



## Infections and the Spleen

By Alan D. Tice, M.D.

*Dr. Alan Tice is an infectious disease specialist who is in private practice in Tacoma. He also serves as a Clinical Assistant Professor of Medicine at the University of Washington School of Medicine. A graduate of Columbia College of P and S, Dr. Tice served his internship and residency at The Roosevelt Hospital and Manhattan Veterans Administration Hospital, both in New York City. He completed a fellowship in infectious disease at Tufts-New England Medical Center, Boston, and taught at the Brown University Medical School. Dr. Tice is currently a member of the Pierce County Medical Bureau Board of Directors, the School Health/Public Health Committee and Tacoma General Hospital's Medical Education Committee.*

The spleen's important role in host defense has been recognized over the last several decades and led to attempts to preserve its function by salvage and even auto transplantation procedures when the spleen is damaged by trauma and incidentally at surgery. When the spleen is totally removed, pneumococcal vaccine is necessary to help prevent infection. The occasional fulminant infection may still occur and should be closely looked for. The role of prophylactic antibiotics, vaccines against meningococcus and *Hemophilus influenza* type B, Levamisole and prompt therapy with intravenous immune globulin remain unclear.

---

**B**ecause of the number of times the spleen has come up in questions about patient management, I decided to review the recent literature about the spleen — especially in relation to infections.

The average adult spleen is an organ of approximately 12 by 7 by 3 cm in size. It weighs only 150 grams, but it comprises at least one-quarter of the lymphoid tissue in the body (4). Although it was not until recently the spleen was recognized to have a significant function, we now know that it has multiple contributions to host immunity aside from its

hematologic activities.

One of the important functions it has is to serve as a filter for defective red cells in the body. It can destroy some of the red cells or even remove abnormalities from within the cells as they pass through the barriers the spleen presents. In addition, it serves as a filter for other material in the blood stream, such as bacteria, parasites and particulate matter. It is a most important organ for clearance of bacteria from the blood stream and hence is important in preventing the overwhelming infections that occur in

patients without a spleen. This organ also serves as a significant reservoir of platelets (30 to 40 percent of those in the peripheral circulation are stored there) — to be released should bleeding or trauma occur.

### **The spleen and infection**

Aside from its action as a filter, the spleen is also an important organ for production of opsonins which are important in the control of infections. Opsonins are the coating or "glue" the body produces to adhere to the surface of bacteria to destroy them or change the surface to allow phagocytosis and killing by granulocytes.

One of the opsonic factors the spleen produces is early organism-specific immunoglobulin IgM. In animals, this IgM can be produced in the spleen within hours of a bacterial challenge — earlier than it can be produced by any other organ in the body. The other opsonins that we know of include tuftsin which is essentially absent in people without a spleen. Properdin and probably other elements of a complement system are also produced by the spleen. Aside from the immediate elements of host defense such as IgM, complement and tuftsin, the spleen also contributes to the processing of antigens by lymphocytes and macrophages for additional IgM and IgG production (2).

The spleen may be enlarged from a variety of causes. Among the most common are infections. As might be expected, it enlarges when asked to deal with chronic or difficult infections such as with parasites (from malaria to leishmania to babesia), syphilis, tuberculosis, viral infections (particularly Epstein-Barr virus and cytomegalovirus), as well as some

bacterial infections which may be chronic such as endocarditis and typhoid fever (8). The spleen also enlarges with connective tissue disorders, hematologic disorders (particularly with hemolysis but also with leukemias and lymphomas), lipid storage diseases, liver disease and some neoplasms. With age, there is a gradual involution of the spleen with decreasing size. The reason for this and the significance of it is not clear, but it may relate to a waning host immunity which also occurs with age.

### **Splenectomy and potential complications**

Although the majority of people have a single spleen, there are reports of one-fifth to one-third of people having accessory spleens on post-mortem examinations (12). The significance of these spleens is uncertain, but they certainly present a potential problem if it is necessary to remove splenic tissue, as may be necessary in idiopathic thrombocytopenic purpura. How much splenic tissue

---

*"Aside from its action  
as a filter, the spleen  
is also an important  
organ for production  
of opsonins . . ."*

---

is actually necessary for normal function in humans is unclear, but studies in animals suggest that three-fourths of the spleen can be removed without affecting the response to bacterial challenge (5).

Approximately 35,000 splenectomies are performed each year. The rea-

sons for splenectomy vary. In a survey done at Ohio State from 1973 to 1978, 27 percent were done for Hodgkins disease, 20 percent were "incidental", 16 percent were for hypersplenism and 14 percent were performed because of trauma (7). There is a significant mortality associated with splenectomy but often it's because of complicating factors such as underlying malignancy,

---

***"The overall incidence of sepsis after splenectomy appears to be 10 to 50 times that of the normal population with a spleen."***

---

trauma or other surgery performed at the time. The primary post-operative complications of splenectomy include respiratory infections, hemorrhage, subphrenic abscess and thrombo-emboli. The peri-operative mortality is approximately 6 to 13 percent overall but somewhat higher with "incidental" and trauma cases (7).

