

## ULTRASTRUCTURE OF SHAGREEN PATCH

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**Abstract.** Shagreen patches, fibrotic nodules and normal-appearing skin of patients were studied in the electron microscope. The patches and the fibrotic nodules showed thick compact bundles of collagen fibrils in the lower corium, the individual fibrils of which were normal. Abnormal collagen fibrils and tropocollagen-like fibrils were seen in groups or singly in thick compact bundles. Elastic fibres were few in the lower corium of the patches.

Tuberous sclerosis manifests itself variously in other organs besides the brain, i.e. heart, kidney, lung, bone and eye as well as skin. The dermal lesions derive, mainly from angiofibromatous processes (6, 8). Adenoma sebaceum, shagreen patches, ungual fibroma and fibrotic nodule of the forehead and scalp are both characteristic and diagnostic (7). The latter three skin manifestations in particular are extremely fibroplastic in the lower corium. The histopathologic findings of shagreen patch may mimic morphea (7). The present study concerns the electron microscopic lesions in shagreen patch, and the changes are compared with fibrotic nodules of the forehead and normal-appearing skin of the patients.

### PATIENTS

*Patient 1.* Twenty-six-year-old female. She has suffered from epilepsy and adenoma sebaceum since childhood. Mental retardation was evident, and subungual fibromata of her right 1st, 4th, and 5th toes and shagreen patches on her back were found. Biopsies were taken from one of the shagreen patches as well as from normal dorsal skin.

*Patient 2.* Twelve-year-old girl. She has suffered from epilepsy since the age of 6. Adenoma sebaceum of the nasolabial fold was found as well as shagreen patches and depigmented macules on her back. Biopsies were taken from one of the shagreen patches as well as from normal dorsal skin.

*Patient 3.* A 2-year-old girl who had had convulsions

since the age of 2 months. Epilepsy was diagnosed 1 year ago. Hypopigmented macules and angiomata were seen on her extremities and, in addition, retinal phacomata were demonstrated. A biopsy was removed from a firm fibrotic nodule on her forehead.

### METHOD

The specimens were fixed in a 6% glutaraldehyde solution in Veronal acetate buffer, pH 7.2, with 7.5% sucrose, and osmicated with 1% osmic acid. After dehydration of the specimens in alcohol, they were embedded in Epon 812, and ultrathin sections were stained with uranyl acetate and lead citrate. A Siemens electron microscope (Elmiskop IA) was operated at 80 kV with a double condenser system.

### OBSERVATIONS

In the lower corium, the collagen bundles were thicker and more compact in the shagreen patches than in the normal skin of the same patient. The findings in the fibrotic nodules were similar to those in the shagreen patches. The collagen fibrils of the compact bundles were straight, with a parallel arrangement and were uniformly thick (about 80 nm) with a distinct periodicity of 55 nm (Fig. 1). Here and there, abnormal collagen fibrils were seen in the thick bundles, either separately or in groups (Figs. 1, 4). They showed straight, curled and twisted shapes with normal axial periodicity in longitudinal section and round, oval and irregular cut-surfaces (Figs. 2, 3). The irregular cut-surface showed a zig-zag margin and fine lucent spots. The large transversely cut fibrils appeared flower-like (1). However, no round collagen fibril was found in the centre (Fig. 4). The thicknesses of abnormal collagen fibrils varied from about 20 to 100 nm (Figs. 2, 3, 4). These abnormal collagen fibrils were embedded in a

