was found in the blood vessels at this later occasion none could have been deposited.

Lungs: Signs of stasis and fairly advanced oedema. In places small bronchopneumonal infiltrates. No evidence of tumour. No definite signs of thorotrast deposits. Round the vessels, and especially subpleurally, there were moderate atherotic deposits. The subpleural parenchyma of the lung showed increased fibrosis. The small reddish-brown formations on the visceral pleural surfaces consisted of granulation tissue rich in teleangiectatic vessels. The parietal pleural membrane showed marked fibrous thickening, with sporadic granulation tissue.

Lymph nodes: In sections from the nodes situated near the hilus of the liver and para-aortally and showing macroscopically evidence of metastases there was growth of tumour similar to that found in the liver. The tumour tissue in the metastases, however, was strikingly necrotic and in places imbibed with blood. Small foci of thorotrast particles were seen in the lymph nodes.

Kidneys: Moderate arterio- and arteriosclerosis. There were no thorotrast deposits.

Thyroid gland: Acini enlarged and rich in collagen, though with no evidence of increased cell activity. No evidence of tumour. No evident deposits of thorotrast.

"Radiologic measurements by radiation spectrum analysis" (performed at the Radiophysical Institute, Stockholm) confirmed the presence of thorium in the liver, spleen and bone marrow.

In brief, a man of 64 years, who 21 years previously had had injection of thorotrast in connection with cerebral angiography. At autopsy thorotrast deposits were found in the liver, spleen, bone marrow and lymph nodes. In connection with the large foci of thorotrast in the hilus of the liver, a moderately differentiated adenocarcinoma had developed from the intrahepatic bile ducts. Metastases were found in the liver and in the regional lymph nodes. The patient died in secondary heart failure.

DISCUSSION

In both cases the thorotrast tumours were probably elicited by radiation from thorium particles deposited in the tissues. As regards the latter case, where there was cancer of the bile duct, importance attaches

24861012

to the low incidence of such tumours in man in the Scandinavian countries. According to *Ringertz & Ericsson* (1961) only 0.7 per cent in Sweden.

The question of the carcinogenic action of thorotrast has been thoroughly discussed among radiologists, pathologists, radiophysicists and others. Many, including *Baserga et al.* (1960), consider that the number of cases of such tumours is definite proof of the carcinogenic effect of thorium. Others point to the fact that in spite of the large numbers of thorotrast injections given over many years, only about 60 cases have been reported or even noticed, owing to various circumstances such as absence of autopsy, and the fact that the physician was unaware that thorotrast had been used. That rather few cases of malignant thorotrast tumours have been described is certainly due in some degree to the long latency period. Radiographic examination, involving thorotrast have probably been performed most frequently on patients who were elderly or seriously ill, many of whom die from old age or disease long before the tumours are due to appear. If all the patients receiving thorotrast had been followed for 20 to 30 years many more such tumours would certainly have been recorded. This is being increasingly realized and follow-up studies are being carried out in various parts of the world. It is therefore important that all cases of thorotrast tumours are recorded so that, with the information so obtained, we can widen our knowledge of the carcinogenic action of thorotrast.

SUMMARY

In connection with the reporting of two new cases of thorotrast tumours a survey of the literature in the field has been made which includes 59 cases. The latency period between the injection of the contrast medium and the appearance of the malignant tumour is about 18 years.

Two cases described are of a neurofibrosarcoma in the soft tissues of the neck, appearing in a 40 year-old man, 19 years after angiography with thorotrast, and a cholangiocellular carcinoma, which appeared in a 64 year-old man 21 years after cerebral angiography with thorotrast.

ADDENDUM

Since this paper was submitted, two more cases of malignant tumours following administration of thorotrast have been published.

1. *A. Nettleship* and *W. Fink* describe a hemangioendothelioma of liver in a 54 years old man, who 16 years before death received an intravenous injection of 75 cc thorotrast. (*Am. J. Clin. Path.* 35: 422-426, 1961).

2. *E. Suckow, G. Henegar* and *R. Baserga* report a case with a bile-duct carcinoma of liver, appearing 15 years after an intravenous injection of thorotrast. Amount of thorotrast is not mentioned. (*Am. J. Path.* 38: 663-676, 1961).

