TREATMENT OF HAEMANGIOMATOUS NAEVI WITH THORIUM X

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The unsightly nature of haemangiomatic naevi of the skin causes much distress and makes the patients or their parents seek treatment in almost all cases. The object of this paper is to assess the results likely to be obtained with thorium X in the treatment of capillary naevi, and to make certain observations regarding the application of this method.

Natural History of Haemangiomatica

Before considering how or whether these naevi respond to treatment, it is necessary to take into account the possibility of spontaneous resolution; and for this purpose it is convenient to divide them into two common varieties—the flat and the raised. Histologically, the flat ("port-wine") haemangiomatica are composed of dilated capillary-like vessels, while the raised (strawberry) lesions contain not only dilated capillaries but also many large intercommunicating blood-filled spaces which give them the name of cavernous naevi. Many of these raised lesions contain both superficial and subcutaneous elements or they may be purely subcutaneous; but, apart from their position in the skin, the two varieties of cavernous naevus appear and behave the same in every respect.

The so-called spider naevi are really very small haemangiectases, sometimes of toxic origin, as in liver disease. They are not true naevi.

Except for the faint reticular lesions of the glabellar and nuchal regions, which often resolve spontaneously (Airey, 1944a), the flat capillary naevi are nearly always persistent; hence they are often seen in adults.

By contrast, the raised (cavernous) naevi carry quite a different prognosis. It was realized for many years (Stelwagon, 1902; Jadassohn, 1932a) that complete spontaneous resolution was a possibility; later it was shown by Lister (1938) and confirmed by many other observers that the great majority resolve spontaneously by the age of 5 or 6—a happy outcome which differs from that of many forms of treatment in that it is unaccompanied by anything more than the faintest scarring. The ordinary cavernous lesions are never seen in adults. It is not proposed to discuss their treatment here, but the above remarks do not mean that active therapy is never desirable.

Some haemangiomatica remain flat for a time but become raised by the third or fourth month of life; these resolve spontaneously in the same way as the ordinary cavernous naevi. They provide, however, a possible source of error when one comes to assess the usefulness of a given treatment, for when the child is first seen the naevus may be noted as "flat" or "capillary"; its subsequent disappearance is recorded as the successful treatment of a capillary naevus, whereas it is nothing more than the spontaneous cure of a cavernous growth which in its earliest stages appeared flat and whose intermediate raised stage was not observed.

Apart from certain rare growths not mentioned here, there are two outstanding exceptions to the general rule

that the raised haemangiomatica disappear spontaneously. Both conditions are uncommon, and both usually involve large areas of skin. The first is the extensive slightly raised deep-red stain on the side of the face which often covers an area roughly corresponding to one or more divisions of the trigeminal nerve; it may even bear pedunculated excrescences. This type is just as persistent as the ordinary "port-wine" stain; it is sometimes part of the Sturge-Weber syndrome (naevus, buphthalmos, pial angiomas, and cerebral calcification on the same side, with contralateral hemiplegia and often mental defect and epileptic fits).

The second exception is the large spongy raised naevus which sometimes appears to be composed of varices and may bear areas of hyperkeratosis. It is very unsightly, is extremely difficult to treat, and may be accompanied by haemangiomatica elsewhere than in the skin; the underlying bones may be greatly rarefied. In the case reported by Silverman (1946) the patient had also a paraplegia due to an extradural haemangioma; that author mentions several other cases in the literature. Jadassohn (1932b) and Ewing (1940) say that the expansion of such cutaneous naevi may do serious damage, but this must be a very exceptional occurrence.

Treatment

Treatment of "port-wine" stains has been, and in many cases still is, very unsatisfactory; nearly all the common methods in use before the introduction of thorium X produced scarring or worse, and thorium X was welcomed as a practicable and apparently safe treatment for these lesions. Scholtz (1937) recommended it for this purpose; Prosser-Thomas (1939) reported favourable results in an unanalysed series of 50 cases; and similar reports, but dealing only with one or two patients, came from Corsi (1943) and Feeney (1944). I have been unable to trace any large series of cases treated in this way.

Thorium X is a radioactive substance whose preparation and properties were described by Lomholt (1923, 1936) and more recently reviewed by Prosser-Thomas (1945); it is sufficient to say here that it has a half-decay period of 3.64 days, emitting alpha-particles of such small penetrating power that when it is applied to the surface of the skin in alcoholic solution its effect is demonstrable histologically for a distance of only 0.2 to 0.3 mm. beneath the surface. Its effect is very similar to that of a small dose of poorly penetrating x rays: short-lived vascular dilatation progresses, after repeated doses, to an obliterative endangiitis; the possibility of serious skin damage is very small, but is considered below.

