Perinephric Infection

1 patient suffered a complication which was attributed to perinephric infection. He was a child, aged 7, with severe nephrotic syndrome and moderate azotemia due to type-I nephritis. His renal biopsy was without incident. Culture of the washings from the biopsy needle was sterile, but coliform organisms were found in the first midstream urine after biopsy. He was given a seven-day course of sulfanamides to which the organisms were sensitive; at the same time (forty-eight hours after biopsy) prednisone therapy was begun. There was no improvement in the nephrotic syndrome, but there were no complaints referable to the biopsy. Two weeks later he suddenly complained of pain in the right loin, and became extremely tender there and on the right side of the abdomen. His temperature rose to 100°F, and a leukocytosis of 18,000 per c.mm. developed over the next twenty-four hours. Urine culture was sterile. He was treated with erythromycin and furadatan, and made a satisfactory recovery.

Pain

Slight aching in the loin, usually at the biopsy site, and commonly related to movement, was often present in the first twenty-four hours. 5 patients had more severe pain during or after biopsy. 1 adult complained of loin discomfort for three days after biopsy and another had fairly severe pain immediately after the procedure, which gradually subsided over the next four days. Both were tender over the affected kidney and, although tomograms showed no evidence of large extravasation, it was thought that a small subcapsular hematoma might be responsible for the pain. Kark et al. (1958) commented that relatively small subcapsular and perinephric hematoma could cause quite severe discomfort.

A child with relapsing nephritis and probable Henoch's purpura, had discomfort in the loin in the first twenty-four hours after biopsy; and, five days later, a further attack of loin pain associated with slight hematuria. In view of the time interval, the second attack may have been due to a flare-up of the illness following biopsy.

A child with nephrotic syndrome and azotemia, in whom biopsy material was obtained with difficulty, had pain in the right loin and iliac fossa for two days afterwards. There was guarding and rebound tenderness over the right side of the abdomen, but no fever or leukocytosis, and the condition cleared up spontaneously. It was thought that, on the initial insertion, the biopsy needle had passed below the lower pole of the kidney and may have produced a small amount of peritoneal bleeding. There was no fall in hemoglobin level.

A 5th patient suffered some loin pain in association with no infection after biopsy.

References


Experimental Staphylococcal Infections in Man

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The earliest attempt to test staphylococcal virulence in man was made by Garré (1885), who rubbed an entire slope culture into the skin of his forearm. This resulted in multiple pustules from which a carbuncle later developed. Since this dramatic demonstration of staphylococcal virulence little experimental work has been performed in man, for obvious reasons. Recently, however, Elek (1956) and Elek and Conen (1957) injected staphylococci intradermally and were able to produce small pustules with doses of over a million organisms; they were unable to produce lesions with killed cocci, and the addition of toxin did not influence the outcome.

In the experiments we describe here we attempted to simulate more closely the conditions obtaining in a wound by using artificial skin lesions into which staphylococci were introduced. By this method we hoped to determine whether local conditions induced by the biopsy included a portion of myocutaneous muscle. Neither patient appeared to suffer any arm, which is interesting in view of Kark's conclusion that biopsy of the myocutaneous muscle might be responsible for pain at the time of biopsy. This patient was carefully questioned; but had felt no pain whatever after the procedure.

Comparison of the incidence of complications in different series is of questionable value since so much depends on the observer's opinion, of instance, where mild discomfort ends and pain begins. However, the incidence of uncomfortable complications in this small series (12%) is reasonably close to that in Kark's much larger one (10%).

Summary

A technique of renal biopsy is described which employs a modified Menghini needle and in which the position of the kidney is determined, when possible, by pyelography at the time of biopsy. The results of 50 biopsy attempts are reported.

In this series the success-rate is higher than with the standard method, using the Vim-Silverman needle. The incidence of complications is similar.

The specimens obtained by the present method contain a higher proportion of renal cortex than those taken with a Vim-Silverman needle, and are therefore more useful to the histologist.
It will be seen from table I that the covered lesions showed considerable increase in the numbers of organisms between 2 and 8 hours, followed by a slower increase over the next 14 hours, whereas there was virtually no increase in numbers in the uncovered lesions even after 24 hours. Macroscopically, the covered lesions showed a purulent exudate after a few hours in contrast to the uncovered lesions, which formed a scab with scanty exudate.

