RESPONSE OF SCHOENLEIN-HENOCH
SYNDROME TO ACTH*
REPORT OF A CASE WITH SERIAL SKIN BIOPSIES

BY
JOSEPH E. LEVINSON, MARK HORWITZ, J. PETER KULKA,
LOT PAGE, and WALTER BAUER
From the Medical Clinic, Massachusetts General Hospital, the Departments of
Medicine and Pathology, Harvard Medical School, and the Massachusetts
Department of Public Health, Boston, Mass.

The Schoenlein-Henoch syndrome, a condition of unknown aetiology, is defined
as the clinical combination of gastro-intestinal symptoms, articular symptoms,
and a characteristic exanthema which is usually purpuric. Nephritis may be an
associated finding. The few available histological studies stress inflammation
of the minute vessels as the dominant pathological feature (Gairdner, 1948).
Because of the similarity of these manifestations of systemic disease to those of
rheumatic fever, disseminated lupus erythematosus, polyarteritis nodosa, and
serum sickness, it was of interest to note whether ACTH would effect as striking
symptomatic relief in the Schoenlein-Henoch syndrome as it does in these clinically
similar conditions.

In the present study, ACTH was employed in the treatment of a case with the
classical features of the Schoenlein-Henoch syndrome, including nephritis.
Although the administration of ACTH was followed by symptomatic improvement,
exacerbations occurred after the cessation of each course of therapy, and the
nephritis persisted. The study of seven serial skin biopsies afforded the oppor-
tunity of observing what, if any, histological changes took place in consequence of
ACTH therapy.

Case Report
Clinical History.—M.B., a 15-year-old schoolgirl, was admitted to the Massachusetts
General Hospital on May 11, 1950, complaining of malaise, severe anorexia, joint pains,
and a rash. She had been well and gave no history of infection or drug administration
preceding the appearance of a pruritic maculopapular exanthema on the dorsum of the
ankles and the extensor surfaces of the elbows and wrists 5 weeks previously. The rash
extended progressively up the legs to the knees, thighs, and buttocks. Some of the
maculopapular lesions on the extensor surfaces of the lower legs became haemorrhagic
bullae, then dried and became scabbed. Simultaneously with the appearance of the
exanthema, she had developed malaise, severe anorexia, and generalized abdominal
pain which tended to localize in the right iliac fossa. Appendectomy had been performed
at another hospital on April 12, 1950, several days after the onset of these symptoms.
The surgeon reported a "subacute appendix" though no histological examination was
made. Colicky pain accompanied by vomiting had persisted intermittently after the
operation. Two and a half weeks after the onset of symptoms, the knees, elbows, and

* Publication No. 122 of the Robert W. Lovett Memorial for the study of crippling disease, Harvard Medical School. The expenses of this investigation were defrayed in part by a grant from the Common-
wealth Fund.
Physical Examination.—The patient appeared thin, pale, and ill, but in no acute distress. The rectal temperature was 100.2°F.; pulse 110 per minute; blood pressure 160/120. The lower eyelids were slightly puffy and the dorsum of the feet and ankles showed slight pitting oedema. The abdomen was not tender. The liver was palpable one fingerbreadth below the right costal margin and was firm. The spleen was palpable two fingers-breadth below the left costal margin. No abnormalities were noted on examination of heart, lungs, fundi, and central nervous system. Both knee joints exhibited slight soft tissue thickening and small effusions. Movements of the elbows were painful. On the extensor surfaces of the lower legs there were numerous lesions of the following types: red maculopapules, purple papules, petechiae, and raised purple maculopapules on the arms, thighs, and buttocks. On the extensor surfaces of the lower legs there were numerous lesions of 3 to 10 mm. in diameter (see Fig. 1a, p. 259). There were red and purple maculopapules on the arms, thighs, and buttocks.

Laboratory Findings

Blood.—Haemoglobin 12.2 g. per 100 ml., white-cell count 12,700 with 81 per cent. neutrophils, eosinophil count 70-125 per c.mm., no red-cell abnormalities, platelets present in usual numbers. Corrected sedimentation rate (Rourke-Ernstene) 1.0 mm. per min. (haematocrit of 40 per cent.). Bleeding and clotting times normal. Prothrombin activity 61 per cent. Rumpel-Leede tourniquet test positive.