Present Study

Late in 1947 I began to review all available cases of haemangiomatic naevus treated with thorium X at St. Thomas's Hospital. The investigation was originally undertaken at the suggestion of Dr. E. W. Prosser-Thomas in order to study the possible occurrence of radiodermatitis or atrophy; but it soon became evident, as many others have discovered, that the effects of thorium X on these naevi are variable in the extreme, some patients being apparently cured, while others receive little or no benefit.

The patients and their records were therefore re-examined in the hope of finding (a) the response to be expected from the treatment of various types of naevus;

and (b) the point at which treatment of unsatisfactory cases should be abandoned as unlikely to produce further improvement.

Material Available.—The records of 48 patients with naevi treated with thorium X since 1939 were available. Four of these were not complete enough for analysis, nor could the patients be traced by letter; they were therefore omitted from the study. The remaining 44 were mostly seen by me personally.

Methods of Treatment.—In most cases thorium X in alcohol, 1,500 E.S.U./ml., was applied by a slight modification of the technique recommended by Roxburgh (1947). The erythema produced was allowed to subside and was followed about a week later by the next application, the interval between treatments being usually three to four weeks. In some patients colloidion was applied after painting, or the interval was reduced to two weeks or even one week when less intensive treatment had failed; but, apart from an increased incidence and degree of erythematous reactions, the ultimate results seemed no different.

Radiodermatitis and Atrophy

The possibility that these two ill effects might follow painting of the skin with thorium X has been suggested in the literature, but there is considerable uncertainty about their incidence, or even whether they occur at all in the dosage usually given (Airey, 1944b; Feeney, 1947; Forman, 1948).

Several authors state that they have seen a little thinning and atrophy of the skin as a result of treatment with thorium X, but these statements must be accepted with reserve, as this degree of skin-change often follows the spontaneous disappearance of an untreated cavernous naevus.

In the present series no serious damage was seen which could be attributed to the thorium X. The largest number of paintings recorded was 109 in about four years; in this case one part of the treated area became pigmented. One child, after 81 paintings spread over seven years, had questionable atrophy of the skin, with absent lanugo hairs on two small areas; one had a shiny and scaly appearance of the skin after about 63 paintings given over three and a half years, but this child was a congenital ichthyotic. Two children had definite atrophy—one with pigmentation—after 16 and 24 paintings (Cases 3 and 17), but each of these had had carbon dioxide snow as well; in view of the small amount of thorium X given, and the large amount used with impunity in other cases, it is probable that the carbon dioxide was responsible for some or all of this damage. A boy (Case 30) developed stippled brown pigmentation after 54 treatments in two years.

It is not unusual to see a shiny appearance of the skin after repeated treatments. Under the skin-microscope this appears to be due to hyperkeratosis: in my experience it is reversible in its early stages, though no doubt it indicates the need for caution.

Results

The results were grouped as follows: (a) Good, when the site of the naevus was invisible, or needed at most a faint dusting with powder to make it so. (b) Moderate, when there had been marked fading of only part of a naevus, or definite but incomplete fading of the whole naevus but only to such a degree that fairly heavy

cosmetic applications were still needed. (c) Bad, when there had been little or no change.

The differentiation of degrees (b) and (c) was by no means easy: parents are usually over-optimistic, tending to see improvement where none has occurred; this was confirmed in the few cases in which black-and-white or colour photographs taken at the beginning of treatment were available for comparison.

The clinical details of the cases are summarized in the Table. Out of 44, the results were: good, 20; moderate, 12; and bad, 12.

Good Results.—Analysis of the good results discloses the very interesting fact that 13 of the 20 cured had naevi which, though classed as "capillary" or "port-wine" when first seen, were raised at some stage of their evolution. It is suggested that at least these 13 recovered spontaneously, being in fact examples of small cavernous naevi; and that the thorium X was not an appreciable factor in their cure. This hypothesis is supported by the following facts: (1) There was no raised naevus in the moderate or bad groups. (2) Four of this group improved only a little during the treatment, but afterwards disappeared completely (11, 11, 9, and 4 paintings). (3) Ten of this group at one time raised and subsequently cured had fewer than 25 paintings, and five of these had 15 or less. This contrasts sharply with the number of paintings given to the moderate and bad groups, in which few of the patients had under 30. It would therefore seem that the degree of improvement was almost inversely proportional to the amount of treatment, a fact showing sustained enthusiasm rather than therapeutic efficacy. (4) The known tendency of cavernous naevi to spontaneous cure (see above). (5) All these cases were cured by the age of 4½ years, by which time most cavernous naevi are known to resolve.

