Infective endocarditis continues to be a life-threatening disease despite the availability of antimicrobial agents. Even with successful antibiotic treatment, death in intractable heart failure is common because of aortic valve destruction. Furthermore, with the increased scope of cardiac surgical procedures, one of the most serious causes of postoperative failure is infection upon prosthetic valves. This type of endocarditis is very difficult to sterilize with antibiotics, and emboli from sterile thrombi are hazardous. Endocarditis is also an increasingly common disease among narcotics users. Yet another area of interest is that of the presumed immunologic sequelae of infective endocarditis. Glomerulonephritis in this infection is one of the forms of glomerulonephritis not due to type A Beta hemolytic streptococci. Thus, there are many common clinical problems that might be better understood were there a simple model in small animals suitable for the laboratory study of bacterial endocarditis. Experiments were undertaken in the hope of developing such a model.

Since it is well known that polyethylene catheters become easily infected in man, it was reasoned that placement of such catheters within the vascular system in animals might produce continuous bacteremia, thus mimicking bacterial endocarditis. When this procedure reliably induced right-sided bacterial endocarditis, the focus of the study sharpened upon this remarkable experimental lesion.

MATERIALS AND METHODS

White New Zealand rabbits weighing about five pounds were the test animals. To anesthetize them, they were injected with 50-60 mg. of sodium pentobarbital intravenously and were made to inhale ethyl ether. The femoral vein was exposed, tied distally with 4-0 silk, and a sterile polyethylene catheter ("Intramedic," Clay-Adams, PE-90, radiopaque, I.D. 0.034", O.D.: 0.050") was inserted to various lengths. The end of the catheter remaining outside the vessel was folded and kept in this position...
with a loop of silk suture. The wound was closed over the folded end of the catheter with silk. The procedure required an average of 20 minutes; strict sterile technique was not employed, and local wound infection did not occur.

Experimental animals (Groups 1 and 2) had appropriate dilutions of an overnight culture (10^8 colony-forming units per ml. trypticase soy broth) of the Giorgio strain of *Staphylococcus aureus* filling the catheter before it was inserted. The diameter of the catheter was such that it contained approximately 0.1 ml. per inch. In addition, 0.2 ml. of the test culture was injected to prevent formation of a blood clot at the catheter tip, and to insure the egress of bacteria from the catheter lumen. It was frequently possible to see pulsations of the heart transmitted along the column of fluid in the catheter and the syringe attached to it. Groups 3 and 4 were control animals with identical operations; however, the catheters contained sterile saline. Group 5 were control animals receiving only an intravenous injection of 10^8 colony-forming units of the test organism.

Periodically 0.5 ml. of blood was drawn, using sterile techniques, from an ear vein of test rabbits and was cultured overnight on an agar pour plate. White blood cell counts and hematocrits were done upon the same samples.

**Catheter placement.** In 8 of the 21 animals in Group 1 the catheters exited from the venous system at the time of placement. This would have been easily demonstrable in five of these cases by X-ray. Moreover, with experience it was possible to tell with a high degree of certainty when the catheter was in the vein.

**Pathologic and bacteriologic studies.** Groups 1 and 2 animals were usually sacrificed when they were moribund, or following several positive blood cultures or elevated white blood cell counts of over 10,000/mm^3. The animals were killed with 120 mg. of sodium pentobarbital intravenously after a terminal blood culture had been drawn. Post-mortem examination was carried out with aseptic technique. After study of the thoracic and abdominal organs and removal of pathological specimens, the organs were homogenized and cultured quantitatively. Enumeration of viable bacterial units in test cultures and organ homogenates was accomplished by counting colonies 24 hours after incubation of serially diluted agar pour plates.

**RESULTS**

**Group 1:** Thirteen of 21 animals in whom long catheters (10-12 inches) containing 10^8 staphylococci were inserted and found at autopsy to be within the venous system in the vicinity of the heart were designated Group 1-A. All had staphylococcal endocarditis except one which had healed endocarditis (Table 1). Animals with similar catheters containing 10^8 bacteria were designated Group 1-B. Three of four animals had active bacterial endocarditis and the fourth had sterile endocarditis (Table 2).

**Pathology of the heart**

Bacterial vegetations in the heart (Fig. 1) bore a striking resemblance to human infective endocarditis. Grossly the lesions were friable, rounded multiple grey-pink excrescences varying in size from 1 to 5 mm.

