

APPENDIX NO. 5

CONSIDERATIONS IN THE STUDY OF BURNS

SEQUELAE IN ATOMIC BOMB SURVIVORS

by

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I. Introduction

Members of the Commission have been impressed during their observations of atomic bomb survivors by the fact that many of the burns have healed with accumulations of large amounts of elevated scar tissue--the so-called keloids. Considerations pertaining to this problem and plans for the study during the next two months are here discussed.

II. Present gross appearance of the burned areas

The burned areas are largely limited to exposed regions of skin and were flash burns as described in reports dealing with early studies on atomic bomb casualties. Nearly all of these are now completely healed. Ulcerated areas are still seen in burn scars of an occasional individual, such areas being located at points of stress as contractures or in scarred areas receiving a poor blood supply or where edema is relatively prominent as at ankle areas.

The scarred areas vary greatly in appearance. A few are composed of rather thin atrophic depigmented scar tissue. In others the scar tissue is extremely thick and elevated above the surface of surrounding skin. The vascularity as noted by gross observation varies much. Some, especially those located on the face, are pink in color, more elastic to pressure, and warmer to touch than surrounding normal skin. These are thought to represent a comparatively early stage in development of scar tissue--the vascularity and cellularity being more prominent than in later stages. Other areas appear white or brown in color, are firm to touch, and are the same temperature to touch as surrounding skin tissue. These are thought to be a later stage in the series of alterations that occur in scar tissue--vascularity and cellularity presumed to have decreased while hyaline connective tissue composition increased. Between these two stages are many intermediate stages according to gross appearance. The surfaces of a few burns are still marked by crusting. Dilated blood vessels are visible on the surfaces of some. Many contractures are seen at locations where these usually occur.

Pigmentary changes are still evident, but the intensity of the hyperpigmentation previously observed on the exposed skin surfaces has apparently decreased much and in some cases has practically disappeared. Some scarred areas, especially those on the hands and feet, are characterized by complete depigmentation centrally.

Skin grafts of all types have been used where contractures or "keloids" have been excised. Nothing unusual is noted in these other than that in some cases where grafts were applied at locations where "keloids" had been excised, elevated masses of scar tissue recurred. Members of the Commission were impressed by the fact, however, that "keloids" have

occurred in donor sites on a few patients on whom skin grafts were placed at locations where "keloids" secondary to atomic bomb burns had occurred.

The striking feature noted is the large number of burns that have healed with excessive quantities of scar tissue, having a relatively flat surface elevated above that of surrounding skin. Margins of these lesions are sharply defined. The area involved varies very much, some being as small as one centimeter in diameter while others may involve most of the face or the back. The maximum growth of such tissue evidently was reached about eight to ten months following the injury. None seem to be enlarging in size now. Their appearance varies also as described in the above paragraphs. The bulk of the scar tissue also varies much in these cases. These are the so-called keloids. In some cases a burn involving only a few centimeters diameter apparently occurred, yet a keloid-like scar has resulted within the limits of this area with sharply defined edges separating it from normal appearing surrounding skin. Many individuals with such keloid formation complained much of hyperesthesia and paresthesias in the areas. However, these symptoms have decreased with time and changes in the scar tissue.

Several questions have arisen regarding these so-called keloids.

1. Is the apparently high incidence of keloids in these individuals to be expected considering the severity of the burns and the etiology?
2. Was the incidence of keloid formation increased as a result of poor treatment, delayed healing, infection, and the poor general condition of the survivors of the atomic bombings?
3. Was there any other factor operating in the cause or course of healing of the burns to result in greater accumulation of scar tissue (keloids)?

An attempt to answer such questions requires a complete clinical and laboratory study of a group of the survivors in addition to a similar study of a control group of Japanese individuals who sustained burns of other etiology. It may be found desirable to continue these observations at intervals throughout the lifetime of individuals who sustained flash burns.

III. Plans for the interim study of the problem

1. Objectives
 - a. Examine, question, photograph a group of atomic bomb survivors to obtain a cross-section view of the appearance of burned areas as they now appear.
 - b. To obtain specimens of excised scar tissue on a large group of survivors (75 to 100) for microscopic study.
 - c. To obtain as much similar information on a control group of Japanese who suffered burns of other etiology during the past several years.

d. To obtain information on the subject now available in the Japanese literature.

e. All work is to be done as a joint undertaking with Japanese physicians now working on the problem.

2. Details of methods of study

It would seem best to work on a basis of cooperation with Japanese physicians now studying the problem. Therefore, it is planned to first contact Dr. Masao Tsuzuki, chairman of the Committee for the Study of Medical Effects of the Atomic Bomb of the Japanese Research Council, to discuss and formulate more detailed plans and methods.