Urine.—Examination revealed macroscopic haematuria; sediment contained many red cells and occasional red-cell and granular casts per high-power field. Protein present in large amounts. Specific gravity 1.025.

Stools.—Guaiac reaction repeatedly positive during first 2 weeks in hospital. Some stool specimens contained flecks of red blood.

- Serum albumin 3.55 g. per 100 ml.
- Serum globulin 2.27 g. per 100 ml.
- Serum sodium 135.9 mEq, potassium 4.5 mEq, carbon dioxide content 29.4 mEq per litre.
- Non-protein nitrogen 21 mg. per 100 ml.
- Cephalin flocculation test negative after 48 hours.
- Bromsulphalein retention 1 per cent. after 45 minutes.
- Phenolsulphonphthalein test 25 per cent. excretion of dye after 15 minutes and 75 per cent. after 2 hours.

Electrocardiogram.—Normal.

X-Ray Examination.—Chest, abdomen, and joints no abnormalities.

Clinical Course

May 11 to May 24.—During the first week in hospital her general condition was unchanged. Rectal temperatures 100° to 101° F. Tachycardia, anorexia, malaise, splenomegaly, hepatomegaly, hypertension, proteinuria, and haematuria persisted. The eyelids remained puffy but the pitting oedema of the ankles subsided. The joint pains and the slight soft tissue swelling continued, though the knee effusions decreased in size. She received 300,000 U. penicillin every 12 hours for 4 days because the throat culture revealed β-haemolytic streptococci. Biopsy (May 16) of two maculopapular lesions on the legs was consistent with the Schoenlein-Henoch syndrome.

On May 18, severe abdominal cramps recurred, the joint pains increased, and she looked much worse. New maculopapular lesions appeared on the legs, forearms, and buttocks on May 24. The liver increased in size to two fingers-breadth below the right costal margin. ACTH therapy was begun at this time and the sodium in the diet was simultaneously reduced to less than 20 mEq daily.

May 25 to May 29 (First Course of ACTH Therapy).—25 mg. ACTH were administered at 6-hourly intervals for 4 days. Symptomatic improvement commenced 1 day after the institution of therapy. She felt well, her appetite returned, the abdominal cramps ceased...
ACTH AND SCHOENLEIN-HENOCH SYNDROME

completely, and the joint pains subsided. The rectal temperature was 99° to 100° F. No new skin lesions appeared and the exanthema which had developed on May 24 had become much less prominent by May 29, when a biopsy was performed. The eosinophil count fell from 81 before therapy to 31 per c.mm. 4 hours later and remained below 50 during the treatment period. The hypertension, haematuria, and proteinuria (3 to 6 g./24 hrs) persisted.

May 30 to June 5.—12 hours after the cessation of ACTH therapy, malaise, anorexia, and abdominal cramps and tenderness recurred. Marked transitory peri-orbital oedema appeared the following day. At this time the Rumpel-Leede test was negative. The eosinophil count had risen to 188. The symptoms gradually subsided only to become more severe than ever on June 4, with vomiting, and abdominal tenderness and rigidity. Fresh petechiae appeared on June 5 on the arms and legs, and the Rumpel-Leede test was found to be positive. Another skin biopsy was performed. The patient voided only 100 ml. on this day despite a fluid intake of 1,000 ml., and the blood pressure rose to 170/135. The white-cell count was 16,500 with 80 per cent. neutrophils, and there were 119 eosinophils per c.mm. It is of interest that the polymorphonuclear leukocytosis which occurred during this crisis was not accompanied by a significant fall in eosinophils such as occurs in most acute infections and surgical emergencies. It was decided to resume ACTH therapy.