There was obvious tricuspid valve involvement on gross examination in eight animals. The vegetations were most commonly located on the right
| Rabbit no. | Days followed | Blood cultures | Organ findings                                      | Other findings                                      | Catheter tip site |
|-----------|---------------|----------------|-----------------------------------------------------|-----------------------------------------------------|-------------------|
| 11        | 36            | Neg. × 12       | Calcified vegetation in R.A. & R.V.                 | Lungs: hemorrhagic foci. Liver: passive congestion. L. kidney: cortical scar. Spleen: 1.5 grams | At entrance to R.A. |
| 12        | 8             | Pos. day 7 and terminally | T. valve: large vegetation. Myocardial involvement of R.V. | R. kidney: focal abscess in medulla. Spleen: 15.0 grams | At entrance to R.A. |
| 13        | 23            | Pos. day 9, Neg. day 8 | Vegetation in R.A. | L. kidney: cortical scar. Spleen: infarct, weight: 2.5 grams | At entrance to R.A. |
| 15        | 12            | Pos. × 5        | Many vegetations in R.A., R.V., T. & P. valves and on papillary muscles | Peritoneal effusion Spleen: 7.0 grams | At entrance to R.A. |
| 16        | 27            | Neg. × 5        | Vegetations in R.A., R.V., T. & M. valves. Pericardial inflammation near catheter tip | R. & L. kidney: several medullary abscesses Spleen: 5.0 grams | R.V. |
| 18        | 25            | Neg. × 4        | Vegetation in R.A., T. valve and P. outflow tract | Liver: passive congestion Spleen: 3.5 grams | R.V. |
| 21        | 40            | Weakly pos. day 3 Neg. × 5 | Vegetation in R.A., T. valve and P. outflow tract | Liver: passive congestion Spleen: 1.4 grams | R.A. |
| 23        | 37            | Pos. day 1 & 28 Neg. days 9, 13, 22, 29, 36, 37 | Vegetations in R.A. and papillary muscles | Spleen: 1.9 grams | R.A. |
| No. | Date | Status | Description                                                                 | Other Findings                                                                 |
|-----|------|--------|------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| 26  | 10   | Pos. × 3| Vegetations on T. & M. valves and in R. V. & R.A.                             | Liver: passive congestion. R.V. L. kidney: infection in medulla and cortex. Lung: hemorrhagic. Spleen: 9.0 grams |
| 27  | 17   | Neg. day 8 Pos. day 16 & terminally | Vegetations T. valve & R.V. myocardium                                      | Lungs: numerous abscesses. R. & L. kidney: cortical abscesses. Spleen: 3.0 grams R.V. wall, tip beneath pericardium. |
| 31  | 13   | Neg. day 2 | Vegetations in R.A., R.V. and T. valve                                      | R. kidney: abscess in medulla. Spleen: 4.0 grams Tip on T. valve |
| 33  | 36   | Neg. × 4 | Vegetations in R.A., R.V. and T. valve                                      | L. kidney: cortical abscess. Spleen: 2.5 grams R.A. |
| 35  | 41   | Day 9 - neg. 14 - pos. 16 - neg. 23 - pos. 26 - pos. 37 - neg. 41 - neg. | Vegetations in R. A. & R.V., T. valve and pulmonary outflow tract. M. valve thickened. | Lung: hemorrhagic foci. Microscopic kidney infection. Spleen: 2.4 grams At entrance to R.A. |

R.A. = right auricle
R.V. = right ventricle
T. = tricuspid valve
M. = mitral valve
P. = pulmonary valve
I.V.C. = inferior vena cava
Table 2. Long Catheters Filled With 10⁶ Staphylococci (Group 1B)

| Rabbit no. | Days followed Blood cultures | Heart                         | Other                        | Catheter tip site |
|------------|------------------------------|-------------------------------|------------------------------|-------------------|
| 63         | 12                           | -                             | T. valve vegetation          | Kidneys normal    | R.V.              |
|            |                              |                               | Spleen: 5.44 grams           |                   |
| 64         | 18                           | Neg. X 2                       | Sterile vegetation in R.A.   | Spleen: 1.6 grams | R.A.              |
| 78         | 9                            | Neg. X 2                       | T. & P. valvulitis           | Spleen: 5.6 grams | At entrance to R.A.|
|            |                              | Hemopericardium                |                              |                   |
| 83         | 12                           | Pos. day 6                     | T. valvulitis. Hemorrhagic   | Bilateral kidney infections. | R.V.              |
|            | Pos. day 11                  |                               | vegetations on T. valve, R.A.| Spleen: 3.5 grams |                   |
|            | Pos. day 12                  |                               | and chorda tendineae         |                   |
Fig. 1. Rabbit No. 15. Vegetations in right auricle and on tricuspid valve 12 days after placement of catheter containing $10^5$ staphylococci.

