ANNALS OF SURGERY
Vol. 219, No. 3, 225–235

Autologous Splenic Transplantation for Splenic Trauma

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Objective

The authors reviewed the experimental evidence, surgical technique, complications, and results of clinical trials evaluating the role of autologous splenic transplantation for splenic trauma.

Summary Background Data

Splenorrhaphy and nonoperative management of splenic injuries have now become routine aspects in the management of splenic trauma. Unfortunately, not all splenic injuries are readily amenable to conventional spleen-conserving approaches. Heterotopic splenic autotransplantation has been advocated for patients with severe grade IV and V injuries that would otherwise mandate splenectomy. For this subset of patients, splenic salvage by autotransplantation would theoretically preserve the critical role the spleen plays in the host's defense against infection.

Methods

The relevant literature relating to experimental or clinical aspects of splenic autotransplantation was identified and reviewed. Data are presented on the experimental evaluation of autogenous splenic transplantation, methods and complications of autotransplantation, choice of anatomic site and autograft size, and results of clinical trials in humans.

Results

The most commonly used technique of autotransplantation in humans involves implanting tissue homogenates or sections of splenic parenchyma into pouches created in the gastrocolic omentum. Most authors have observed evidence of splenic function with normalization of postsplenectomy thrombocytosis, immunoglobulin M levels, and peripheral blood smears. Some degree of immune function of transplanted grafts has been demonstrated with *in vivo* assays, but the full extent of immunoprotection provided by human splenic autotransplants is currently unknown.

Conclusions

Multiple human and animal studies have established that splenic autotransplantation is a relatively safe and easily performed procedure that results in the return of some hematologic and immunologic parameters to baseline levels. Some aspects of reticuloendothelial function are also preserved. Whether this translates into a real reduction in the morbidity or mortality rates from overwhelming bacterial infection is unknown and requires further investigation.

For more than half of this century, splenectomy was the mainstay in the surgical management of splenic trauma. Despite early convincing laboratory evidence to the contrary,[1] the spleen was considered a rather superfluous organ, and splenectomy was believed to be of no long-term consequence to the patient. In the early 1950s, an association between splenectomy and subsequent septic death was noted in infants with hereditary spherocytosis.[2] For nearly two decades, this risk was thought to be confined to children undergoing splenectomy for hematologic disorders.[3] In 1970, however, a detailed analysis by Singer[4] revealed that the risk of postsplenectomy sepsis was actually much more significant than first was appreciated. The risk of sepsis after splenectomy was observed to extend to both adults and children and could occur at any time after splenectomy, regardless of the indication for the splenectomy.

A gradual appreciation of the relationship between splenectomy and postsplenectomy sepsis and the evidence that asplenia is associated with an increased risk of thromboembolic complications[5] has fostered a re-examination of the indications for splenectomy in patients with splenic trauma. The important immunologic role of the spleen was recognized, and early reports established that splenic conservation was possible in some cases of traumatic splenic injury.[6–8] Ultimately, splenorrhaphy and even nonoperative management of splenic injuries have now become routine aspects of the management of splenic trauma.[9] However, many splenic injuries are so extensive that they cannot be managed by spleen-conserving techniques. Heterotopic splenic autotransplantation has been advocated for patients with severe (grade IV and V[10]) injuries that would otherwise mandate splenectomy. Initial clinical and research interest in autogenous splenic transplantation was stimulated in the 1970s when it was observed that there was some residual splenic function in patients with postoperative splenosis after splenectomy for trauma.[11] The salvage of some splenic parenchyma with subsequent regeneration would theoretically preserve the critical role the spleen plays in the host's defense against infection. This review examines the clinical and basic research that has been published to date and establishes a perspective on the methods, choice of anatomic site, results of animal studies, and results of clinical trials completed to date for autogenous splenic transplantation.

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Accepted for publication April 21, 1993.