The role of the spleen is preventing infection was recognized in animal studies done as early as 1919, but it was not recognized as a problem in humans until 100 patients were reported by King and Schumacher in 1952 (9, 11). Their study noted six patients under the age of 6 who developed fulminant infections, two of which were fatal. Since that time, there has been a significant controversy in the literature in terms of how significant the post-splenectomy infection potential really is. From the varying data there seemed to be some accepted principles that apply.

Young children are clearly more at risk for fulminant infections than adults; a summary of 4,500 reported cases indicates that there is a 4.1 percent incidence of sepsis in children vs 1.9 percent incidence in adults (7). This correlation with age is particularly acute within the first two years of life. The overall incidence of sepsis after splenectomy appears to be 10 to 50 times that of the normal population with a spleen (7).

The greatest controversy about infection rates is in adults. Studies vary from suggesting that adults without a spleen have such a high rate of fulminant sepsis that they should be placed on penicillin (13), to a well-controlled study at the Baltimore Cancer Research Center which suggested that even in their Hodgkins disease patients splenectomy does not increase the incidence of pneumococcal sepsis or other infections above the control group of patients who had Hodgkins but without spleen removal (2).

### **Complicating factors**

Another principle that seems to hold is that the incidence of sepsis increases with associated disorders such as malignancy, chemotherapy and radiation therapy, as would be expected in patients with hematologic malignancies for which the spleen was removed.

Another factor that seems important is the fatality rate once an infection occurs. In children, more than one-half of the cases of sepsis are fatal and in adults about one-third of sepsis episodes are fatal. Both these figures are higher than those for the normal population (7).

There appears to also be an inverse correlation with the likelihood of sepsis and the duration of time since splenectomy. In animal studies as well as studies

of children, there appears a clear increase in mortality if an infection occurs soon after splenectomy. Two-thirds of the cases of sepsis occur within two years of splenectomy (7). The higher fatality rate with splenectomized patients is probably related to a higher concentration of bacteria in the blood once bacteremia occurs and is associated with disseminated intravascular coagulation. Sepsis without a spleen is usually of more rapid onset as well as more severe.

Pneumococci comprise about 50 percent of the bacteria isolated when children and adults are grouped together. The second most likely bacteria is *Hemophilus influenza* followed by *Neisseria meningitidis*, beta-hemolytic streptococcus, *Escherichia coli* and pseudomonas (7).

The top bacteria which account for sepsis in splenectomized patients have a polysaccharide capsule which is a deterrent to opsonization, especially without a spleen. It is also interesting that the infections are not simply related to the polysaccharide capsules, but include a variety of other bacteria as well. Some studies suggest a significant incidence increase in staphylococcus infections with associated higher mortality. In addition to the bacteria, some viral infections may be more likely or more severe in splenectomized patients. This appears to be true for cytomegalovirus although good studies have not been done for infectious mononucleosis (1). The significance of accessory spleens in preventing infection is unclear, but presumably they offer some protective effect. In animals, only 25 percent splenic tissue is necessary to control bacteremia. There have been reports of sepsis in patients with multiple fragments of splenic tissue following splenectomy for trauma (13).

## Recent developments

The frequency and severity of infections in splenectomized children indicates a need to prevent or better treat the infections that do occur. If you accept that there is a higher incidence of infection in adults as well, then many of the same principles apply. The first consideration should be to examine any means that may reduce the incidence of splenectomy.

Many spleens are removed for diagnostic or therapeutic purposes. However, in the trauma patient or with the "incidental" splenectomy, it may be worthwhile trying to repair the spleen. Studies from England suggest it is possible to salvage significant splenic tissue with half or more of the patients with significant splenic damage (4). Salvage can be accomplished through closure or coverage of a laceration, oversewing the

---

*"The first consideration should be to examine any means that may reduce the incidence of splenectomy."*

---

laceration with omentum, covering the spleen with a polyglycolic mesh, ligation of the main splenic artery and ligation of the lower polar artery with partial splenectomy. There is some doubt as to the usefulness of ligating the main splenic artery as this may prevent adequate blood flow for the filtration action of the spleen.

Despite the above surgical considerations, the spleen must still often be re-

moved with trauma. When this is necessary, additional considerations include auto-transplantation wherein fragments of residual splenic tissue are placed within the omentum or possibly abdominal wall (4, 10). Infusion of splenic tissue into the portal vein has also been tried. The question of the amount of splenic tissue necessary to return normal splenic function remains unclear and there have been no good studies demonstrating a lower incidence of infection following auto-transplantation in humans.

### Prophylaxis

If a spleen has been removed in the past and no auto-transplantation done and there is presumably no useful amount of accessory splenic tissue, there are additional considerations which should be made in terms of prevention of infection.

---

*“The newer bacterial vaccines are another area of advance in preventing infections in splenectomized patients.”*

---

The situation of children is relatively clear particularly for the first few years of life. In this situation, penicillin has been quite useful in preventing sepsis although one may postulate that ampicillin or amoxicillin would be better, particularly in children who may have infections with *Hemophilus influenza*. The adult dose of penicillin should be 250 to 500 mg twice daily. The usefulness of penicillin therapy is probably related to the age of the child, but it should be continued for at least

three years following splenectomy and possibly into adolescence.