June 6 to August 7 (Second Course of ACTH Therapy).—A total of 3,470 mg. ACTH was administered in divided doses every 6 or 12 hours as follows:

<table>
<thead>
<tr>
<th>Dose (mg.)</th>
<th>Duration (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>6</td>
</tr>
<tr>
<td>80</td>
<td>8</td>
</tr>
<tr>
<td>100</td>
<td>6</td>
</tr>
<tr>
<td>80</td>
<td>6</td>
</tr>
<tr>
<td>60</td>
<td>4</td>
</tr>
<tr>
<td>40</td>
<td>7</td>
</tr>
<tr>
<td>30</td>
<td>12</td>
</tr>
<tr>
<td>20</td>
<td>13</td>
</tr>
<tr>
<td>10</td>
<td>On the last day of treatment</td>
</tr>
</tbody>
</table>

The sodium intake during the period of therapy is recorded in the Table.

About 8 a.m. on June 6, a number of grand mal seizures occurred, followed by stupor and restlessness lasting 36 hours. Several minor seizures were noted later in the same day in spite of one intravenous and three subcutaneous injections of 0·1 g. sodium luminal each, and two doses of 0·2 g. dilantin. There were no abnormal neurological signs apart from a transitory extensor plantar reflex during the post-convulsive period. The optic fundi were normal. The blood pressure varied between 160/120 and 210/140. The cerebrospinal fluid was clear and the pressure was 165 mm. of water. It contained 29 red cells and two polymorphonuclear leukocytes per c.mm.

Oliguria continued through June 6. The non-protein nitrogen was 54 mg. per cent. on June 7, when the urine output rose to 750 ml. and the patient’s general condition improved. On June 8 she was fully conscious, felt well, and had a normal appetite. There was no recurrence of abdominal pain. She had a retrograde amnesia for the entire period of hospitalization prior to the seizures. This gradually cleared during the next few weeks. This episode was thought to be "hypertensive encephalopathy" complicating the renal disorder. The role of ACTH in initiating the convulsions was considered non-contributory since the patient had had only 25 mg. ACTH when the encephalopathy became apparent. Moreover, the convulsions ceased and she improved rapidly despite the continuation of ACTH. The improvement in her condition was progressive and she remained free of symptoms throughout the rest of the period of ACTH therapy (Table). Her general health and appetite were excellent. The soft tissue swelling of the knees was imperceptible after 2 weeks. The spleen became impalpable on June 25 and the liver on July 4, 19 and 28 days respectively after the resumption of ACTH therapy. No new skin lesions appeared and the scabbed haemorrhagic areas present on admission slowly involuted, leaving brown, depressed scars. Skin biopsies were performed on June 13 and 19. The Rumpel-Leede test was negative on June 17 and remained negative thereafter. The blood pressure, however, continued to be persistently elevated. Haematuria varied
from gross to microscopic but was never absent. Proteinuria continued at levels between 1·9 and 16·5 g./24 hrs during this period. The specific gravity of the urine varied from 1·007 to 1·024. The non-protein nitrogen fell to 31 mg. per cent. on June 10 and remained within normal limits. There were no significant alterations in serum albumin and globulin. The phenolsulphonphthalein tests were normal (see Table). The corrected sedimentation rate varied irregularly between 0·4 and 1·3 mm. per minute, while the haematocrit and haemoglobin remained essentially unchanged. The white-cell count stayed between 11,000 and 23,000, with 75 per cent. neutrophils, during June and July, and became normal at the end of July. The eosinophil count fluctuated between 6 and 93 per c.mm. The serum sodium, potassium, and chloride values were normal, but the serum carbon dioxide content rose to 31 mEq per litre on two occasions. The electrocardiogram showed transitory flattening of T2 on June 12 and flattening of TV5 and 6 on August 2.

Marked acne of the face developed after 2 weeks of therapy. By June 25, after 3 weeks of treatment, she had gained 12 lb. in weight and there was marked pitting oedema of the feet, sacrum, and vulva, and rounding of the face. The daily dose of ACTH, which had been 100 mg., was reduced to 80 mg., and the daily sodium intake was further restricted to 8·7 mEq. The oedema subsided completely during the ensuing 3 weeks and did not recur during this treatment period.

ACTH therapy was terminated on August 7. When the patient was discharged on August 16, the only abnormalities were hypertension (varying between 140 and 160 systolic and 95 and 110 diastolic), proteinuria, haematuria, and residual skin lesions (Fig. 1b).