Fig. 2. Rabbit No. 12. Bulging vegetation as seen from ventricular surface of the tricuspid valve 8 days after placement of catheter containing $10^6$ staphylococci.
Fig. 3. Rabbit No. 15. Low power view of tricuspid vegetation 12 days after placement of catheter containing $10^8$ staphylococci. Bacterial colonies (large black masses) are enmeshed in a laminated matrix containing very few polymorphonuclear leucocytes.

Fig. 4. Rabbit No. 26. Proliferation of the endothelium of a large artery in the lung and infiltration of the endothelium with inflammatory cells.
Fig. 5. Rabbit No. 36. Marantic endocarditis, tricuspid valve, 38 days following placement of catheter, the tip of which was found to be at the entrance to the right auricle.
atrial wall and the atrial surface of the tricuspid valve, occupying the leaflets entirely in some instances and bulging through to the ventricular surface (Fig. 2). The right ventricle and pulmonary outflow tract were less commonly involved, with the pulmonic valve involved in one animal. Tiny vegetations were found upon the mitral valve in two animals.

Microscopically the features of the lesions depended upon their age, as described by McGeown. Rabbits that had a fulminating course showed vegetations with central necrosis and colonies of bacteria enmeshed in laminated material (probably platelets and fibrin) with mononuclear and fibroblast infiltration at the base of the lesion and endothelial cells spreading over the fibrin but never resting directly on bacterial colonies (Fig. 3). Polymorphonuclear leucocytes were consistently sparse around bacteria. When the disease process was older, granulating tissue was seen at the bases of the vegetations, and Anitchkow myocytes and small new vessels were present. Myocardial involvement in association with a vegetation or a catheter was present in the right ventricles of two rabbits. No myocarditis or microinfarcts were observed.

Rabbit 11 had healed bacterial endocarditis by clinical and pathologic criteria: negative blood cultures, sterile vegetations and a reduced number of bacteria in the catheter, which was plugged with leucocytes. Calcification was observed in the healed vegetation.

Thus, bacterial endocarditis was produced in 12 of 13 rabbits with a catheter containing $10^5$ staphylococci. The remaining animal had healed endocarditis.

In Group 1-B were four animals in which long catheters containing $10^2$ colony-forming units per ml. were inserted. Three developed bacterial endocarditis with splenomegaly. One of the three had bloodstream and bilateral kidney infections. The fourth animal was found to have sterile vegetations in the right atrium, no splenomegaly and no bloodstream infection.

Pathology of other organs

Lung. The lungs appeared somewhat edematous in all animals in Group 1, and were strikingly edematous with foci of hemorrhage in three. Lesions resembling infarcts were observed in several animals. Two animals, Rabbits 11 and 13, had arteritis, presumably a consequence of embolic or immune manifestations of the endocarditis (Fig. 4).

Spleen. Splenomegaly (over two grams in rabbits of this size), was observed in 10 of the 12 animals with active disease. Microscopically, the enlarged spleens showed increased white pulp. One spleen was noted to be infarcted in its distal third.
Liver. Passive congestion was noted in four animals.

Kidneys. One animal had a kidney infection detectable only microscopically. Four had cortical and medullary abscesses in one or both kidneys. Glomerulonephritis was not observed. There were two rabbits in which interstitial nephritis, an occasional finding in our laboratory stock, was seen.

Bacteriologic findings

Blood cultures were negative throughout in two animals that had courses longer than 25 days and were found to have endocarditis at autopsy. In six animals, cultures were positive on only one of several determinations; in five animals, cultures were repeatedly positive.

Quantitative culture of the vegetations yielded 10^8 colony-forming units per gram of tissue. Error is inherent in this calculation because of the irregular distribution of the bacteria evident on microscopic examination.