METHODS AND COMPLICATIONS

Because the majority of patients with simple splenic injuries undergo nonoperative management or splenorrhaphy *in situ,* patients who are candidates for autogenous transplantation have extensive splenic injuries that preclude whole organ transplantation. Table 1 outlines the major methods of splenic autotransplantation used in the human studies published to date. The most common methods involve implanting tissue homogenates or variably sized sections of splenic parenchyma into pouches created in the gastrocolic omentum (Figs. 1 and 2). One group has implanted parenchymal slices into a preperitoneal, subfascial pouch.[12] The autograft should be implanted well away from the liver, and the margins of the graft site should be marked with radiopaque clips to facilitate postoperative splenic scintigraphy. Postoperative studies, including liver–spleen scintigraphy, with normalization of the platelet count and peripheral blood test results confirm the presence of viable splenic tissue.

Relatively few complications have been reported after splenic autotransplantation in humans. Two cases of intestinal obstruction were reported,[13,14] one of which was clearly documented to be a consequence of adhesions to a small perigraft abscess.[13] Focal abscess formation also was described after (1) placement of the splenic homogenate into an omental pouch,[15] (2) implantation of splenic sections into an omental pouch,[16] and (3) extraperitoneal graft placement.[13] Most investigators have not implanted splenic tissue in the presence of coincident bowel injury because the relatively devascularized autograft may serve as a nidus for subsequent infection. Moore et al.,[16] however, had the largest published experience with autotransplantation and do not believe that coincident peritoneal contamination represents a contraindication to graft placement. In their series of 43 splenic autotransplants, fully 23 had associated hollow visceral injuries, and in only 1 of these patients, did a postoperative infectious complication develop (intra-abdominal abscess).

ANATOMIC SITE AND AUTOGRAFT SIZE

Autogenous splenic transplantation has been attempted in a variety of species in both intraperitoneal and extraperitoneal locations (Table 2). In many animal studies, sites were selected to facilitate the investigation of specific aspects of the regenerative process or posttransplant splenic function. Intrarenal implantation, for example, allows for scanning electron microscopic evaluation of the process of vascular regeneration because of the relative paucity of intraparenchymal connective tissue in the kidney.[17,18] These diverse anatomic sites fa-

Table 1. METHODS OF AUTOGENOUS SPLENIC TRANSPLANTATION IN HUMANS

Author	Year	n	Graft Site	Method
Patel et al.[48]	1981	4	Omentum	2 sections of whole spleen 3 mm thick
Velcek et al.[50]	1982	3	Omentum	15–20 sections 15 × 15 × 2 mm
Moore et al.[16]	1984	43	Omentum	5 sections 40 × 40 × 3 mm
Durig et al.[51]	1984	9	Omentum	Splenic homogenate 50–100 g
Nielsen et al.[15]	1984	6	Omentum	Splenic homogenate in 10 cm^3 pouches ⅓ total spleen
Nicholson et al.[52]	1986	6	Omentum	2–3 mm cubes 30–50 g
Traub et al.[12]	1987	7	Preperitoneal subfascial	25–30 g thin sections
Buyukunal et al.[14]	1987	16	Omentum	2–4 sections 30 × 50 × 5 mm
Mizrahi et al.[49]	1989	10	Omentum	3 mm thick sections 50 g

cilitate specific animal research studies but are not generally applicable to human autogenous splenic transplantation. Human transplants have been primarily into omental pouches, with one notable exception (Table 1). The experimental basis for this was outlined in a series of studies that compared different anatomic sites for graft placement to identify an optimal site for both splenic regeneration and the recovery of splenic function. These comparison studies are summarized in Table 3 and demonstrate that, compared with extraperitoneal graft placement, autogenous splenic grafting into the omentum results in better splenic regeneration and subsequent immunologic function. Ostensibly, this would appear to be the result of the rich blood supply of the omentum with its generous supply of inflammatory cells, growth factors, and cytokines,[19] but the precise reasons for superior graft regeneration and function in the omental position are unknown.