The next step planned is to work with Dr. Tsuzuki and members of the Faculty of Medicine, Tokyo Imperial University, who have been working on this problem in obtaining information now available regarding the incidence of keloids in Japanese, especially following burns, incidence of neoplastic changes in such lesions, and any other pertinent information.

The period of time to the middle of January, 1947 is to be spent in study of patients at the First and Second National Hospitals in Tokyo examining, questioning, photographing and obtaining specimens of excised scar tissue on individuals who sustained burns from other causes than the atomic bomb during the past several years. It is desired that this work be done with Japanese physicians of the Tokyo Imperial University Faculty of Medicine.

A visit to Hiroshima is contemplated for the middle of January, 1947. Similar work would be done then at the Red Cross, Post Office, and Ujina Hospitals. If feasible and indicated, a few days trip to Nagasaki would then be made for this type of work there.

It may be desirable at some time in the study to treat cases pre- and post-operatively with penicillin to determine the significance of infection on the healing after plastic surgery of keloid areas. This is being deferred at present for further considerations and judgment as to feasibility.

Specimens and data are to be returned to Tokyo during the first week of February for organization and further study. Histological preparation and examination of specimens is being arranged with the 40th Medical Laboratory in Tokyo.

All American persons in Japan engaged in the follow-up studies of atomic bomb survivors will be kept well acquainted with the progress of the study so that continuity will never be lost. Progress reports will also be forwarded to interested persons in the United States. It is hoped that the foundations will be laid for continued work on the problem as is necessary.

Japanese physicians who have already been studying the problem and with whom it is desired to be associated in the work include:

Tokyo:

Dr. Masao Tsuzuki

At the Tokyo Imperial University, Faculty of Medicine

Dr. Shigeru Matano

Dr. Junichi Uchida

Dr. Tetsu Watanuki

Hiroshima:

Red Cross Hospital
Dr. Ken Takenouchi
Post Office Hospital
Dr. Michihiko Hachiya
Ujina Hospital
Dr. Tomosuke Komiyama
Nagasaki:
Dr. Raisake Shirabe

IV. Supplies and requirements for the study include:

1. Solutions
 - a. Zenker's
 - b. Formalin
 - c. 70% alcohol
 - d. 10% formalin
2. Bottles, wide-mouth, specimen (200), with stoppers
3. Bottles, wide-mouth, 1000 cc.
4. Questionnaire forms printed
5. Developing and printing of photographs
6. Flash or photoflood bulbs
7. Interpreter at Tokyo, Hiroshima, Nagasaki
8. Services of a photographer for perhaps one week
9. Labels, syringes, needles, forceps, medicine droppers

Questionnaire and data forms have been prepared for use in the study. These are to be mimeographed in necessary numbers.

It should be possible to obtain the necessary supplies through supply channels available to the Commission in Tokyo.

V. Considerations of factors involved in the keloid problem of atomic bomb survivors

1. Comparison with results that would occur in healing of similar lesions of any etiology:

It is desirable that the usual reparative and healing processes that would occur under any circumstances in lesions of comparable severity as to depth and area involved due to any cause, as simple excision, for example, be understood. This involves, actually, knowledge of the fundamental factors of tissue repair, especially pertaining to the skin and subcutaneous tissues. Would granulation tissue continue to accumulate until a markedly elevated mass of granulation tissue would be present before completion of healing would occur? When does completion of healing occur? What are the factors operating to control the amount of reparative tissue which does appear? What are the fundamental contributions of leucocytes in the healing processes? Work done on factors involved in epithelialization of skin lesions should be consulted. This involved a study of healing itself, not considering other variables, as treatment, infection, etc.

2. Comparison with the outcome in healing of burns of comparable severity but of other etiology:

a. If possible, fundamental characteristics of healing of burns themselves should be understood. Are there differences associated with the healing process, depending on the physical force which caused the tissue destruction: What are the characteristics of burns produced by various wave lengths of the ultra-violet, radiant, and infra-red spectra?

b. The time-intensity factor:

What are the differences in the lesion and in the healing of similar lesions as to severity when caused by heat applied with varied intensities over varied intervals of time?

Nearly all burns of the survivors were flash burns. The members of the Commission have seen some Japanese who sustained burns from other causes during the war -- flash burns from incendiary bombs, gasoline fires, and powder explosions. A few were seen who did develop keloids upon healing. Most of such cases that were seen, however, did heal with scar tissue not excessive in quantity.

3. Importance of infection in the healing of such lesions:

The influence of infection in healing of lesions as discussed in 1 and 2 above should be considered.

4. Factor of treatment:

The changes in healing resulting from various forms and degrees of treatment should be considered in the healing of such lesions as discussed in 1 and 2 above. This includes local treatment (dressings, grafting), general treatment (transfusions, nutritional care, drugs), time of application of the treatment, adequacy of treatment, ability of the person who carries out the treatment, etc.