Quantitative determination of organisms in various body organs, as shown in Table 3, revealed that animals with terminal positive blood cultures generally had many bacteria in various organs, while few bacteria were detected in animals with terminal negative blood cultures.

White counts were not a useful index of infection. They were usually elevated in animals who appeared listless and ill and who had positive terminal blood cultures. Some animals, however, had normal white counts and one (Rabbit 15) had a low white count.

Approximately 10^8 colony-forming units/ml. were recovered from most of the catheters after they were removed at autopsy and no catheter contained fewer than 10^8 colony-forming units.

Group 1-C is the designation for eight animals in which the catheter went astray at operation (Table 4). With the exception of Rabbit 30, whose right renal vein was catheterized, and Rabbit 20, whose pericardium was catheterized after the right atrium had been punctured, no infections developed at the tips of these catheters, although three lay free in the peritoneal cavity, one was lodged in the right psoas muscle, and one had dissected along the intima of the inferior vena cava and lay beneath the endocardium in the anterior wall of the right atrium. In the six rabbits without bloodstream infections, white counts remained normal and there was no splenomegaly. No less than 10^8 colony-forming units of staphylococcus were recovered from the catheters. There was a fibrous reaction around the tip of the catheters and adhesions in the cases of those in the peritoneum.

Group 2 animals were those with short catheters (6-7 inches) containing staphylococci (Table 5). None of the four developed infections, positive blood cultures or elevated white counts. At autopsy all organs were normal,
| Rabbit | Spleen (*/gram) | Liver (*/gram) | R. Kidney (*/gram) | L. Kidney (*/gram) | Urine (*/ml) | Retrieved catheter (*/ml) | Vegetation (*/gram) | Terminal blood culture |
|--------|----------------|---------------|-------------------|-------------------|--------------|---------------------------|-------------------|------------------------|
| Group IA |
| 11     | 0              | 0             | 0                 | 0                 | 0            | 10<sup>9</sup>            | 10<sup>9</sup>     | neg.                   |
| 12     | 10<sup>9</sup> | 10<sup>9</sup>| 10<sup>9</sup>    | 10<sup>9</sup>    | 0            | 10<sup>4</sup>            | 10<sup>9</sup>     | pos.                   |
| 13     | 10<sup>9</sup> | 10<sup>4</sup>| 0                 | 0                 | 0            | 10<sup>9</sup>            | 10<sup>9</sup>     | pos.                   |
| 15     | 10<sup>9</sup> | 10<sup>9</sup>| 10<sup>9</sup>    | 10<sup>9</sup>    | 10<sup>9</sup> | 10<sup>9</sup>            | —                 | pos.                   |
| 16     | 10<sup>9</sup> | 10<sup>9</sup>| 10<sup>9</sup>    | 10<sup>9</sup>    | 0            | 10<sup>9</sup>            | 10<sup>9</sup>     | pos.                   |
| 18     | 10<sup>9</sup> | 10<sup>9</sup>| 10<sup>9</sup>    | 10<sup>9</sup>    | 0            | 10<sup>9</sup>            | 10<sup>9</sup>     | pos.                   |
| 21     | 10<sup>9</sup> | 10<sup>9</sup>| 10<sup>9</sup>    | 10<sup>9</sup>    | 0            | 10<sup>9</sup>            | 10<sup>9</sup>     | neg.                   |
| 23     | 0              | 0             | 0                 | 0                 | 0            | 10<sup>9</sup>            | 10<sup>9</sup>     | pos.                   |
| 26     | 10<sup>9</sup> | 10<sup>9</sup>| 10<sup>9</sup>    | 10<sup>9</sup>    | 10<sup>9</sup> | 10<sup>9</sup>            | —                 | (M.V. 10<sup>9</sup>) |
| 27     | 10<sup>9</sup> | 10<sup>9</sup>| 10<sup>9</sup>    | 10<sup>9</sup>    | 10<sup>9</sup> | 10<sup>9</sup>            | —                 | (lungs: 10<sup>9</sup>) |
| 31     | (found dead; bacteriology incomplete) | 10<sup>9</sup> | 10<sup>9</sup>    | 10<sup>9</sup>    | 10<sup>9</sup> | 10<sup>9</sup>            | 10<sup>9</sup>     | pos.                   |
| 33     | 0              | 0             | 0                 | 0                 | 0            | 10<sup>9</sup>            | —                 | neg.                   |
| 35     | 0              | 0             | 0                 | 10<sup>9</sup>    | 10<sup>9</sup> | 10<sup>9</sup>            | 10<sup>9</sup>     | neg.                   |
| Group IB |
| 63     | (found dead; bacteriology incomplete) | 10<sup>9</sup> | 10<sup>9</sup>    | 10<sup>9</sup>    | 10<sup>9</sup> | 10<sup>9</sup>            | —                 | —                      |
| 64     | "              | "             | "                 | "                 | "            | 10<sup>9</sup>            | 10<sup>9</sup>     | —                      |
| 78     | "              | "             | "                 | "                 | "            | —                        | 10<sup>9</sup>     | —                      |
| 83     | 10<sup>9</sup> | 10<sup>9</sup>| 10<sup>9</sup>    | 0                 | 0            | 10<sup>9</sup>            | —                 | pos.                   |
### Table 4. Catheters That Went Astray (Group 1C)