No human studies and only a few animal studies have addressed the relationship between the amount of splenic tissue transplanted and the mass of subsequent regenerated spleen. Obviously, there is a limit to which the tissues of the graft bed can adequately nourish avascular transplanted autograft. Beyond this limit, the graft undergoes additional necrosis and, as such, serves as a nidus for infection. Early investigations using a rodent subcutaneous graft model suggested that there was a linear relationship up to 100 mg of autograft between the weight of the transplanted tissue and the mass of splenic tissue recovered at 5 weeks.[20] This study has been criticized, however, because others noted that, using different-aged animals or other graft sites or allowing a longer period for regeneration, could significantly alter this conclusion.[21] These results should not be generalized to other animal models and, certainly, not to human autografts. In a porcine omental graft model, there was no

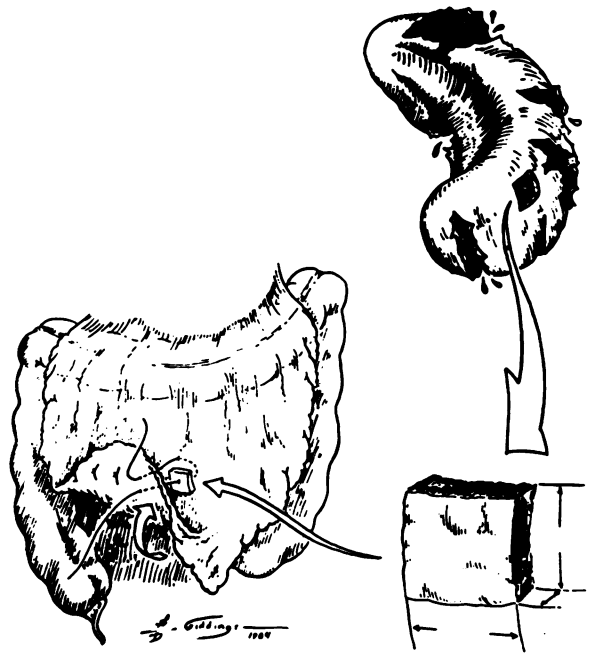

Figure 1. Technique for transplantation of autogenous splenic sections (40 × 40 × 3 mm) into an omental pouch. Used with the permission of Dr. Ernest E. Moore, University of Colorado, Denver, CO.

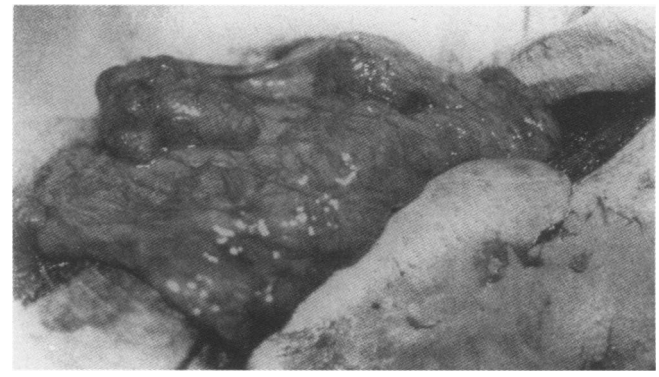

Figure 2. Operative photograph demonstrating three splenic implants within omental envelopes. Used with permission of Dr. Ernest E. Moore.

relationship between the regenerated splenic mass at 6 months and the size of the implants or the total mass of grafted tissue.[22] This study, using a model more analogous to human splenic autotransplantation, does not allow a recommendation to be made in regard to the optimal graft size or total mass. The human studies needed to address this issue would require an accurate indirect method to assess the regenerated splenic mass because "second-look" laparotomy is not ethically acceptable. To date, human studies of splenic autotransplantation have evaluated regenerated splenic mass with radionuclide splenic scintigraphy—a technique that lacks sufficient precision to be helpful in comparative human studies designed to identify an optimal implant size or total mass.

EXPERIMENTAL EVALUATION OF AUTOGENOUS SPLENIC TRANSPLANTATION

A review of autogenous splenic transplantation is incomplete without some discussion of the experimental basis for this technique. This topic, including investigations addressing the phases of splenic regeneration, immunohistologic findings of the regenerated spleen, morphometry of regenerated implants, enhancement of splenic regeneration, and autograft lymphocyte subsets and production, recently was reviewed.[21-24] We present a brief overview that specifically addresses the immunoprotective effect of splenic autotransplantation. There is no debate about the feasibility of splenic autotransplantation. There are multiple animal models (Table 2) and several human studies (Table 1), which when taken together, demonstrate that viable splenic tissue with structure (Fig. 3), immunoarchitecture, and scintiscanning characteristics similar to normal spleen can be recovered after a period of regeneration. However, because the purpose of autotransplantation is to preserve immunocompetence, the central question remains as follows. Are these autografts functional, that is, what degree of immunoprotection is provided to the host?