There are some who advocate penicillin or other prophylactic therapy for adults as well as children. Unfortunately, compliance is a problem over the years that are potentially necessary to prevent the infection. It is also possible that the patient may have an infection with a penicillin or ampicillin-resistant bacteria. The chronic penicillin treatment may also result in the production of resistant strains of pneumococcus.

The newer bacterial vaccines are another area of advance in preventing infections in splenectomized patients. The pneumococcal vaccine is the best studied and seems effective in children (7). The newer 23-strain vaccine may be even more effective than prior older preparations which had only 18 types of pneumococcal antigen included. The value of meningococcal vaccine has not been proven but it is theoretically of benefit even though only the less frequent two of three primary strains are available in the vaccine. The recent release of *Hemophilus influenza* type B vaccine may be of additional benefit in splenectomized children. Unfortunately, the removal of the spleen seems to limit the responsiveness of patients to a vaccine. If a splenectomy is to be performed electively, it would be most useful to give the vaccines a month before surgery to allow a full stimulation of the immune system by the vaccines.

Unfortunately, there are many other bacteria which may cause significant infections in splenectomized patients — for which no vaccine is available. The value of repeated administration of a vaccine which is not recommended more than once per lifetime in patients with a spleen is unclear. Although some question about

the significance of infection in adults remains, it is standard practice to vaccinate all splenectomized patients against pneumococcus — despite their age and the time period since splenectomy. In some major medical centers, splenectomy cases over the last 20 years have been tracked down to be sure that they have received the vaccine since surgery. The primary value of the vaccine seems to be in preventing certain pneumococcal infections from occurring. It has not been shown valuable in preventing the overwhelming type of sepsis once a significant infection has begun.

### Looking to the future

Another very important consideration in splenectomized patients is the value of the patient knowing that he or she is susceptible to infections and must be more alert to the early signs of infection than the normal person. With early diagnosis and potentially early therapy, the incidence of sepsis and mortality from it should be lessened. It is a frustrating experience, however, to care for a patient with a fulminant onset who does not respond to even the most aggressive therapy. Perhaps people without a spleen should be given antibiotics to keep with them and take at the first sign of any infection.

Future considerations and areas of interest include the possibility of replacing or adding factors which may improve host immunity aside from the vaccines and antibiotics. Among the considerations are *Lavamisole*, an investigational drug which is an immune stimulator and at least in animals has been shown to be valuable in preventing pulminant sepsis (6). The usefulness of intravenous immune globulin is unclear but it offers some theoretical benefit if given early in

the treatment of sepsis. Tuftsin and other opsonic factors have not been tried in attempts to replace normal immunity but this may be possible in the future.



### References

1. Baumgartner, J.D., Glauser, M.D., et. al. Severe cytomegalovirus infection in multiple transfused, splenectomized, trauma patients. *Lancet* July 10:63-65, 1982.
2. Coker, D.D., Morris D.M., et. al. Infection among 210 patients with surgically staged Hodgkin's Disease. *Amer. J. Med.* 75:97-109, 1983.
3. Cooper, M.J., Williamson, R.C.N. Splenectomy: indications, hazards and alternatives. *Br. Jnl. Surgery* 71:173-180, 1984.
4. Cooney, D.R., Dearth, J.C. Swanson, S.E., et. al. Relative merits of partial splenectomy, splenic reimplantation, and immunization in preventing post-splenectomy infection. *Surgery* 86:561-569, 1979.
5. Dajee, H., Buhr, A.J., et. al. Prevention of death of post-splenectomy sepsis with lavamisole and penicillin. *Current Surgery* 39(3): 167-170, 1982.
6. Ellison, E.C., Fabri, P.J. Complications of splenectomy. *Surgical Clinics of North America* 63:1313-29, 1983.
7. Fefer, A. Enlargement of lymph nodes and spleen in *Principles of Internal Medicine* (10th edition). Petersdorf, R.G., et. al. (ed.) Ch 56, pp 300-304. McGraw-Hill, New York, 1983.
8. King, D.H., Bullock, R.D. The importance of the spleen in resistance to infection. *Annals of Surgery* 70:513, 1919.
9. Livingston, C.D., Levine, B.A., Sivinek, K.R. Site of splenic autotransplantation affects protection from sepsis. *Am. J. Surgery* 146:734-36, 1983.
10. Morris, D.H., Bullock, R.D. The importance of the spleen in resistance to infection. *Annals of Surgery* 70:513, 1919.
11. Robbins, S.L. Lymph nodes and spleen in *Pathology* (3rd edition). Ch 18, pp 683-698. W.B. Saunders Co., Philadelphia 1967.
12. Zarrabi, M.H., Rasner, F. Serious infections in adults following splenectomy for trauma. *Arch. Intern. Med.* 144:1421-24, 1984.