| Rabbit no. | Days followed | Blood cultures                      | Organ findings                              | Catheter tip site |
|------------|---------------|-------------------------------------|---------------------------------------------|-------------------|
| 20         | 14            | Pos. day 2 and terminally. Neg. days 4, 9, 11 | normal                                      | Pericardium       |
| 30         | 14            | Pos. day 13. Neg. × 2 previously Neg. terminally | normal                                      | Rt. renal vein    |
| 19         | 25            | Pos. day 4, Neg. days 6, 11, 13, 17, 23 | normal                                      | Free in peritoneal cavity |
| 22         | 36            | Neg. × 4                             | normal                                      | Free in peritoneal cavity |
| 24         | 35            | Neg. × 5                             | normal                                      | Rt. psoas muscle  |
| 32         | 32            | Neg. × 5                             | normal                                      | Inside rt. atrial wall |
| 28         | 34            | Neg. × 5                             | normal                                      | Free in peritoneal cavity |
| 25         | 38            | Neg. × 5                             | sterile vegetation in R.A. Spleen : 1.5 grams | R.A. wall         |
| Rabbit no. | Days followed | Blood cultures | Organ findings | Catheter tip site |
|-----------|---------------|----------------|----------------|------------------|
| 14        | 7             | Neg. × 1        | normal         | I.V.C. above diaphragm |
|           |               |                 | 10⁶ bacteria recovered from catheter |                  |
|           |               |                 | Spleen: 4 grams |                  |
| 17        | 27            | Neg. × 7        | normal         | I.V.C. above diaphragm |
|           |               |                 | 10⁶ bacteria recovered from catheter |                  |
|           |               |                 | Spleen: 1 gram |                  |
| 29        | 35            | Neg. × 5        | normal         | I.V.C. at liver   |
|           |               |                 | 10⁶ bacteria recovered from catheter |                  |
|           |               |                 | Spleen: 1.2 grams |                  |
| 34        | 32            | Neg. × 5        | normal         | I.V.C. at renal veins |
|           |               |                 | 10⁶ bacteria recovered from catheter |                  |
|           |               |                 | Spleen: 0.6 grams |                  |
save for one animal that had an enlarged spleen. Cultures of the fluid from the catheters removed at the time of sacrifice grew $10^8$ colonies of staphylococci per ml.

Group 3 consisted of control animals in which long catheters containing sterile saline were in place for 7 to 38 days (Table 6). Of great interest were the gross findings at autopsy that all seven animals had developed marantic endocarditis (Fig. 5). Grossly the vegetations had the same distribution as the infected ones in Groups 1-A and 1-B but were smaller, firm, flat, and pale. There was no evidence of tricuspid valve destruction by these sterile vegetations. Microscopically the vegetations consisted of fibrin and rare white cells of mononuclear series. Bacteria were not seen and cultures were sterile. There were no other myocardial or valve lesions. None of the animals had splenomegaly and white counts were generally less than 10,000/mm$^3$.

The lungs of the animals in Group 3 had foci of hemorrhage and slight edema; the livers and kidneys appeared normal.

Group 4 animals had short catheters containing saline left in place up to 21 days before sacrifice (Table 7). All three animals had negative blood cultures and none had elevated white counts or splenomegaly.