Table 2. ANATOMIC SITES FOR AUTOGENOUS SPLENIC TRANSPLANTATION

Site	Species/Reference
Intraperitoneal	
Omental pouch	Human[14-16,48-52]
	Dogs[55]
	Pigs[25,56-58]
	Rabbits[59,60]
	Rats[19,37,39,46,61-67]
Between leaves of small bowel mesentery	Rats[31,32,38]
	Mice[44,68]
Transportal intrahepatic	Rats[32,40,41]
Transhepatic intrahepatic	Rats[41]
Free peritoneal ("Splenosis")	Dogs[55]
	Rats[33]
	Mice[44]
Extraperitoneal	
Preperitoneal	Human[12]
Retroperitoneal	Rats[35,45,47]
Intrarenal	Rats[17,18]
Subcutaneous	Dogs[55]
	Rats[19,31,38,67]
	Mice[44,68,69]
Intramuscular	Dogs[55]
	Mice[68]

The experimental design of studies investigating the immunoprotective effects of splenic autotransplants has been of two basic types: bacterial challenge followed by measurement of either (1) microorganism clearance or (2) host mortality rates. However, a direct comparison of these studies is problematic because a variety of animal models, infecting organisms, infecting routes (*e.g.*, intravenous, intraperitoneal, or aerosol inhalation), and inoculum sizes were used. This is further complicated by the use of different-aged animals, heterogeneous transplantation techniques, and a variable time interval from transplant to bacterial challenge, all of which have significant effects on the amount of regenerated splenic tissue present at the time of the inoculation. Table 4 summarizes several immunoprotective studies and emphasizes the heterogeneous nature of these investigations. Although broad conclusions are difficult to draw from these data, several comments are warranted.

The vast majority of experimental studies evaluating the immunoprotective effect of splenic autotransplantation have been done in rodent and murine models for reasons of cost and convenience. However, it has been suggested that the spleen seems to play a more important role in host defense in rodents.[25] Considerably higher relative splenic mass and blood flows have been noted in rodents compared with humans.[26,27] Furthermore, rodents appear to be highly susceptible to pneumococcal infection.[28,29] Thus, the use of rodent models to evaluate immunoprotection against pneumococci may be suboptimal.

Most investigators have evaluated the host's response to intravenous pneumococci. It has been suggested, however, that an experimental design that simulates the pulmonary route of inoculation may be more meaningful because it evaluates immunoprotection during a microbial challenge pathogenetically similar to human pneu-

Table 3. EXPERIMENTAL EVALUATION OF AUTOGENOUS SPLENIC GRAFT SITE

Authors	Model	Graft Sites Investigated	Significant Finding
Herbert et al.[68]	Murine	Omental *vs.* subcutaneous	More extensive regeneration with less fibrosis in the omental graft group
Vega et al.[44]	Murine	Omental *vs.* subcutaneous	Improved reticuloendothelial function (^{99m}Tc labeled isologous RBC scans) in the omental graft group
Schwartz et al.[70]	Rodent	Omental *vs.* subcutaneous	Higher antibody titer following injection of sheep erythrocytes in omental graft group
Thalhamer et al.[67]	Rodent	Omental *vs.* subcutaneous	Development of spleen-like immunoarchitecture in omental group. Functional evaluation revealed B cell defect after LPS stimulation in subcutaneous group but not in omental graft group
Bowman et al.[71]	Rodent	Omental *vs.* subcutaneous	Greater spleen cell counts, numbers of plaque forming cells, hemolysin titre after intravenous injection of sheep erythrocytes in omental graft group
Livingston et al.[38]	Rodent	Between leaves of SB mesentery *vs.* subcutaneous	Intraperitoneal graft provided immunoprotection against an epidemic of murine mycoplasmosis
Livingston et al.[31]	Rodent	Between leaves of SB mesentery *vs.* subcutaneous	Intraperitoneal graft found to have more advanced histologic regeneration with less fibrosis. Reduced mortality following pulmonary challenge with Strep. pneumonia in omental group
Reilman et al.[58]	Porcine	Omental *vs.* subfascial	Significantly more follicles and more advanced histologic regeneration with less fibrosis in omental graft group