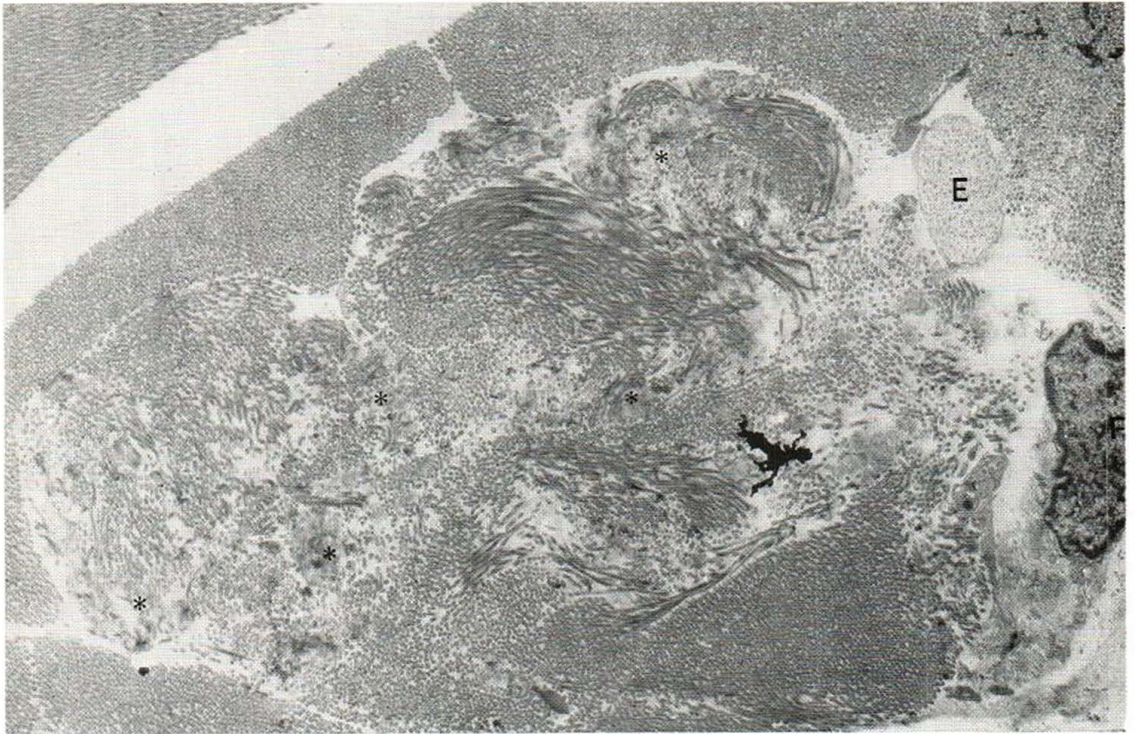
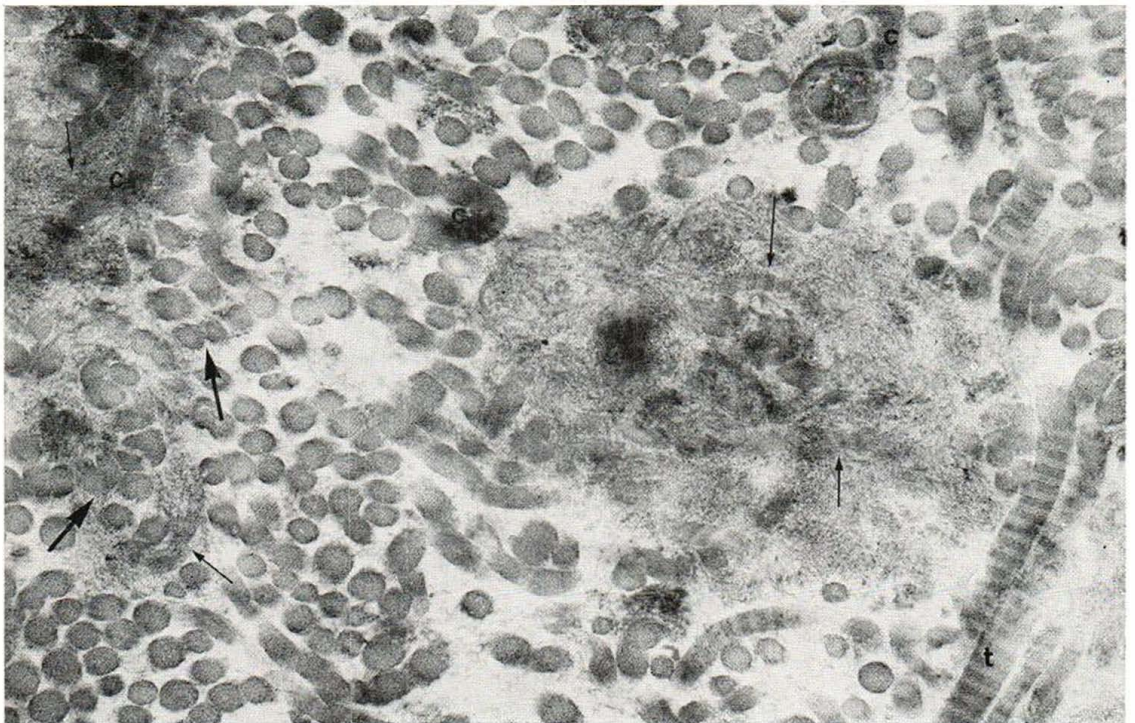