August 8 to April 8.—On August 18, while she was leading a life of moderate activity at home without dietary restrictions, she developed a mild exacerbation characterized by generalized headaches, intermittent vomiting of clear mucoid material, and painful swelling of the knees and fingers. Oedema appeared in the face and the dependent portions of the legs. The liver and spleen both became palpable two fingersbreadth below the costal margins. The blood pressure remained unchanged. She was placed on a more exacting regimen, with reduction in physical activity and sodium restriction to 20 mEq per day. A complete symptomatic remission occurred within 2 weeks, but the hypertension, proteinuria, and haematuria persisted. A skin biopsy was performed on August 24.

There were no further exacerbations in the 8 months after ACTH was discontinued. She felt well and her weight remained constant. The liver and spleen slowly receded in size. The residual pigmentation in the old skin lesions gradually faded.

The phenolsulphonphthalein excretion test and urine concentration remained within low normal limits. The endogenous creatinine clearance three months after discharge was 91 ml. per minute and after four months 99 ml. per minute corrected to 1·73 square metres of body surface (normal: 125 ± 15 ml.). The total plasma protein rose from 5·36 g. per 100 ml. to 6·3 g. per 100 ml. with a normal Albumin/Globulin ratio. The nonprotein nitrogen and serum cholesterol remained normal. The corrected sedimentation rate fell to 0·2 mm. per minute on November 30 with an haematocrit of 42 per cent. At that time the white-cell count was 9,300, the eosinophil count 86, and the Rumpel-Leede test negative (Table).

**Biopsy Findings**

A total of seven punch biopsies varying from 4 to 8 mm. in diameter were obtained from as many skin lesions over a period of 14 weeks.

1 and 2.—On May 16, 1950, 9 days before the start of hormonal therapy, and 5 to 6 weeks after the first appearance of skin involvement, two of the lesions, one "early" and one "old" (Fig. 1a), were removed to serve as a basis of comparison with subsequent biopsies.
ACTH AND SCHOENLEIN-HENOCH SYNDROME

Fig. 1(a).—May 16, 1950 (5 weeks after onset). Maculopapules, petechiae, and scabbed haemorrhagic lesions 9 days before ACTH therapy.

Fig. 1(b).—August 14, 1950 (18 weeks after onset). Depressed pigmented scars 1 week after cessation of ACTH therapy.

The "early" lesion, a red maculopapule, was examined microscopically (Figs 2a and b). A subacute inflammatory process centred in the blood vessels of the upper corium and reached its greatest intensity in the centre of the lesion. The branches of the arteriolar plexus, in particular, were outlined by heavy cellular infiltration of their walls and the perivascular connective tissue.

The infiltrate consisted of varying proportions of neutrophils, lymphocytes, and moderate-sized mononuclear cells, with large, polymorphic, vesicular nuclei and a relatively small amount of pale-staining indistinct cytoplasm. Occasional eosinophils were also present. The vascular lumens appeared to be narrowed by endothelial hypertrophy, and were occluded in several places by leukocytic and fibrin thrombi. In rare instances, there was fibrin infiltration and frank necrosis of vessel walls.

Haemorrhage was limited to the dermal papillae in the centre of the lesion, where some of the capillary loops were disrupted and surrounded by small collections of red cells. The connective tissue of the upper corium showed moderate diffuse inflammatory cell infiltration with neutrophils predominating. Occasional collagenous bundles were unusually thick and straight. The elastic fibres seemed to be fragmented. A sweat duct ran up through the centre of the lesion. The
epidermis was slightly acanthotic. In the central portion of the lesion there was some necrosis and neutrophil infiltration.

Intra-epidermal vesicles containing fibrino-purulent and haemorrhagic exudate were present both in the necrotic portion and the adjoining region. The lesion was consistent with those described as characteristic by Gairdner (1948).

The "old" lesion, which was grossly hard, purple, and papular, was covered by a thin crust of old purulent and haemorrhagic exudate interposed between layers of keratinized material (Fig. 3). The epidermis showed some flattening of the rete pegs. In the papillary layer of the corium there was slight proliferation of a loose, oedematous-appearing connective tissue within which there were occasional minute pericapillary extravasations and haemosiderin deposits. Rhexis of vessel walls was not seen but endothelial hypertrophy was common. The collagenous bundles in this region were unusually delicate, and elastic fibres were almost completely absent.