RBC = red blood cell; SB = small bowel; ^{99m}Tc = Technetium-99m pertechnetate.

mococcal sepsis. In this context, three studies are widely quoted as demonstrating immunoprotection during aerosol inhalation[30] and intratracheal injection.[31,32] Unfortunately, the sham-operated control groups in these studies had significant mortality rates in excess of 75%, making definitive conclusions difficult. Only Moxon et al.[33] demonstrated improved clearance and mortality rates (splenectomy, 70%; control, 0%; and transplant, 0%) after intranasal challenge with *Haemophilus influenzae.*

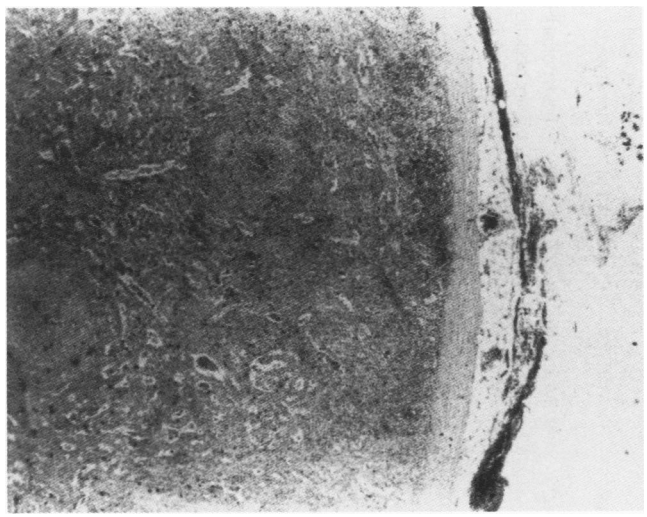

Figure 3. Photomicrograph of a splenic autotransplant demonstrating normal splenic architecture. The capsule is intact, and areas of white pulp are present with a normal sinusoidal pattern. Used with permission of Dr. Ernest E. Moore.

In studies evaluating pneumococcal clearance, only one group demonstrated complete clearance (although clearance kinetics were delayed compared with the control animals).[34] Several investigators observed partial clearance,[26,33,35] which was significantly less than that observed in control animals. Others, however, have observed no effect on microorganism clearance.[25,36] The results of experimental studies using host death as an end point also were equivocal with some studies demonstrating a definite immunoprotective effect of autotransplantation.[37–39] Other studies suggest a partial immunoprotective effect, but high mortality rates (> 75%) in the control group make definitive comparisons difficult.[31,32,39] The majority of investigators, however, observed no immunoprotective effect in rodent,[30,35,40–43] murine,[44] or porcine[25] models.

Several studies investigated the potential benefits of immunization combined with autografting.[45–47] Immunization does appear to augment the pneumococcal clearance, although this may be a consequence of increased hepatic reticuloendothelial clearance rather than improved autograft function.[47] Immunized autografted animals also had a survival advantage when challenged with pneumococci.[45,46] These experimental data provide support for the clinical practice of immunizing patients with pneumococcal vaccine after heterotopic autotransplantation. No other broad conclusions can be drawn from the heterogeneous studies reported to date.