Fig. 1. Lower corium in shagreen patch. Thick compact bundles of normal collagen fibrils show uniform thickness and a parallel arrangement. Within a bundle, abnormal

collagen fibrils were seen in groups (marked by asterisk). An elastic fibre (E) and a fibroblast (F) are seen.  $\times 4500$ .



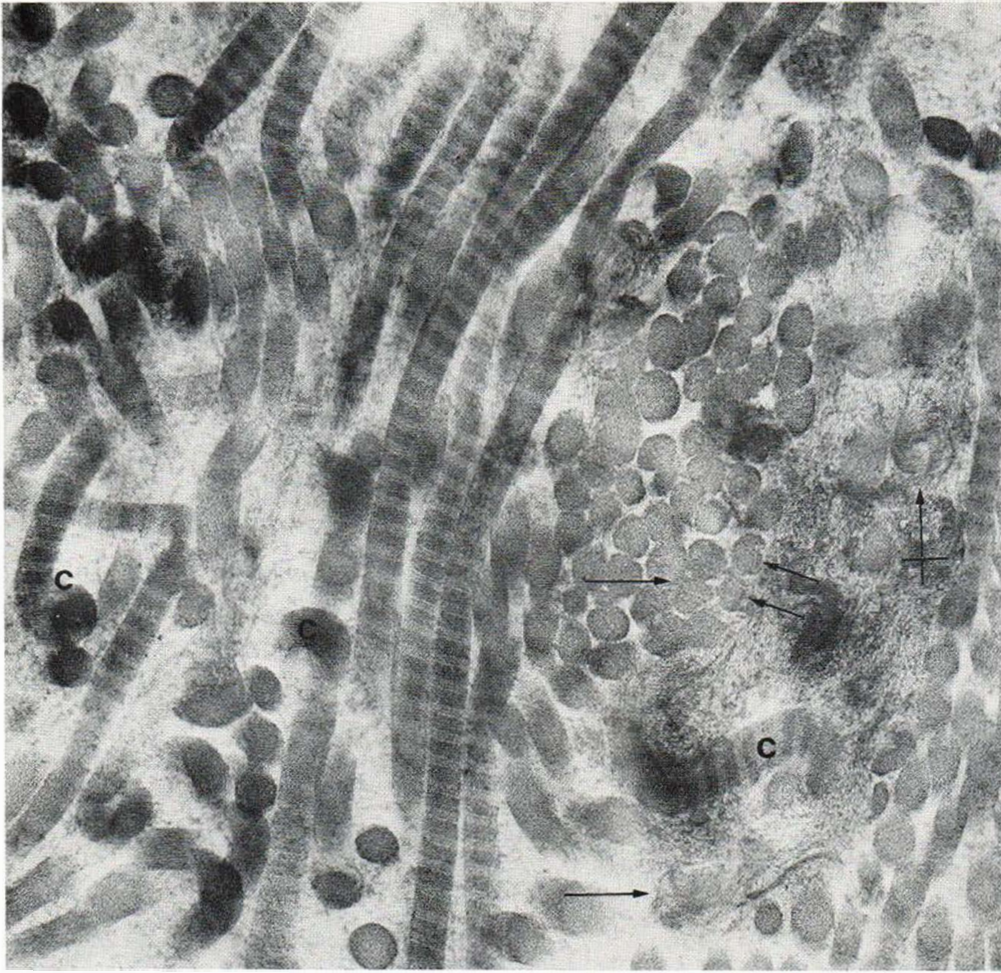


Fig. 3. Shagreen patch. Abnormal collagen fibrils (left) show thicknesses of 70 to 80 nm with distinct bandings and curling (c). To the right, a wide curled collagen fibril (c) shows distinct bandings and a whisk-like ending.