Abrahamson, L. associated
Alken, C., Rouc-
Carcinom-
137-156, 1
Austoni, B.: Epi-
Chirurgia.
Backer, O. G.: P.
Baserga, R., Yo-
13: 1021-1
Batzenschlager,
thorotrast
Boemke, F.: Th-
Brody, H. & Cul-
with thoro
Budin, E. & Ger-
medium.
Caroli, J., Etène
foie. Rev.
Gattell, R. B. &
Ekström, G. & L
Thorotrast
Ekström, G. & L
Thorotrast
Fallot, P.: Comi
l'administ
Federlin, K. & S
tion. Fran
Foulds, L.: The
by injecti
Friedrich, W.: I
philes Ade
Fruhling, L.: Sa
subi 12 a
thorotrast
Fruhling, L. &
généralisé
Gardner, D. L. &
of neoplas
133-144, 1
Gieser, J. & Sch
lung einer
Grampa, G. &
venous inj
Grebe, S. F.: Bei
311-319, 1
Gros, C., Fruhtin
15 ans apr
Cancer. 42
Gros, M., Fruhtin
cancer du
Grossoird, A., R.
du Foie av
hôpital. Paris
Guimaraes, J., L
tion. Brit.
Huckenthal, P.: a
biagerum
Wittman, W.: C
Chirurg. 2

24861013

REFERENCES

- Abrahamson, L., O'Connor, M., & Abrahamson, M.: Bilateral alveolar lung carcinoma associated with the injection of Thorotrast. *Irish J. Med. Sc.* 6: 229-235, 1960.
- Alken, C., Roucayrol, J., Oberhausen, E., Taupitz, A., & Ueberberg, H.: Zur Frage der Carcinom-Entstehung nach Pycelographie mit Thorotrast. *Urol. internat.* 10: 137-156, 1960.
- Austoni, B.: Epithelioma mammario maschile in sede di mastite cronica da Thorotrast. *Chirurgia*, 5: 145-152, 1950.
- Backer, O. G.: Periphere Veränderungen des Blutbildes nach Angiographie mit kolloidalem Thoriumdioxid. *Acta med. Scandinav.* 159: 195-217, 1957.
- Baserga, R., Yokoo, H., & Henegar, G.: Thorotrast-induced cancer in man. *Cancer*, 13: 1021-1031, 1960.
- Batzenschlager, A., & Wilhelm, E.: Cancer primitif de la travée hépatique sous thorotrast. *Ann. anat. path.* 2: 39-50, 1957.
- Boemke, F.: Thorotrastschäden der Nieren. *Zentralbl. allg. Path.* 95: 464-470, 1956.
- Brody, H., & Cullen, M.: Carcinoma of the breast seventeen years after mammary injection with thorotrast. *Surgery*, 42: 600-606, 1957.
- Budin, E., & Gershon-Cohen, J.: The danger of cancer from thorotrast as a diagnostic medium. *Am. J. Roentg.* 75: 1188-1193, 1956.
- Caroli, J., Eténié, J., & Platteborse, R.: Thorotrast et hémangio-épithéliome du foie. *Rev. Med.-Chir. mal. Foie*, 31: 53-68, 1956.
- Cattell, R. B., & Kahn, F.: Thorotrast and carcinogenesis. *J.A.M.A.* 174: 413-415, 1960.
- Ekström, G., & Lindgren, A.: Gehirnschädigungen nach cerebraler Arteriographie mit Thorotrast. *Zentralbl. für Neurochir.* 3: 227-248, 1958.
- Ekström, G., & Lindgren, A.: Cerebral Injuries after Arteriography of the Brain with Thorotrast. *Acta Chir. Scandinav.* 82: 291-302, 1959.