Table 4. EXPERIMENTAL EVALUATION OF THE IMMUNOPROTECTIVE EFFECT OF SPLENIC AUTOTRANSPLANTS

Authors	Study Design	Model	Graft Site	Regeneration Time	Infectious Challenge	Inoculum Size	Results
Brown et al.[36]	Clearance	Guinea pig	Free peritoneal "splenosis"	2 wks–5 mos	Pneumococcus IV	1×10^8	No difference in clearance (TP *vs.* splenectomy)
Horton et al.[26]	Clearance	Rabbit	Retroperitoneal	3 mos	Pneumococcus IV	4×10^6	Improved clearance in TP group (*vs.* splenectomy) but still less than controls
Patel et al.[34]	Clearance	Rabbit	Slices SC Homogenate IP Slices omentum Homogenate omentum	16 wks	Pneumococcus IV	1×10^7	Complete clearance in 3 hrs in omental slice TP (*vs.* 2 hrs in controls); partial clearance with homogenized TPs; no clearance in SC TPs
Schwartz et al.[42]	Mortality	Rodent	Free peritoneal "splenosis"	18 wks	Pneumococcus IV	$4 \times 10^{3-}$ 4×10^8	No difference in mortality (LD_{50}) *vs.* splenectomy
Dickerman et al.[72]	Mortality	Murine	Free peritoneal "splenosis"	8 wks	Pneumococcus Aerosol inhalation	2.5×10^9	Mortality rate: TP (75%), control (85%), splenectomy (100%)
Whiteside and Thomas[30]	Mortality	Rodent	Intraperitoneal Transportal IH	4 wks	Pneumococcus IP	1×10^8	No difference in mortality (LD_{50}) *vs.* splenectomy
Tesluk and Thomas[73]	Mortality	Rodent	Not stated	5 wks	Pneumococcus IV	$5 \times 10^{2-}$ 5×10^8	TP group slight improvement in LD_{50} but not equal to control
Greco and Alvarez[41]	Mortality	Rodent	Transportal IH Transhepatic IH	4 mos	Pneumococcus IV	$1 \times 10^{3-}$ 1×10^7	No difference in mortality *vs.* control or splenectomy
Vega et al.[44]	Mortality	Murine	Free peritoneal "splenosis" Subcutaneous	10 mos	Pneumococcus IP	4 CFU	No difference in mortality; whole organ SC TP had slight decrease in mortality rate
Patel et al.[39]	Mortality	Rodent	Omental pouch	16 wks	Pneumococcus IP	2×10^7	Protective effect; MR: splenectomy (48%), control (0%), TP (11%)
Oakes et al.[40]	Mortality	Rodent	Transportal IH	8–12 mos	Pneumococcus IV	1×10^5	No difference in mortality *vs.* splenectomy or control
Livingston et al.[32]	Mortality	Rodent	SB mesentery Subcutaneous	12 wks	Pneumococcus intratracheal	5×10^7	MR: splenectomy (92%), control (76%), SB mesentery TP (86%), SC TP (96%)
Livingston et al.[31]	Mortality	Rodent	SB mesentery Transportal IH	12 wks	Pneumococcus intratracheal	5×10^7	MR: splenectomy (100%), control (75%), SB mesenteric TP (84%), IH TP (91%); no protective effect with SC TPs

Table 4. EXPERIMENTAL EVALUATION OF THE IMMUNOPROTECTIVE EFFECT OF SPLENIC AUTOTRANSPLANTS

Authors	Study Design	Model	Graft Site	Regeneration Time	Infectious Challenge	Inoculum Size	Results
Livingston et al.[38]	Mortality	Rodent	SB mesentery Subcutaneous	Approximately 10 wks	Murine mycoplasma epidemic	—	MR: splenectomy (45%), control (20%), SB mesentery TP (22%), SC TP (35%); no protective effect with SC TPs
Malagoni et al.[43]	Mortality	Rodent	Omental pouch	9 wks	Pneumococcus IP	1×10^5	MR: splenectomy (92%), control (0%), transplant (88%)
Cooney et al.[35]	Clearance and mortality	Rodent	Retroperitoneal	4–5 wks	Pneumococcus IP	3.3×10^4	Clearance improved in TP group *vs.* splenectomy but not equal to control; MR: splenectomy (95%), control (0%), TP (95%)
Moxon and Schwartz[33]	Clearance and mortality	Rodent	Free peritoneal "splenosis"	3 mos	Hemophilus influenzae intranasal	3×10^8	TP group: improved clearance with delay in development of meningitis, but equal to control; MR: splenectomy (70%), control (0%), TP (0%)
Fasching and Cooney[45]	Clearance and mortality	Rodent	Retroperitoneal	1 yr	Pneumococcus IV	10–20 (non-immunized)	Bacteremia in TP and splenectomy group despite low dose; MR: splenectomy (95%), control (0%), TP (85%)
						1×10^7 (immunized)	All groups responded to immunization; MR: splenectomy (70%), control (0%), TP (30%)
Dawes et al.[46]	Clearance and mortality	Rodent	Omental pouch	11 wks	Pneumococcus IP	1×10^5 (non-immunized)	Some protective effect; MR: splenectomy (96%), control (10%), TP (64%)
						1×10^5 (immunized)	All groups responded to immunization; MR: splenectomy (19%), control (0%), TP (10%)
Steely et al.[37]	Clearance and mortality	Rodent	Omental pouch	16 wks	Pneumococcus IV	4×10^3	Protective effect; MR: splenectomy (63%), control (4%), TP (27%)
Izbicki et al.[25]	Clearance and mortality	Porcine	Omental pouch	16 wks	Pneumococcus IV	1×10^9	No significant differences in clearance or mortality rates