Inflammatory cell infiltration was limited to a minimal perivascular scattering of round cells. This lesion was evidently old both by its clinical and microscopic features. It exemplified a lesion in the course of natural evolution.

3.—The third lesion, of 5 days’ duration, was removed on May 29 after 4 days of ACTH treatment. Its gross as well as microscopic appearance (Figs 4a and 4b, overleaf) was essentially similar.
Fig. 2(b).—Higher magnification of vascular lesion in corium shown in Fig. 2(a). Note obliteratorative endothelial hypertrophy, intramural and perivascular infiltration of neutrophils, lymphocytes, and larger mononuclear cells, and the unusually thick and straight collagenous bundle in the adjacent connective tissue. Haematoxylin and eosin. × 400.

Fig. 3.—Purple papule before treatment. Note crust of old exudate, flattening of rete pegs, and oedematous-appearing papillary layer of corium with loss of elastic fibres. The arrow points to a small extravasation of red cells in this layer. Inflammatory cell infiltration is minimal. Verhoeff's elastic-tissue stain and Van Gieson. × 340.
FIG. 4(a).—Red maculopapule of 5 days' duration after 4 days of ACTH therapy. In the lower left-hand corner an arteriole and its branches are outlined by inflammatory cell infiltration. Haematoxylin and eosin. × 110.

4.—The fourth lesion was removed on June 5, 7 days after cessation of the first course of therapy and 1 day after the onset of an exacerbation of the disease with abdominal pain and appearance of new petechiae. The lesion was of the “old” papular type representing a healing haemorrhagic bulla. Microscopically, it showed a rather diffuse scattering of well-preserved extravasated red cells in the superficial layer of the corium. This layer was thickened, and consisted of newly-formed, loose, pale-staining connective tissue with delicate collagenous bundles, absence of elastic fibres, a slightly haematoxylinophilic ground substance, and plump fibroblasts. The cells of the blood-vessel walls were hypertrophied and the lumens were narrowed by the...
inward bulging endothelium. There was no increased vascularity or disruption of vessels. There was minimal lymphocytic infiltration and slight perivascular haemosiderin deposition, mostly in the deeper portions of the corium. The epidermis over the central part of the lesion was somewhat atrophic, with absence of the rete pegs, and was separated slightly from the underlying corium, leaving a small fluid-filled cleft. The general features of this lesion were essentially similar to those of the purple papule examined before the start of therapy, but the amount of haemorrhagic extravasation and fibrous proliferation in the corium were more extensive. The extravasation appeared to be the result of the escape of red cells through the intact vessel walls, and was thus quite different from the inflammatory rhexis of capillaries in the acute lesions. The possibility that operative trauma was a causative factor could not be excluded. The localization of the extravasation to the region of proliferating connective tissue may have been related to the absence of supporting perivascular elastic fibres (Peck and others, 1937), to the immature character of the endothelium, or to a change in the ground substance.

5.—The fifth skin biopsy was performed on June 13, 1950, 7 days after the start of the second course of ACTH, and 8 days after the last exacerbation of the disease. The lesions were all somewhat flatter and browner than those previously described. The histological findings differed
FIG. 5.—Depressed brown scar after 13 days of ACTH therapy. The epidermis is atrophic. The superficial corium is devoid of elastic fibres, appears oedematous, and contains diffusely scattered red cells. Verhoeff's elastic-tissue stain and Van Gieson. × 340.

little from those of the fourth biopsy. Fibrosis of the corium, haemosiderin deposition, and atrophy of the epidermis, were slightly more advanced. Haemorrhagic extravasations were more discreet but measured up to 0.5 mm. in diameter. One small subpapillary vessel contained a necrotic thrombus.

6.—The sixth biopsy was performed on June 19, after 13 days of ACTH therapy. The lesions had become depressed brown scars. Microscopically (Fig. 5) the features resembled those of the fifth biopsy. Fresh-appearing extravasated red blood cells were again diffusely scattered through the newly-formed connective tissue of the upper corium.