Effect of Foreign Material
In view of the possibility that foreign material might influence the results, the effect of rubbing starch and French chalk into the lesions was investigated.

Six standard skin lesions were made and treated as indicated in table III. They were then covered with the lids of small bijou bottles which were strapped on to the arm, keeping the lesions moist but avoiding the direct pressure inevitable with a coverslip. The lesions were left for 24 hours, after which they were inspected and organism-counts were made.

The results show no apparent macroscopic difference between the lesions produced in this series and those in which coverslips had been used, although the rate of multiplication of organisms was slower with the bijou-cap method. There was also no significant difference between the lesions to which foreign material had been added and those which were uncontaminated.

Inflammatory Responses in Skin Lesions Infected by Staphylococci
Three skin lesions were made, one of which acted as a control, while the other two were inoculated with a standard loopful of a 24-hour culture of Staph. albus or Staph. aureus (phage-type 36:57:1) respectively (table IV). The lesions were then covered with coverslips, which were changed at intervals during the next 24 hours. The cellular exudate on these coverslips was stained by methylene-blue and examined microscopically. The state of the lesion was recorded after 24 hours.

The essential cytological difference between the infected and the control lesions was the increasing numbers of degenerate polymorphonuclear leucocytes in the infected lesions, whereas...

### Table II—Comparison of Multiplication of Organisms in Standard Skin Lesions Sealed with Coverslips and Left Exposed

<table>
<thead>
<tr>
<th>Time after inoculation</th>
<th>Lesions sealed with coverslips</th>
<th>Lesions allowed to dry</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 min</td>
<td>0.7 x 10^6</td>
<td>0.7 x 10^6</td>
</tr>
<tr>
<td>2 hours</td>
<td>1.8 x 10^6</td>
<td>0.8 x 10^6</td>
</tr>
<tr>
<td>3 hours</td>
<td>1.8 x 10^6</td>
<td>0.8 x 10^6</td>
</tr>
<tr>
<td>17 hours</td>
<td>2.5 x 10^6</td>
<td>2.5 x 10^6</td>
</tr>
<tr>
<td>37 hours</td>
<td>5.5 x 10^6</td>
<td>5.6 x 10^6</td>
</tr>
</tbody>
</table>

Lesions were then sealed with circular flamed coverslips which were held in position with Sellotape.

### Table III—Comparison of Organism-Counts and Macroscopic Appearances in Lesions Treated with Foreign Material

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Appearance at 24 hours</th>
<th>Organism-count at 24 hours</th>
<th>Appearance at 48 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Serous exudate</td>
<td>0</td>
<td>No erythema</td>
</tr>
<tr>
<td>Standard loopful of Staph.</td>
<td>Purulent exudate</td>
<td>19 x 10^6</td>
<td>Erythema</td>
</tr>
<tr>
<td>Standard loopful of Staph., french chalk</td>
<td>Dry exudate</td>
<td>17 x 10^6</td>
<td>No erythema</td>
</tr>
<tr>
<td>French chalk</td>
<td>Purulent exudate</td>
<td>13 x 10^6</td>
<td>Erythema</td>
</tr>
<tr>
<td>Staph. — Starch</td>
<td>Slight serous exudate</td>
<td>0</td>
<td>No erythema</td>
</tr>
<tr>
<td>Starch</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
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<td>Erythema</td>
</tr>
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<td>Slight serous exudate</td>
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<td>No erythema</td>
</tr>
<tr>
<td>Starch</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table IV—Comparison of the Inflammatory Responses in Skin Lesions Infected by Staphylococci

<table>
<thead>
<tr>
<th>Time of application of coverslips</th>
<th>Cytology</th>
<th>Control (uninoculated)</th>
<th>Staph. albus</th>
<th>Staph. aureus</th>
</tr>
</thead>
<tbody>
<tr>
<td>5–6 hours</td>
<td>Polymorphs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9–13 hours</td>
<td>Dragneromorphs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13–24 hours</td>
<td>Mononuclears</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococci</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table V—Macroscopic Appearance at 34 Hours