IV = intravenous; IP = intraperitoneal; IH = intrahepatic; TP = splenic transplant; SC = subcutaneous; SB = small bowel; CFU = colony forming unit.

Table 5. ASSESSMENT OF HUMAN SPLENIC AUTOGRAFT FUNCTION

Authors	Year	n	Graft Site	Functional Assessment	Results
Patel et al.[48]	1981	4	Omentum	Platelet count	Returned to normal
				Peripheral blood smear	Loss of Howell-Jolly bodies and target cells
				IgM	Returned to normal
				C3	Returned to normal
				Radionuclide scintiscans	Functional splenic tissue (uptake at 8 wks)
Velcek et al.[50]	1982	3	Omentum	IgM	Returned to normal
				Antipneumococcal antibody*	Normal response (2× or greater)
				Radionuclide scintiscans	Functional splenic tissue (radionuclide uptake)
Moore et al.[16]	1984	43	Omentum	Platelet count	Returned to normal
				IgM	Returned to normal
				Radionuclide scintiscans	Functional splenic tissue (radionuclide uptake)
Durig et al.[51]	1984	9	Omentum	Lymphocyte subsets	50% reduction in T helper/T suppressor cell ratio
				^{99}Tc RBC scintigraphy	Functional splenic tissue (radionuclide uptake at 3, 6, and 12 mos)
Nielsen et al.[15]	1984	6	Omentum	Platelet count	Returned to normal
				Peripheral blood smear	Returned to normal
				IgA, IgG, IgM	Returned to normal
				^{99}Tc RBC scintigraphy	Functional splenic tissue (radionuclide uptake)
Nicholson et al.[52]	1986	6	Omentum	Platelet count	Returned to normal
				Peripheral blood smear	Post splenectomy morphology in 5/6
				^{99}Tc RBC scintigraphy	Functional splenic tissue (radionuclide uptake)
				^{99}Tc-labelled heat damaged autologous RBC scan	Positive scans in 4/6
Traub et al.[12]	1987	7	Preperitoneal subfascial	Platelet count	Persistant thrombocytosis
				Peripheral blood smear	Increased pocked RBCs, but less than asplenic state
				^{99}Tc sulphur colloid scintiscan	Functional splenic tissue (7/7 at 2 yrs)
				^{51}Cr-RBC clearance	Reduced half-time clearance compared to splenectomy but, not equal to control
Buyukunal et al.[14]	1987	16	Omentum	Lymphocyte subsets	No difference *vs.* splenectomy group (n = 10)
				Peripheral blood smear	Fewer Howell-Jolly bodies than splenectomy group
				IgA, IgG, IgM	No difference *vs.* splenectomy group (n = 10)
				Complement C3, C4	Increased C3 *vs.* splenectomy
				Opsonic activity	No difference *vs.* splenectomy group (n = 10)
				Radionuclide scintiscans	Functional splenic tissue (radionuclide uptake)
Mizrahi et al.[49]	1989	10	Omentum	Peripheral blood smear	Loss of Howell-Jolly bodies
				IgM	Howell-Jolly bodies
				^{99}Tc sulphur colloid scintiscan	Functional splenic tissue (10/10 at 10 wks)

* Antibodies to tetradecavalent pneumococcal vaccine.

SPLENIC AUTOTRANSPLANTATION IN HUMANS

There are remarkably few reports documenting clinical experience with autotransplantation in humans. This seems somewhat surprising in view of the well-known risks of asplenia and the relative ease with which otherwise unsalvageable spleens can be autotransplanted. These clinical reports, all published in the 1980s, are outlined in Table 1 and represent data accrued in the treatment of traumatized patients,[14–16,48–51] iatrogenic splenic injuries,[15] and splenectomy for chronic pancreatitis.[52] For the most part, these reports are feasibility studies. They demonstrate that heterotopic splenic autotransplantation can be performed safely, even in the presence of associated hollow visceral injuries with minimal complications (discussed earlier).