5. The factor of the patient's general condition in healing of lesions as discussed in 1 and 2 above.

The condition of the patient throughout the healing of the lesion and the ability of the patient to provide essentials for the steps in the reparative process should be evaluated as to significance in healing of these lesions.

6. Associated factors operating in atomic bomb survivors:

a. Radiation injury:

Many of these individuals were also suffering from some manifestations of radiation injury -- decreased white blood cell counts, anemia, hemorrhagic tendency, etc. Disturbances in the steps of the reparative processes secondary to these changes are difficult to evaluate completely. It is obvious that to fully appreciate the importance of this, one must understand the part that leucocytes play in wound healing, etc.

b. The individuals concerned here were affected also by a number of the factors discussed in 3, 4, and 5 above. Many burned areas were said to have been infected. This could also have increased

the severity of the lesions as to depth of tissue necrosis and as to areas involved. Also prolonged healing with greater accumulation of infected or partially infected granulation tissue could result in part from this. The ability to combat infection must have been decreased in these individuals. Many of the survivors undoubtedly were suffering from poor nutrition, especially following the bombing.

Treatment was of necessity minimal in these cases for the most part. It was not possible to graft the burned areas as is now customary in the United States. Large areas had to heal themselves by granulating in the case of most of the survivors.

c. The burns were largely flash burns. The time-intensity data should be examined. Also the wavelengths of the spectrum concerned should be considered.

d. Factor of ionizing and neutron radiation:

It seems impossible to definitely evaluate the significance of this factor. The fact that many patients with keloids were at areas distant enough from the center of the explosion that the amount of ionizing and neutron radiation that they received must have been very low plus the fact that most of the burns were limited to exposed areas and were apparently flash burns tends to minimize the importance of the direct action by these radiations. It does seem most probable that any radiation received by survivors at the time of the bombings was "hard" in character and consisted of gamma rays and neutrons.

e. Pigmentary changes associated with the burns:

These were characteristics and have been well described in previous reports dealing with early studies of the survivors. Both depigmentation and hyperpigmentation occurred. The areas of hyperpigmentation have decreased in intensity with time and in many cases seem to have almost disappeared at the present time.

7. Existing knowledge regarding the nature and characteristics of keloids should be examined.

8. Miscellaneous

a. Question of a keloid tendency in Japanese:

Japanese physicians deny a keloid tendency in their race. However, members of the Commission have observed overgrowths of scar tissue which could be called keloids in scars of surgical incisions as well as in other healed skin lesions. However, the incidence is apparently not remarkable in scars from surgical incisions. Such wounds differ definitely from burns though in many respects (type of tissue injury, area involved, treatment, antisepsis, closure, depth). Evidence indicates that races with skins of dark color do have a higher incidence of keloids in healed scars than fair skinned races.

It is interesting that in several atomic bomb survivors elevated areas of scar tissue (keloids) were seen in donor areas where skin was removed for grafting of other areas where keloids had been excised, these keloids having developed in areas of flash burn from the atomic bomb. Keloids are said to have recurred also in individuals on

whom keloids had been simply excised and the skin edges undermined and closed.

Accumulations of scar tissues comparable in appearance to those in atomic bomb survivors have also been seen in Japanese who sustained burns from other causes -- incendiary bombs, gasoline fires, and powder explosions. However, in most of these cases the appearance of the scar tissue was not unusual in quantity.

b. That varying degrees of accumulation of granulation tissue did occur followed by a gradual change to scar of more dense connective tissue seems evident. The unusual incidence of very thick and elevated scar tissue is the striking thing. The word keloid has been used to describe such thick elevated areas of scar tissue -- this, however, necessitates definition before classification and determination of the incidence of such can be accomplished. This is a problem at present.

Apparently the burns did go through the process of granulation tissue accumulation which went on to become large in quantity in many cases, surface epithelialization finally occurring. With time, vascularity decreased gradually while the density of hyaline connective tissue increased so that the histological picture apparently was that of tissue gradually becoming more mature with fewer cells and a greater fibrous tissue composition. Contractures have occurred as usual while grossly the scar tissue has become more dense, less elevated and less red in color. Although epithelialization of the burned areas had occurred in most cases by three to four months after the injury, the scar tissue continued to increase in many so that keloid-like lesions resulted. It seems that the maximum growth of this tissue was reached eight to ten months after the bombings. Since then the amount of scar tissue has not increased as judged by gross examination.

9. The future

The natural history of the keloids does not yet seem to be completed.

Present knowledge indicates that the incidence of neoplastic changes in such lesions is increased above that for normal skin. This applies especially to burns which are slow in healing and which tend to break down at intervals. Such changes may not occur for many years, however. Locations in which chronic ulceration occurs in atomic bomb casualties should especially be observed.