There remained seven patients in the cured group whose naevi were never noted as raised. One of these was of the suboccipital type, with a known tendency to spontaneous cure. The very little treatment given to four others (2, 9, 13, 15 applications) makes it probable that some of these, too, were cases of spontaneous resolution. Of these seven all except one (aged 40) were cured by the age of 4 years.

Moderate Results.—Of the 12 patients noted as moderately improved, all had flat naevi, the majority of which were small or faint at the start of treatment. Their naevi have not regressed further since the discontinuance of treatment, but in every case it was thought that treatment had been worth while.

Bad Results.—The outstanding feature here is the large number of applications which were given with no useful improvement.

Conclusions

It is concluded from the above that, although many of the good results were unconnected with the use of thorium X, nevertheless the favourable results in the moderately improved group were due to that substance; and it is thought that certain observations can be made which will help in the management of similar cases. (1) Deep-red capillary naevi are difficult to treat, whereas the faint ones are easier. (2) A capillary naevus which is likely to undergo worth-while improvement on thorium X shows definite signs of it not later than the twelfth painting; a strong impression has been gained that even in these favourable cases no useful improvement is seen after a total of 30 to 35 applications. Case 5

was the only exception to this rule—a woman of 40 who began to improve after 20 paintings and was virtually cured after 64 in five and a half years. (3) It is often stated that treatment with thorium X should be started as early in infancy as possible. It is probable that this idea has arisen because, as in this series, a proportion of children seen in the youngest age group have naevi which are going to heal spontaneously; in the series given here are included patients of 44, 40, 38, 13, and 10 who showed cure or improvement, while children whose treatment was begun early are no more frequent in the improved than in the bad groups.

Ancillary Treatments

Two patients who were considerably improved by thorium X derived further benefit from pin-point cauter-

ization of residual telangiectases. This can be done without anaesthesia in an intelligent adult; it is not suitable for unanaesthetized children. A loop-cautery must never be used instead of a pin-point, as it leaves unsightly pock-like scars.

Carbon dioxide snow is difficult to control, is unpleasant for the patient, and children treated by this method seldom return for a second application. It may leave some atrophy and pigmentation if applied in effective amounts, but occasional good results may be seen in adults.

The use of heavy cosmetic applications is of the greatest possible value when "port-wine" stains persist into adult life. Judiciously applied, they can in most cases be relied on as an effective disguise, and it is unfortunate that at present they are so expensive.