7.—At the time of the seventh biopsy on August 24, 17 days after the cessation of the 2-month course of ACTH, and 3 months after the last crop of skin lesions had appeared, brown scars persisted but were somewhat less depressed (Fig. 1b). On histological examination, the epidermis, which had been atrophic, appeared almost normal with re-formed rete pegs. Haemorrhages had disappeared, and the upper corium showed a normal pattern of elastic fibres. However, slight perivascular infiltration of lymphocytes and plasma cells, as well as scattered haemosiderin granules, remained.

In summary, the 5-day-old maculopapular lesion removed at the end of the first 4-day course of ACTH treatment did not differ significantly from the ‘early’ lesion removed before the start of treatment. Both were characterized by an intense subacute angiitis of the upper corium with mononuclear as well as polymorphonuclear leukocytic infiltration, some capillary rhexis, and segmental vascular necrosis, slight perivascular extravasation of red cells, and necrosis and vesicle formation in the overlying epidermis. A biopsy of a papular lesion, taken 7 days after cessation of the first course of therapy at a time when new purpuric lesions were appearing, and biopsies of comparable lesions, taken respectively on the seventh and thirteenth days of the second course of ACTH, were all essentially similar on microscopic examination. They resembled the involuting
ACTH AND SCHOENLEIN-HENOCH SYNDROME

pretreatment lesion in showing only minimal inflammatory cell infiltration. Fibrosis, epidermal atrophy, haemosiderin deposition, and extravasation of fresh-appearing red cells were more extensive in all three of these lesions than in either of the pretreatment "controls", despite the absence of capillary rhesis. The seventh biopsy, taken 17 days after cessation of the 2-months' course of ACTH, showed almost complete reversal of all microscopic changes, except for slight perivascular round-cell infiltration.

Discussion

The nosological status of the Schoenlein-Henoch syndrome is difficult to evaluate. Some (Gairdner, 1948) believe it to be a "clear entity"; others (Osler, 1914; Davis, 1948) suggest that a variety of aetiologic factors, which may or may not be related, evoke a similar host response and result in a similar clinical picture. It is known that the triad of non-thrombopenic purpura, articular symptoms, and gastro-intestinal symptoms can occur in disseminated lupus erythematosus, polyarteritis nodosa, rheumatic fever, and serum sickness, and that nephritis may be a manifestation of these diseases. Unfortunately, no systematic comparative study has yet been made of the purpuric lesions in these diseases, purpura simplex, and the Schoenlein-Henoch syndrome. Nevertheless, Gairdner (1948) believes that the exanthema of the Schoenlein-Henoch syndrome is sufficiently characteristic to be recognizable both clinically and histologically. He points out that recurrent crops of red maculopapules, with or without purpura, are found in variable combination with gastro-intestinal symptoms, articular symptoms, and nephritis, all of which, as he believes, probably result from a vascular lesion. He stresses that an acute aseptic inflammatory reaction around the vessels of the upper corium, frequently associated with a tissue eosinophilia, forms the basis of the exanthema. Our case fulfils both the clinical and the histological criteria of Gairdner's definition.

The clinical course of the syndrome is variable. There may be only one attack or there may be attacks recurring for periods of a few months up to 50 years (Osler, 1914; Davis, 1948). Individual skin lesions may disappear within a few hours, days, or weeks, but may persist as pigmented scars for many months. Gairdner (1948) states that the maculopapules typically disappear within 2 weeks. The gastro-intestinal and articular symptoms are also variable in both duration and severity. The inconstant incidence and course of the renal lesions in illustrated by the fact that eleven of Gairdner's twelve cases had renal involvement, of whom one died in renal failure and four went on to chronic or latent nephritis, whereas only four of the 44 cases of Davis (1948) showed renal disease, and only one of these had albuminuria at the end of 3 months.

The difficulty of assessing any therapeutic procedure in a disease so subject to spontaneous exacerbations and remissions as the Schoenlein-Henoch syndrome is self-evident. None of the modes of therapy other than ACTH, which have been tried in this condition, has been shown to exert a consistently favourable influence. The use of ACTH for a 2-week period in one case has been reported by Stefanini and others (1950), who found that the abdominal pain, which had been present intermittently in the 24 days before therapy, subsided "early" during therapy and that the petechial rash, which appeared 6 days before ACTH was administered, did not
disappear until after 6 days of treatment. Small numbers of new petechiae appeared in the skin even during this period. Urinary findings showed a slight though transient improvement. The biopsy of an area of fresh haemorrhage taken at the start of therapy showed mainly active inflammation centred about the small vessels of the corium. The biopsy of a similar area of fresh haemorrhage taken at the cessation of therapy showed massive haemorrhage but only minimal peri-vascular lymphocytic infiltration. Purpuric spots and abdominal symptoms recurred briefly 6 days after the suspension of treatment. An exacerbation of skin and renal symptoms occurred one month later.