Group 5 included seven control rabbits that received $10^7$ colony-forming units of staphylococcus intravenously, 100 times the number of bacteria used in Groups 1 and 2 (Table 8). These animals had positive blood cultures for 48 hours after injection, but white counts remained normal and subsequent blood cultures were negative. They were studied 17-23 days after inoculation. There was no evidence of endocarditis and all organs appeared normal with the exception of the kidneys of two animals, which had small abscesses. None of the animals had splenomegaly.

DISCUSSION

This study derived from the observation in man that indwelling intravenous catheters and other prosthetic devices are easily liable to infection, leading to blood stream sepsis, and endocarditis. The experiments in rabbits have fully confirmed the ease with which bacterial endocarditis results from the placement of infected catheters in the heart. This is a new technique for the study of bacterial endocarditis in animals that have not been subjected to serious alterations of their immunologic or hemodynamic systems.

That the vegetations were infected in 12 of 13 cases when the catheter contained organisms is evidence that this is a reliable method of producing bacterial endocarditis with positive blood cultures, splenomegaly, leucocytosis, and a variety of metastatic lesions. Of note is the fact that all or-
Table 6. Long Catheters Filled With Saline and Left in Place up to 21 Days (Group 3)

| Rabbit no. | Days followed | Blood cultures | Organ findings | Catheter tip site |
|------------|---------------|----------------|----------------|------------------|
| 36         | 38            | Neg. × 6        | Vegetations; R.A., T. valve | No bacteria recovered from catheter. R. kidney infection. Spleen: 0.9 grams | At entrance to R.A. |
| 37         | 38            | Neg. × 5        | Vegetations; R.A. | No bacteria recovered from catheter. Spleen: 1.5 grams | At entrance to R.A. |
| 43         | 15            | Neg. × 3        | Vegetations; R.A. R.V., T. valve | No bacteria recovered from catheter. Spleen: 0.8 grams | R.A. |
| 60         | 19            | Neg. × 3        | Vegetations; R.A. T. valve | No bacteria recovered from catheter. Spleen: 0.83 grams | R.V. |
| 62         | 19            | Neg. × 3        | Vegetations; T. valve | No bacteria recovered from catheter. Spleen: 0.38 grams | R.V. |
| 74         | 29            | Neg. × 2        | Vegetations; R.A. R.V., T. valve | No bacteria recovered from catheter. Spleen: 1.9 grams | R.V. |
| 75         | 29            | Neg. × 2        | Vegetation: R.A. | No bacteria recovered from catheter. Spleen: 1.08 grams | Displaced at autopsy: probably at entrance to R.A. |
| Rabbit no. | Days followed | Blood cultures | Organ findings                                                                 | Catheter tip site          |
|------------|---------------|----------------|---------------------------------------------------------------------------------|----------------------------|
| 7          | 9             | Neg. × 6        | normal Died of intercurrent disease. No bacteria recovered from catheter         | lower I.V.C.               |
| 8          | 21            | Neg. × 12       | normal No bacteria recovered from catheter                                       | lower I.V.C.               |
| 42         | 15            | Neg. × 3        | normal Clot extended from catheter to R.A. No bacteria recovered from catheter  | I.V.C. at renal vein       |
|            |               |                | Spleen: 1.3 grams                                                               |                             |
TABLE 8. 10⁶ STAPHYLOCOCCI I.V. (Group 5)

| Rabbit no. | Days followed | Blood cultures | Organ findings |
|------------|---------------|----------------|----------------|
|            |               |                | Heart          | Other                        |
| 38         | 23            | Pos. initially | normal         | normal                      |
| 39         | 23            | Pos. initially | normal         | normal                      |
| 40         | 23            | Pos. initially | normal         | normal                      |
| 41         | 23            | Pos. initially | normal         | Sterile peritoneal effusion  |
|            |               | neg. × 3       | normal         | Left kidney infection (10⁶ organisms) |
| 44         | 17            | Neg. × 2       | normal         | normal                      |
| 45         | 17            | Neg. × 2       | normal         | Right kidney grew 10⁶ colonies. Left kidney sterile. |
| 46         | 17            | Neg. × 2       | normal         | Scar on cortex of right kidney. |

organisms recovered at autopsy were the *Staphylococcus aureus* placed within the catheters. Quantitative evaluation of the numbers of organisms per gram in various tissues indicated that the counts were highest in the vegetations and infected valves. This is consistent with quantitation of organisms in experimental endocarditis in dogs produced by Hamburger.⁷-⁸