Details of Cases

Case No.	Age at Start of Treatment. Sex	Description and Site	No. of Paintings	Duration of Treatment	Time from Last Treatment to Last Examination	Remarks
<i>Good Results</i>						
2	7 mths F	Slightly raised, small; forehead	40	4 yrs	3 yrs	Some wrinkling and telangiectasis remain
3	10 wks M	Raised, large; left shoulder	16	8 mths	6 "	Slight atrophy and pigmentation. No scarring. Had received four applications of CO ₂ snow
4	5 " M	Raised; left side occiput	13	14 "	5 "	Slight telangiectasis and wrinkling remain
5	40 yrs F	Flat; forehead and eyelid; present at birth	64	5½ yrs	6 mths	A few telangiectases remain
10	7 mths F	Slightly raised, small; nose	11	1 yr	3½ yrs	Faded away after treatment had been stopped. No trace remains
12	4 " F	Flat; forehead and nose	9	7 mths	4 "	Naevus present at end of treatment, then faded away quite quickly. No trace now
13	8 wks	Slightly raised; right leg	4	4 "	3½ "	Slight thinning of skin and barely perceptible telangiectasis. Faded after stopping treatment
14	9 mths M	"Telangiectatic naevus"; flat; forehead	2	1 mth	4 "	Slight wrinkling. One or two telangiectases
17	1½ yrs F	Raised; nose	24	2 yrs	3 mths	Thinning of skin and patch of absent lanugo hairs. Had received 4 applications of CO ₂ snow
23	4 mths M	Raised; eyelid	18	7 mths	1 yr	No trace of naevus
25	3 " F	Raised; face	21	17 "	2½ yrs	" "
28	3 " F	Slightly raised; lip	28	16 "	8 mths	" "
29	5 " F	Slightly raised; forehead	18	10 "	2½ yrs	Faint "blue fleck" remains
31	2½ yrs F	Flat, small, faint; nose	25	2 yrs	2½ "	Needs a little covering
32	10 wks F	Flat at birth, later raised; face; 2 lesions	29	1½ "	1½ "	One lesion gone. Other resolving slowly without further treatment
35	4 mths F	Flat, moderately faint; nape of neck	6	4 "	6 mths	Faded about 80%
36	9 wks F	Flat; nose	15	10 mths	4 "	Began to fade only at end of treatment; then disappeared in about five months
37	2 mths M	Slightly raised; face	11	10 "	2 yrs	Faded away after stopping treatment
38	6 " F	Flat; deep red, small; front of neck; and faint on glabella	13	1 yr	—	Both disappeared
42	10 wks F	Raised; right cheek	9	7 mths	10 mths	Faded after stopping treatment. A few telangiectases remain
<i>Moderately Improved</i>						
6	13 yrs M	Flat; face	20	1½ yrs	—	Four years later reported by letter that initial improvement had not been maintained
8	38 " F	Flat, faint and patchy; right side neck and face; present since birth	25	2½ "	1½ yrs	
9	44 " F	Flat; left side neck; appeared only since aged 38	20	1 yr and 4 mths		Four years later reported that treatment had bleached skin, but obvious discoloration still present
15	5 " F	Flat, pink; left side face	3	Apr-June 1944		Second course (in 1949) given at another hospital, where she was discharged as improved, not cured
18	2 " F	Flat, large; face	9	1949		Letter 18 months later. No marked change
19	24 " M	Flat; face; marked telangiectasis	34	2½ yrs	6 wks	Ultimately very good result after use of point cautery
22	1 " F	Flat; face; two small pink patches	39	3½ "	3 "	
27	6½ " F	Flat; face; extensive	55	3 "	—	
30	4½ " M	Flat; face; patchy	54	2 "	7 mths	Some pigmentation of treated area
33	7 wks F	Flat	11	7 mths	4 "	Moved away from district
40	10 yrs F	Flat, rather faint right thumb; present at birth and spreading on to wrist since age 5	15	1 yr	6 "	Late-appearing lesions almost gone. Others only moderately improved
41	5 mths F	Flat, pale; left side face and neck	30	1 "	—	Still under treatment. Possibly still fading. Has improved about 50%
<i>Bad Results</i>						
1	7 yrs M	Flat, bilateral; face, hands, neck, and part of trunk	81	7 yrs	1 yr	Questionable atrophy, with absent lanugo hairs, on two patches on cheeks
7	4 " M	Flat, small; chin	77	5 "	3 mths	Virtually no change
11	13 " F	Flat, small; face; fairly deep colour	13	8 mths	4½ yrs	No change at all
16	3 wks F	Flat, deep red; face, body, and legs	63	3½ yrs	1 yr	Painted skin shiny and scaly, but child is ichthyotic
20	3 " F	Flat, deep red, large; face	109	4 "	3 mths	Possibly faded about 30% in parts. Very unsightly. Some pigmentation has appeared
21	5 yrs M	Flat, deep red, fairly large; face	68	2½ "	3 "	Very little change
24	3½ " M	Flat, deep red, fairly large; face	42	4 "	2 "	No marked change
26	5 " F	Flat, large; face	34	2 "	—	Very slight fading
34	2 " F	Flat, faint; chin	13	3 "	—	No change. Still under treatment
39	1½ " F	Flat, not very red; cheeks and forehead	37	(long interruption) 2 yrs	—	Faded about 30% when compared with colour plates taken at beginning
43	11 " F	Flat, rather pale; face	26	13 mths	—	Possibly slight fading
44	7 mths F	Flat, large, deep red; face	24	14 "	—	" " "

Summary

From the results of treating 44 haemangiomatic naevi with thorium X it is concluded that: (1) Some patients derive useful benefit, but complete cure is not common. (2) The complete and spontaneous resolution of slightly raised "port-wine" stains may erroneously be attributed to thorium X. (3) Contrary to previous belief, the age at which treatment is begun does not affect the outcome. (4) There is seldom any point in continuing treatment when improvement is not evident after 12 applications, and it is rarely necessary or desirable to use more than 30 applications in any one area. (5) Atrophy or pigmentation does not occur if moderate numbers of treatments are used.