- Falloy, P.: Commentaire a propos d'une observation de cancer du foie corrélatif a l'administration de Thorotrast. *Rev. Med. Chir. mal. Foie*, 31: 53-68, 1956.
- Federlin, K., & Scior, H.: Spätschäden und Tumorentwicklung nach Thorotrastinjection. *Frankf. Ztschr. Path.* 68: 225-253, 1957.
- Foulds, L.: The production of transplantable carcinoma and sarcoma in guinea-pigs by injections of thorotrast. *Am. J. Cancer*, 35: 363-373, 1939.
- Friedrich, W.: Hypernephroides Carcinom nach Thorotrastanwendung in nephroscopischen Adenom der Hypophyse. *Ztschr. Krebsforsch.* 63: 456-459, 1960.
- Fruhling, L.: Sarcoma endothélial angio-plastique généralisé chez un malade ayant subi 12 ans auparavant une injection intra-artérielle et para-artérielle de thorotrast. *Bull. ass. franç. étude Cancer*, 42: 559-563, 1955.
- Fruhling, L., & Batzenschlager, A.: Diagnostic macroscopique de la thorotrastogénéralisée. *Ann. Anatom. Path.* 2: 32-38, 1957.
- Gardner, D. L., & Ogilvie, R. F.: The late results of injection of thorotrast: The problem of neoplastic disease following contrast angiography. *J. Path. & Bact.* 78: 133-144, 1959.
- Gelzer, J., & Scheidegger, S.: Samenblasencarcinom (14 Jahre nach Kontrastanwendung einer Harnfistel mit Thorotrast). *Oncologia*, 12: 27-33, 1959.
- Grampp, G., & Tommasini Deyna: Hemangioendothelioma of liver following intravenous injection of thorotrast. *Acta Genet. Stat. Med.* 8: 65-78, 1958.
- Grebe, S. F.: Beitrag zur Frage der Thorotrastspätschädigung. *Strahlentherapie*, 31: 311-319, 1954.
- Gros, C., Fruhling, L., & Keilling, R.: Injection de Thorotrast dans le sinus portal 15 ans après. Apparition d'un épithélioma malpighien. *Bull. ass. franç. étude Cancer*, 42: 556-558, 1955.
- Gros, M., Fruhling, L., Batzenschlager, A., & Keilling, R.: L'autoradiographie dans le cancer du foie au thorotrast. *Acta Un. Intern. Cancer*, 16: 429-430, 1960.
- Grossiord, A., Roucayrol, J., Duperrat, B., Cecaldi, P., & Merus-Bith, L.: Adénocarcinome du Foie avec cirrhose 21 ans après une arteriographie au thorotrast. *Bull. hôp. Paris*, 39: 1728-1738, 1956.
- Guimardes, J., Lamerton, L., & Christensen, W.: Late effects of thorotrast administration. *Brit. J. Cancer*, 9: 263-267, 1955.
- Hackenthal, P.: Beitrag zu den morphologischen Veränderungen durch Thorotrastablagerungen. *Zentralbl. allg. Path.* 94: 352-359, 1956.
- Heilmann, W.: Carcinom des Gallengangs und der Leber nach Thorotrastinjection. *Chirurg*, 25: 223-225, 1954.