<table>
<thead>
<tr>
<th>Organism-count</th>
<th>Appearance</th>
<th>Erythema</th>
</tr>
</thead>
<tbody>
<tr>
<td>5–6 hours</td>
<td>Serous exudate</td>
<td>No erythema</td>
</tr>
<tr>
<td>9–13 hours</td>
<td>Dragneromorphs</td>
<td>Erythema</td>
</tr>
<tr>
<td>13–24 hours</td>
<td>Mononuclears</td>
<td>No erythema</td>
</tr>
</tbody>
</table>

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*Staphylococcal Counts from Skin Lesions*

The coverslip and selotape over each lesion were stripped off and dropped into 1 ml of nutrient broth in a wide-mouth universal container. One drop of sterile broth was then added to the underlying lesion, and the whole area was thoroughly rubbed with two sterile alginates wool swabs to remove all exudate and superficial layers of the lesion. Both swabs were then broken off into the same sample of nutrient broth as the coverslip. After capping, the universal container was shaken vigorously until the alginates swabs were disintegrated.

Serial tenfold dilutions were then prepared in broth 1 in 10 ml dropping pipettes, and each dilution was plated out. After overnight incubation the colonies of staphylococci were counted, and from these counts the number recovered from the whole lesion was calculated. In experiments in which coverslips were not used to seal the lesions organisms counts were obtained by firm swabbing of the area with alginates swabs prior to preliminary moistening with broth. The swabs were then dropped into the universal containers as before.

### Results

**Multiplication of Organisms**

Five standard skin lesions were made in two subjects and inoculated as described above with phage-type 36:57:1. In one subject the lesions were covered with coverslips, and in the other they were left exposed. Counts were then made of the numbers of organisms isolated at various times after inoculation.
in the control lesion mononuclear and histiocytic cells increased
for 13 hours, when they dominated the picture. Although phagocyte reactions of organisms by polymorphs was seen on all the
coverslips from the infected lesions most organisms were
extracellular.

Different Types of aureus and Their Inflammatory Responses
Six standard skin lesions were made; five of these were
inoculated with the five different types of Staph. aureus listed in
Table I. The lesions were then sealed with coverslips which
were changed at intervals, as already described. After 24 hours
all the inoculated lesions showed surrounding erythema and
were covered with a purulent exudate, whereas the uninoculated
lesion was not erythematous and showed only slight exudate
(see figure). There was no essential difference between the
lesions produced by the different types of organisms.

Organism Dose and Inflammatory Response

Two sets of five standard lesions were made and inoculated
with dilutions of a 24-hour broth culture of Staph. aureus
(phage-type 3c/55/71). Four of the lesions of one of these sets
were inoculated with 100, 1000, 10,000, and 1,000,000
organisms respectively, while the other set was seeded with 240,
120, 60, 30, and 15 organisms. In each set the fifth lesion
was inoculated with broth as a control.

The results of the larger dose inoculum are shown in Table I.
There was little difference between lesions 2, 3, and 4 although
the exudate was increased slightly with increasing numbers of
organisms. Lesion 5, however, by contrast showed a frankly
purulent exudate, and it was indurated and sore. After removal of
the coverslips all these lesions dried up and were healed
within a week.

The results of the smaller dose inoculum, shown in Table VI,
indicate that as few as fifteen organisms are sufficient to cause
a septic lesion, and they illustrate the rapidity with which the
organisms can multiply.

The Staphylococcal Lesions

In the course of these experiments, two of the three subjects
developed skin lesions of some severity on the inoculated arm.
Soon after inoculation one got a boil and a crop of small
pustules in the hairy part of the arm and over the sites of a
sentinele reaction; 5 weeks after his last inoculation he developed

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Organisms at 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Control</td>
<td>No exudate; no erythema</td>
</tr>
<tr>
<td>2. 100 organisms</td>
<td>Purulent exudate; erythema 5 x 5 mm</td>
</tr>
<tr>
<td>3. 1000 organisms</td>
<td>Purulent exudate; erythema 7 x 7 mm</td>
</tr>
<tr>
<td>4. 10,000 organisms</td>
<td>Purulent exudate; erythema 12 x 12 mm</td>
</tr>
<tr>
<td>5. 1,000,000 organisms</td>
<td>Purulent exudate; erythema 15 x 15 mm</td>
</tr>
</tbody>
</table>

organisms, but were unable to demonstrate any difference in
the smallest pus-forming dose between strains obtained from
lesions or from healthy nasal carriers and epidemic strains.