Our own results (see Table) are similar in many ways to those of previous authors. The institution of the first course of ACTH was followed within 24 hours by striking improvement in the constitutional, abdominal, and joint manifestations, but the constitutional and abdominal symptoms recurred 12 hours after the drug was sustained, improvement within 2 days. A mild temporary return of constitutional, abdominal, and joint manifestations was noted on the eleventh day after the cessation of the second course of therapy. In spite of the prompt improvement of all other features, hypertension, haematuria, and proteinuria persisted throughout the two courses of treatment and were still present 12 months after the onset.

### Table

**Constitutional, Abdominal, Articular, Epidermal, Renal, And Vascular Manifestations**

<table>
<thead>
<tr>
<th></th>
<th>Pre-ACTH</th>
<th>1st R</th>
<th>2nd Course</th>
<th>ACTH</th>
<th>Subsequent Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Well-being</strong></td>
<td>-</td>
<td>-</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Appetite</strong></td>
<td>-</td>
<td>-</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Weight (lb.)</strong></td>
<td>90</td>
<td>86</td>
<td>84</td>
<td>82</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td></td>
<td>94</td>
<td>94</td>
<td></td>
<td>102</td>
</tr>
<tr>
<td><strong>Abdominal Pains</strong></td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Joint Pains</strong></td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>New Skin Lesions</strong></td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Rumpel-LeeDe Tourniquet Test</strong></td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hepatomegaly</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Splenomegaly</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SED Rate (mm/min)</strong></td>
<td>13 1.4  13 1.6  7</td>
<td>6 3  13 1.4</td>
<td>13 1.6  7</td>
<td>13 1.1</td>
<td>3 0 13 1.6  5 4 0.5 4 0.5 0.5</td>
</tr>
<tr>
<td><strong>Leucocytes</strong></td>
<td>5.7</td>
<td>16.5</td>
<td>200-110</td>
<td>140</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td>180</td>
<td>180</td>
<td>100 70-70</td>
<td>12</td>
<td>90</td>
</tr>
<tr>
<td><strong>Acne</strong></td>
<td>-</td>
<td>-</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Oedema</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Haematuria</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Proteinuria</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>G / 24 Hrs.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Blood Pressure</strong></td>
<td>100</td>
<td>100</td>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Diagram

- **PSP**: 15 minutes
- **N.P.N. mg/kg/h**: 25
- **No Intake**: 75
- **ACTH R mg/day**: 100
- **Days**: 8 15 22 29 36 43 50 57 64 71 78 85 90 150 211 272 333
- **Date**: May 8 25 29 June 6 Aug 8 Dec 7 April 8

### Skin Biopsy

- ↑ 2 ↑ ↑ ↑ ↑ ↑ ↑
of the illness. It is still too early to say whether the nephritis will progress in this case, but there is no evidence that the course of the renal disease was significantly affected. This is in agreement with the results of ACTH therapy in other forms of Bright's disease (Farnsworth, 1950; Brunsting and others, 1950; Thorn and others, 1950; Burnett and others, 1950; Shick and others, 1950).

The effect on the cutaneous lesions is difficult to interpret because of the variability in their clinical appearance and course. In favour of a salutary effect are the failure of new lesions to develop during therapy, and the fact that fresh petechiae appeared when the first course of ACTH was stopped. Moreover, inflammatory exudation was minimal in the biopsies taken after more than 4 days of treatment. On the other hand, an untreated "old" lesion, which grossly resembled those removed during therapy, showed equally slight inflammation, and a 4-day course of ACTH failed to alter appreciably the evolution of a lesion which appeared the day before therapy was initiated. The mechanism of fresh haemorrhage in "old" lesions as long as 13 days after the beginning of ACTH therapy is obscure, and the possibility cannot be excluded that operative trauma played a role.