24861014

- Hieronymi, G.*: Kritische Untersuchung sogenannter Thorotrasttumoren nebst Mitteilung zweier Fälle. Zentralbl. allg. Path. 97: 513-523, 1958.
- Hofer, O.*: Kieferhöhlenkarzinom durch radiumhaltiges Kontrastmittel hervorgerufen. Deutsche Zahnärztliche Zeitschrift, 7: 736-741, 1952.
- Jacob, H. & Schostok, P.*: Früh- und Spätfolgen nach Thorotrast Anwendung. Langenbecks Arch. klin. Chir. 285: 341-352, 1957.
- Johansen, C.*: Histological changes in man and rabbits after parenteral thorium administration. Radiobiology symposium 1954.
- Johansen, C.*: Carcinogenesis of Thorium. Acta un. Int. Cancer. 16: 425-426, 1960.
- Klemm, F. W.*: Intrakavitäre Thorotrastablagerungen nach 17 Jahren. Fortschr. Geb. Röntgenstrahlen, 82: 131-132, 1955.
- Klitgerman, M., Lattes, R. & Rankow, R.*: Carcinoma of the maxillary sinus following thorotrast instillation. Cancer. 13: 967-973, 1960.
- Kohoutek, J. & Novák, D.*: Cholangiogeni karcinom jater po thorotrastu. Ceskoslovenská rentgenologie, 14: 110-116, 1960.
- Krůček, K., Lessmann, H. & Pudwitz, K.*: Nierenkarzinom als Thorotrastabschaden. Fortschr. Röntgenstrahl. 93: 313-321, 1960.
- Levy, H.*: Histiocytäre knötchenförmige, nicht geschwulstartige Wucherungen der Leber, Milz und Lymphknoten nach Thorotrastinjektion. Frankfurt. Z. Path. 70: 423-446, 1960.
- Looney, W.*: Late clinical changes following the internal deposition of radioactive materials. Ann. Int. Med. 42: 378-387, 1955.
- Looney, W., Arnold, J. S., Levi, H. & Jee, W.*: Autoradiographie and Histopathological Studies of Thorium Dioxide Patients. A.M.A. Arch. Path. 60: 173-178, 1955.
- Looney, W. B. & Colodzin, M.*: Late follow-up studies after internal deposition of radioactive materials. J.A.M.A. 160: 1-3, 1956.
- Looney, W. B., Hirsch, J. B., Colodzin, M. & Siedman, L. T.*: Tumor induction in man following Thorotrast (Thorium dioxide) administration. Acta un. Int. Cancer. 16: 435-447, 1960.
- Lüdin, M.*: Haemangio-Endotheliomatose von Leber und Milz bei Thorotrastspeicherung. Schweiz. Ztschr. allg. Path. 16: 987-994, 1953.
- MacMahon, E., Murphy, A. S. & Bates, M. L.*: Endothelial-cell sarcoma of liver following thorotrast injections. Am. J. Path. 23: 585-613, 1947.
- Matthes, Th.*: Thorotrastschäden und Krebsgefahr. Arch. Geschwulstforsch. 6: 162-182, 1954.
- Matthes, Th.*: Zur Frage der Entstehung eines Carcinoms auf dem Boden einer Thorotrast-Narbenleber. Strahlentherapie, 99: 94-106, 1956.
- Morgan, A., Jayne, W. & Marrack, D.*: Primary liver cell carcinoma 24 years after intravenous injection of Thorotrast. J. clin. Path. 11: 7-18, 1958.
- Netoušek, M., Boreš, J. & Dvořák, J.*: Chronic Myelosis Following the Use of Thorotrast. Blood, 12: 391-397, 1957.
- Nielsen, G. & Kracht, J.*: Zur Cancerogenese nach diagnostischer Thorotrastanwendung. Frankfurt. Ztschr. Path. 68: 661-667, 1958.
- Okimaka, S., Nakao, K., Ibayashi, H., Nakaidzumi, M., Kakehi, H. & Sugimura, T.*: A case report on the development of biliary tract cancer eleven years after the injection of Thorotrast. Am. J. Roentgenol. 78: 812-818, 1957.
- Plenge, K. & Krückemeyer, K.*: Über ein Sarkom am Ort der Thorotrastinjektion. Zentralbl. allg. Path. 92: 255-260, 1954.
- Ringertz, N. & Eriksson, J.*: Frekvensen av maligna tumörer och leucemi i Sverige 1958 jämte jämförelse med de övriga nordiska ländernas frekvens. Sv. Läkartidn. 58: 565-586, 1961.
- Roberts, J. & Carlson, K.*: Hepatic Duct Carcinoma Seventeen Years After Injection of Thorium Dioxide. A.M.A. Arch. Path. 62: 1-7, 1956.
- Rosenbaum, F.-J.*: Lebersarkom nach Thorotrast. Deutsche med. Wehnschr. 84: 428-433, 1959.
- Roth, F.*: Thorotrastkarzinom der Bronchien. Zentralbl. allg. Path. 96: 417-418, 1957.
- Rotter, W.*: Über Gewebsschäden durch Thorotrast. Unter besonderer Berücksichtigung der Gefäßveränderungen und aplastischer Knochenmarksreaktionen. Beitr. path. Anat. 111: 144-157, 1951.
- Rudolphi, H.*: Spätentwicklung eines Unterlidkarzinoms nach Thoriumoxydinjektion. Beitr. path. Anat. 111: 158-164, 1951.
- Ruf, F. & Philipp, K.*: Zur Radioaktivität des Thorotrasts, ein Beitrag zur Frage

eventuel
genbecks
Rösle, R.: Sp
Scheibe, G.: A
Chir. 80:
Schwenger, A.
Entstehu
Selbie, F.: Exj
1936.
Silva Horta, J.
injektion
trast). A.
Spieler, J., Cluff
trast, J. I
Stemmermann.
trast, Am
Thomas, S., He
Radiolog
Tesluk, H. & N.
administr
Verhaak, R. L. (l
land, 1954
Werthemann, A
autoradio
350-363, 1
Wohlwitz, F.: I
dung dies
allg. Path
Wuketich, S. &
Krebsfors
Vöglin, J. & Mi
Psychograp
1952.
Zollinger, H.: 1
graphie. S