Using a similar organism dose we have shown that it is
possible to demonstrate differences in skin reaction
between an uninfected lesion, one inoculated with Staph. aureus,
and one inoculated with Staph. albus. The Staph. albus
lesion was clearly infected in contrast to the control
but the inflammatory reaction was less than in the lesion
infected by Staph. aureus.

In a similar experiment four types of Staph. aureus
which had not been associated with infections were compared
with a strain (phage-type 3c/55/71) known to have
caused several infections. It was not possible to differen-
tiate between the macroscopic or microscopic features of
these five lesions at the end of 24 hours: all showed a
similar purulent exudate with surrounding erythema.
These results confirm those of Elek and Cohen (1957),
who also attempted to differentiate between lesions produced
by organisms from carriers, and those from
septic lesions, without success.

The multiplication of staphylococci in these standard
infected lesions covered with coverslips followed the
expected pattern of growth, with a lag phase followed by
a phase of rapid multiplication. But in similar experiments
in which the lesions remained uncovered after inoculation,
multiplication was delayed for 8 hours. It seems probable
that keeping the lesion moist was the significant factor
since the 24-hour count after a standard inoculation was
similar whether the lesions were covered with coverslips,
or with small lids which retained moisture without causing pressure on the lesion. No evidence was forthcoming that the application of foreign material, such as French chalk or starch, which are used in glove powders, influenced the multiplication of organisms or the 24 hours inflammatory response. Superficial foreign material, however, cannot be compared with deep foreign bodies, such as sutures. The experimental work of Elek and Conen (1957) has shown that sutures have a significant effect in determining a clinical lesion.

In all the initial experiments in our study the organism numbers in the inocula were mostly of an order similar to those used by Elek (1956), and thus they bore little relation to clinical reality. In our dilution experiments, however, we found that as few as fifteen organisms could still produce significant sepsis in a standard skin lesion, and also that multiplication of organisms was so rapid at the total organism count at 24 hours was not much different from those infected with larger inocula. In so far as these experimental skin lesions simulated operation wounds, the results indicate that wound infection could also develop after superficial contamination with small numbers of organisms. The significance of this finding is enhanced by the observation of Foster (1960), who demonstrated the deposition of occasional staphylococci on an artificial operation site by a carrier using a new aseptic technique.

The unplanned subsequent septic lesions in two experimental subjects curtailed further experiments, but illustrated some additional aspects of the behaviour of Staph. aureus in the body. The boils on the arms were not necessarily at the site of inoculation but were always centred on hair follicles. These findings are in line with clinical experience and with the experimental work of Bockhart (1957), who excised experimentally produced furuncles and showed histologically that the organisms had multiplied in hair follicles. It may be of significance in this connection that of the three subjects of this experiment the one who escaped infection entirely was a woman, and the one most severely affected was the most hirsute. This subject, who later became a naval carrier and developed abscesses on the thigh and buttock, illustrates the propensity of the Staph. aureus to spread all over the body from an initial infective site, and the importance of separating such infected individuals from the neighbourhood of uninfected healing wounds.

Summary

Artificial skin lesions produced in man were inoculated with staphylococci. Organisms multiplied rapidly if the lesions were kept covered. There was a difference between the inflammatory response produced by Staphylococcus albus and Staph. aureus, but no evidence that different types of Staph. aureus varied in their virulence.

The addition of superficial foreign material did not affect the eventual lesion. Multiplication of organisms with the production of a septic lesion could be produced by as few as fifteen organisms.

The experiments had to be terminated because of the development of other septic lesions in two of the subjects.

Our thanks are due to Dr. E. H. Letchner who volunteered to take part in one experiment and to Prof. Ronald Hare for helpful criticism.

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Anderson, G. S., Williams, R. E. O. (1956) J. clin. Path. 9, 94.