Thin arrows point out irregular cut-surfaces of collagen fibrils. A thin arrow with a cross indicates a curly thread with small irregular collagen fibrils.  $\times 60\ 000$ .

thread-like material (Figs. 2, 3). The threads may represent procollagen fibrils, since the profiles were different from acid glycosaminoglycan-filaments (4), amyloid (3) and hyalin (9), in that they appeared as whisk-like ends of collagen fibrils.

Fig. 2. Shagreen patch. Abnormal collagen fibrils with curled (c) and twisted (t) shapes and distinct bandings in longitudinal sections. There are round, oval and irregular cut-surfaces, and zig-zag margins of the fibrils with fine lucent spots. (Thick arrows indicate some distinct figures.) A thread-like material is shown in the centre and to the left of the photograph. Thin arrows (right) indicate bandings of the thread-like material and those to the left end indicate whisk-like ends of the collagen fibrils.  $\times 45\ 000$ .

and occasionally formed bundles with an axial periodicity similar to that of normal collagen fibrils. Elastic fibres and acid glycosaminoglycan filaments were few.

In the upper corium, no thick compact bundles of collagen fibrils were found, while elastic fibres with a granular matrix, acid glycosaminoglycan filaments, mast cells with mature granules, and slim fibroblasts were seen.

#### DISCUSSION

Histopathologically, a shagreen patch consists of thick homogeneous collagen bundles and frag-

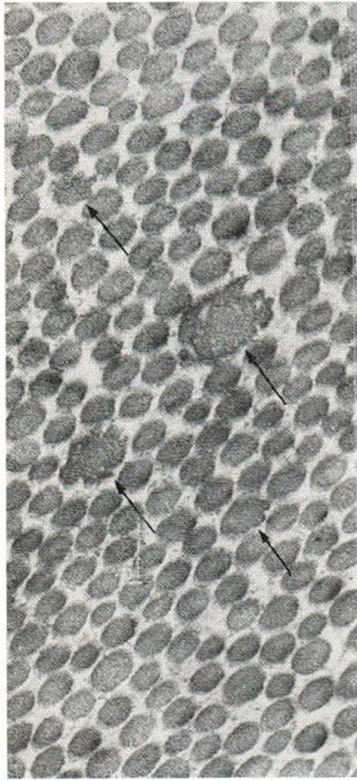


Fig. 4. Abnormal collagen fibrils were seen separately in a bundle (thin arrows) in normal-appearing skin. They showed irregular margins and fine lucent spots inside, but no central fibril was seen.  $\times 48\ 000$ .

mented elastic fibres, and, in contrast to the changes seen in other organs and adenoma sebaceum tissue, vessels are rarely found (7). No specific changes of the fibrous components in the lower corium of shagreen patches have been demonstrated. Identical findings have been described for fibrotic nodules. In all specimens examined in this study, i.e. shagreen patches, fibrotic nodules, and normal-appearing skin, there were changes in the number and thickness of the collagen bundles and in the numbers of abnormal collagen fibrils. In scleroderma, collagen fibrils show a considerable variation in thickness, and no abnormal collagen fibrils or thread-like material are found (5). The abnormal collagen fibrils seen

in this study were unlike those found in senile and pseudoxanthoma-elasticum skin (1, 2). It seems likely that a disturbed formation of collagen fibrils gives rise to such abnormal figures. The paucity of elastic fibres within the collagen bundles is in contrast to previous histological studies (7).

#### ACKNOWLEDGEMENTS

The authors thank Miss Lise Fredebo, Miss Jean A. Sage and Mr John Winther for their technical assistance.

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Received November 17, 1972

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