The observation that sterile endocarditis can be produced by a sterile catheter maintained in close proximity to endocardium and valves suggests that hemodynamic disturbance locally is a critical factor in the development of valvulitis and endocarditis. Some of the vegetations produced in this series developed in areas of low velocity flow, in the right atrium. Direct trauma to endocardium by the end of the catheter is likely to have occurred in one rabbit in Group 3. Damage to the endocardium as a prerequisite to development of endocarditis raises the question of what events follow prolonged cardiac catheterization in man. Reliable production of marantic endocarditis provides a model for the possible study of platelet adhesion and serum factors in endocarditis, previously studied in ill human patients.⁹-¹³

Previous methods of producing experimental endocarditis have utilized severe systemic immunologic reactions, drastic hemodynamic alterations, such as fistulae between the aorta and inferior vena cava,¹⁰-¹⁷ or surgical creation of aortic insufficiency.⁷,¹⁸,¹⁹ Other methods employed have been the disruption of cardiac lymphatic drainage, simulated high altitude with and without hemodynamic stress and bacteremia,²¹,²² stress of many types,²³-²⁶ and finally, injection of large numbers of organisms.²⁷

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These experimental methods rely on disruption of the hemodynamic norm or upon immunologic or endocrine challenge, thus interfering with the course of the endocarditis they produce by altering the animal's susceptibility to infection. In addition, the techniques are difficult, with varying degrees of predictability, and the surgical methods involve placement of suture material which may serve as a nidus of infection. That hemodynamic disturbances are produced by most of these experimental methods corroborated observations that both marantic and infective endocarditis are more likely to occur on valves with structural anomalies and suggest turbulence as an etiologic factor. The presumed flow disruption has also been studied experimentally by Robard, Angrist, et al., on the basis of histologic study, postulate valvular edema with distortion of subendothelial stroma as a predisposing factor. Our findings do not contradict these hypotheses.

Endocarditis with negative blood cultures is consistent with the known clinical variability of blood cultures in this disease. Our observation of positive blood cultures in animals without left-sided infections confirms that the lungs do not, as once postulated, filter all microorganisms passing through them. Bain has provided good clinical evidence that virulent organisms gain access to the arterial circulation in right-sided endocarditis.

We observed positive blood cultures inconsistently. In two animals with infective endocarditis positive blood cultures were never obtained. In six animals, cultures were positive only once in several determinations; in five animals cultures were repeatedly positive. It should be mentioned, however, that our method of performing blood cultures (solid media) differed from that used clinically, and would be expected to be more often negative when there are few circulating bacteria.

Although Rabens produced diffuse glomerulonephritis consistently with Streptococcus mitis, convincing renal lesions of this type were not observed in our experiments. Glomerulonephritis is reported in man to be a rare complication of staphylococcal endocarditis. That staphylococcal infection on the right side of the heart can produce glomerulonephritis was well demonstrated by the findings of glomerulonephritis with florescent antibody to staphylococcus demonstrable in the kidney of patients with infected ventriculoatrial shunts. Noteworthy is the fact that 5 of the 6 patients in this series were infants when originally infected and had an interval of 11 months to 6 years between the first documented infection and the development of renal symptomatology. Perhaps the development of glomerulonephritis in animals with right-sided staphylococcal endocarditis requires a longer period of active infection than was permitted in the present series of experiments.
SUMMARY

Polyethylene catheters with their tips at the entrance to or within the right side of the heart produce sterile marantic endocarditis and tricuspid valvulitis. Introducing as few as $10^4$ microorganisms within the catheter predictably produces staphylococcal endocarditis. The course of the disease is variable, some animals surviving for six weeks. The technique is simple and does not require hemodynamic, immunologic or endocrine manipulations of the animals. Splenomegaly was frequently found in association with endocarditis but positive blood cultures were inconstant. Kidney infections were observed but there were no examples of proliferative glomerulonephritis. This model is suitable for the study of the bacteriologic, pathologic, and immunologic aspects of bacterial endocarditis and reproduces some of the complications of indwelling venous catherization that have been observed in man.

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