24861015

- eventueller Spätschädigungen bei seiner Verwendung als Kontrastmittel. *Langenbecks Arch. klin. Chir.* 263: 573-587, 1950.
- Rösle, R.: Spätschäden durch Thorotrast. *Zentralbl. allg. Path.* 85: 227-228, 1949.
- Scheide, G.: Malignes intraperitoneales Thorotrastom beim Menschen. *Zentralbl. Chir.* 80: 588-592, 1955.
- Schwenger, A. W. & Federlin, K.: Salpingographie mit Thorotrast vor 23 Jahren und Entstehung eines ovarialkarzinoms. *Geburtsh. u. Frauenh.* 17: 225-236, 1957.
- Selbie, F.: Experimental production of sarcoma with thorotrast. *Lancet.* 2: 847-848, 1936.
- Silva Horla, J.: Lebersarkom einer Frau. 3 Jahre und 2 Monate nach Thorotrast-injektion. *Chirurg.* 24: 218-223, 1953.
- Silva Horla, J.: Late Lesions in Man caused by Colloidal Thorium Dioxide (Thorotrast). *A.M.A. Arch. Path.* 62: 403-418, 1956.
- Spier, J., Cluff, L. & Urry, W.: Aplastic anemia following administration of thorotrast. *J. Lab. & Clin. Med.* 32: 147-154, 1947.
- Stennumann, G.: Adenocarcinoma of the intrahepatic biliary tree following thorotrast. *Am. J. Clin. Path.* 34: 446-454, 1960.
- Thomas, S., Henry, G. & Kaplan, H.: Hepatolienography: Past, Present and Future. *Radiology.* 57: 669-684, 1951.
- Tesluk, H. & Yordin, W.: Hemangioendothelioma of liver following Thorium dioxide administration. *A.M.A. Arch. Path.* 60: 493-501, 1955.
- Verhaak, R. L. O. M.: Nierafwijkingen na pyelographie met thorotrast. *Tijdschr. Holl.* 1958.
- Werthemann, A.: Über Spätschäden verschiedener Organe durch Thorotrast und autoradiographischer Nachweis desselben. *Schweiz. Ztschr. allg. Path.* 22: 350-363, 1959.
- Wohlwill, F.: Untersuchungen über die Gewebsreaktion auf Thorotrast bei Anwendung dieser Substanz zu diagnostischen Zwecken am Menschen. *Schweiz. Ztschr. allg. Path.* 5: 25-52, 1942.
- Wuketich, S. & Mark, T.: Doppelcarcinom nach Thorotrast-Arteriographie. *Ztschr. Krebsforsch.* 62: 95-108, 1957.
- Vögtlin, J. & Minder, W.: Ueber Thorotrastschäden nach Bronchographie, retrograder Pyelographie, Salpingographie und Arteriographie. *Radiol. clin.* 21: 96-115, 1952.
- Zollinger, H.: Ein Spindelzellsarkom der Niere. 16 Jahre nach Thorotrastpyelographie. *Schweiz. med. Wchnschr.* 30: 1266-1268, 1949.

24861016A

n Store REG US1C 1316304 B 042M

Time 1-DEC-94 @ 12:17 Needs By:

To Location: 3CA00Staffer: N



Number: 10241204
Title: GIGIENA TRUDA PROF ZABOLEVANIYA

June: 5 Issue: 9 ISSN/ISSN:

DATE: 1961
AGES: 26
Title: VOPROSYI TOKSIKOLOGII V KHIMII VYSOKOMOLEKULYARNYKH SOEDINE
NII

Author: DANISHEVSKII, S L; EGOROV, N M

Note: CAON

36

Page Count	6
Reason Not Filled	

Num: 5393
Co 1: 5393
Co 2: BAN

US1C 1316304 B 042M