Thus, it seems possible that ACTH may inhibit the development of new inflammatory skin lesions, but it is not established that the regression of existing lesions can be significantly altered.

It should be emphasized that further studies are needed before an adequate evaluation of ACTH in the treatment of the Schoenlein-Henoch syndrome is possible. It would seem important to undertake therapy early in the course of the disease. The study of biopsy material would have greater value if the microscopic evolution of the untreated skin lesions were more exactly known, and if lesions removed before and during treatment were matched whenever possible before therapy as regards date of appearance and clinical characteristics.

Summary

(1) A case is presented with the classical features of the Schoenlein-Henoch syndrome, including nephritis.

(2) Each of two courses of ACTH therapy was followed by prompt and progressive improvement in the constitutional, abdominal, and joint manifestations. Exacerbations occurred after withdrawal of the drug in both instances.

(3) No skin lesions appeared during therapy, but there was a new crop of petechiae in the interval between the two courses of ACTH. Histological study failed to establish that the regression of existing skin lesions was significantly hastened.

(4) The evidence of renal involvement (hypertension, proteinuria, and haematuria) persisted in spite of 9 weeks of ACTH therapy, and was still present 12 months after the onset of the illness.

REFERENCES


Action de l'ACTH dans le Syndrome de Schoenlein-Henoch:
Rapport sur un Cas, avec Étude Histologique des Prélèvements de la Peau

RÉSUMÉ
(1) On décrit un cas présentant des traits classiques de syndrome de Schoenlein-Henoch, y compris la néphrite.
(2) Chacune des deux séries de traitement à l'ACTH fut suivie d'une amélioration prompte et progressive des manifestations générales, abdominales, et articulaires. Il y eut des exacerbations chaque fois qu'on arrêtait le traitement.
(3) Pendant le traitement les lésions cutanées n'apparurent pas, mais il y eut une poussée pétéchiale pendant l'intervalle entre les deux séries de l'ACTH. L'étude histologique n'a pas réussi à établir que la disparition des lésions cutanées existantes ait été accélérée d'une manière significative.
(4) Les signes de l'atteinte rénale (hypertension, albuminurie, et hématurie) persistèrent malgré neuf semaines de traitement par l'ACTH et étaient encore présents douze mois après le début de la maladie.

Acción de la ACTH en el Sindrome de Scholein-Henoch:
Informe sobre un Caso, con Biopsias de la Piel

SUMARIO
(1) Se presenta un caso con las clásicas características del sindrome de Schoenlein-Henoch, incluyendo nefritis.
(2) Cada uno de dos tratamientos por la ACTH fue seguido por mejoría rápida y progresiva de las manifestaciones generales, abdominales, y articulares. Exacerbaciones ocurrieron cada vez que se interrumpió el tratamiento.
(3) Durante el tratamiento no aparecieron lesiones cutáneas, pero hubo un brote pétéquial en el intervalo entre las dos series de ACTH. Los estudios histológicos no lograron establecer que la desaparición de las lesiones cutáneas presentes fuese acelerada de manera significativa.
(4) Evidencia de complicación renal (hipertensión, albuminuria, y hematuria) persistió a pesar de que el tratamiento por ACTH se extendiese por nueve semanas y se la pudo constatar aún después de doce meses contados desde el principio de la enfermedad.
Response of Schoenlein-Henoch Syndrome to ACTH: Report of a Case with Serial Skin Biopsies

Joseph E. Levinson, Mark Horwitz, J. Peter Kulka, Lot Page and Walter Bauer

doi: 10.1136/ard.10.3.255

Updated information and services can be found at:
[http://ard.bmj.com/content/10/3/255.citation](http://ard.bmj.com/content/10/3/255.citation)

These include:

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
[http://group.bmj.com/group/rights-licensing/permissions](http://group.bmj.com/group/rights-licensing/permissions)

To order reprints go to:
[http://journals.bmj.com/cgi/reprintform](http://journals.bmj.com/cgi/reprintform)

To subscribe to BMJ go to:
[http://group.bmj.com/subscribe/](http://group.bmj.com/subscribe/)