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The December issue of the *Practitioner* contains an interesting expert article on the estimation of the probable number of casualties in the event of atomic bomb explosion in Britain. Flash burns should form only a small fraction of the total British casualties because the weather is seldom clear, and the amount of haze will greatly cut down the danger area below the two-and-a-half-mile radius found in Japan, while high buildings and narrow streets will have a valuable shielding effect. The fire risk is thought to be small apart from the danger of a fire storm like that which caused 40,000 casualties in a single raid on Hamburg. The danger of exposure to gamma radiation is summarized in three tables which show the percentage mortalities at various doses as reported by the U.S. Atomic Energy Commission, the shielding value of concrete, and the probable casualties among a standard population (one person per 1,000 sq. ft., or 27,900 per sq. mile) all in houses. The first table ranges from 0% mortality for 100 r to 100% after 700 r, with an LD50 at 400 r. At 2,000 ft., over a mile, from the explosion centre of a Nagasaki type of bomb a 30-in. thickness of concrete will cut the radiation dose to 100 r, and 32 in. to 25 r; while at twice this distance from the centre the required thicknesses are 16 and 21 in., respectively. Direct blast injury is of little importance, because the blast pressure necessary to produce serious injury is of the order of 50–100 lb./sq. in., which is only reached directly under the bomb in an air burst at 2,000 ft. The most important risk of all is from debris, which is likely to kill over much of the area where gamma radiation is also lethal. The final estimate of the authors is a total of 31,100 killed and 29,500 injured in a population of 43 per acre all inside houses; or of 14,300 killed and 10,500 injured if everyone were in a reinforced brick surface shelter.

Medical Memoranda

Penicillin and Sulphamerazine in Treatment of Typhoid Carriers

Rumball and Moore (1949) cleared a chronic carrier by use of a combination of penicillin and sulphamerazine. They suggested that it was necessary to maintain the blood sulphonamide level at over 10 mg. per 100 ml. in order to obtain the full synergistic effect of penicillin. Following this report, we treated three typhoid carriers by this method.

CASE REPORTS

Case 1.—A woman aged 63 had been in hospital 39 years. She had had typhoid fever in March, 1915. From that date until September, 1948, she had been kept on an enteric caution card, but was not recognized as a carrier. Following negative urine and stool examinations over a period of three weeks and a negative Vi agglutination, she was taken off her enteric caution card. Six months later, on a routine check, she was found to be excreting *Salmonella typhi* (type F, I) in both urine and faeces. Penicillin, 400,000 units every three hours, was given (total, 24,000,000 units). She also received sulphamerazine, 2 g. eight-hourly, to a total dose of 38 g. Blood sulphonamide levels were estimated on three occasions over the eight-day treatment period. On the second day the level was 5.1 mg. free and 5.8 mg. total sulphonamide; on the third day, 5.8 mg. free and 5.9 mg. total; and on the eighth day, 6.7 mg. free and 7 mg. total. Penicillin estimations were not carried out. During the last 10 months repeated bacteriological examinations of both urine and faeces have failed to produce a culture of *Salm. typhi*.

Case 2.—A woman aged 64. Duration of present admission 26 years. There is no record of this patient ever having had typhoid fever, but she was exposed to an outbreak in 1915, when she had been a patient during an earlier admission. There was also a further outbreak of typhoid fever in 1943. On repeated bacteriological examinations of excreta from all patients in the hospital one year previously, she was discovered to be excreting *Salm. typhi* (type E₁, I). During the past 12 months she has been both a urinary and a faecal carrier. She was given a combined course of penicillin and sulphamerazine—500,000 units of penicillin administered intramuscularly three-hourly, to a total of 30,000,000 units, and at the same time 4 g. of sulphamerazine in the first eight hours, then 1 g. eight-hourly, to a total of 25 g. Eight days after the withdrawal of these drugs both her urine and her stools became positive to *Salm. typhi*.

Case 3.—A woman aged 67 had been in this hospital 19 years. Again there is no history of typhoid fever. She was, however, in the hospital during the minor epidemic of 1943. She has been excreting *Salm. typhi* (type F, I) in both urine and faeces over the past 10 months. This patient was treated similarly as Case 2, with equally disappointing results.

COMMENT

In Cases 2 and 3, which failed to respond to treatment, the blood sulphonamide level was maintained above 10 mg. per 100 ml.

The problem of a typhoid carrier in a mental hospital is one that must continually subject the authorities to a certain amount of anxiety, and particularly that of the carrier from the ambulatory or undetected clinical case. In all cases of pyrexia of unknown origin occurring for three days or longer typhoid fever should be excluded. The history of these three patients shows that only one had had a definite record of typhoid fever; the other