The assessment of splenic function after autotransplantation in humans must rely on indirect laboratory and radionuclide scanning techniques. Various techniques have been used, and these are summarized with results in Table 5. Most authors report a gradual reduction of the postsplenectomy thrombocytosis to normal levels with an associated increase in immunoglobulin M levels to normal. Peripheral blood smears generally reveal a gradual loss of many postsplenectomy features, including Howell–Jolly bodies and target cells. Radionuclide scintiscans have universally demonstrated func-

tional splenic tissue with uptake of the radionuclide. It should be stressed, however, that the mere presence of splenic tissue does not necessarily imply normal immune function. The ultimate test of splenic function is a pneumococcal challenge. Although this is not feasible in human studies, it is interesting to note that there are at least 14 case reports of fatal postsplenectomy infection in patients with evidence of residual or regenerated splenic tissue.[24] Most of these patients had accessory spleens or splenosis documented at autopsy, but at least one case of overwhelming postsplenectomy sepsis was reported after omental splenic autotransplantation.[53] This does not refute a possible immunoprotective effect of autotransplantation however. In fact, the high rate of spontaneous splenosis after splenectomy for trauma (approaching 50%[11]) has been postulated to explain the low incidence of postsplenectomy sepsis seen after traumatic splenectomy.

With one exception,[12] all studies were retrospective. Although only 7 patients underwent autotransplants, the study by Traub et al.[12] is noteworthy because 40 patients with splenic lacerations were prospectively studied with splenectomized patients randomized to undergo or not an autotransplantation. Splenosis was identified after surgery (by scintiscanning) in 8 of 19 splenectomized patients who did not undergo autotransplantation. The autotransplanted group (n = 7) was then compared with the splenectomy group (with splenosis, n = 8; without splenosis, n = 11), a splenorrhaphy group (n = 8), and a partial splenectomy group (n = 6). Reticuloendothelial function (as assessed by clearance of anti-Rh antibody-coated ^{51}Cr-radiolabeled autologous erythrocytes) was better preserved after partial splenectomy and splenorrhaphy than after splenic autotransplantation. Autografted patients, however, had significantly better splenic function than did asplenic patients. This suggests that autotransplantation can restore at least partial reticuloendothelial function. Whether this is sufficient to reduce overwhelming postsplenectomy sepsis rates compared with those in asplenic patients is unknown. Others observed that patients with sickle cell disease had a graded risk of major infection commensurate with the degree of splenic function.[54] Thus, by inference, it can be suggested that the small volume of functioning splenic tissue resulting from autotransplantation may provide some degree of immunoprotection. In view of the fact that the extent of possible immunoprotection provided by human splenic autotransplantation is unknown, it is important to emphasize that all patients who have had a splenectomy, irrespective of the method used to preserve the autogenous splenic tissue, should receive immunoprophylaxis (pneumococcal, *Haemophilus influenzae,* and meningococcal vaccines).

SUMMARY AND CONCLUSIONS

The past two decades have witnessed significant progress in the management of patients with splenic injuries. There has been a gradual appreciation of the definite relationship between the asplenic state and the development of postsplenectomy sepsis. The spleen is no longer considered a superfluous organ, and its complex roles in cellular and humoral immunity are slowly being understood. This has fostered a climate of splenic preservation whenever possible, and indeed, many patients with early-grade injuries are now managed by nonoperative means or splenorrhaphy. The ideal management of high-grade (IV and V) splenic injuries, however, is not as clear. The multiple human and animal studies published to date on splenic autotransplantation have established that this is a relatively safe and easily performed procedure that results in the return of some hematologic and immunologic parameters of splenic function to baseline levels. Some aspects of splenic reticuloendothelial function are also preserved. Whether this translates into a real reduction in morbidity or mortality rates from overwhelming bacterial infection is unknown.

It is clear that little is to be gained by the repetition of the same laboratory experiments in a variety of animal models without any change in the underlying hypothesis. Given the frequently fatal outcome of overwhelming postsplenectomy sepsis, not withstanding its infrequent occurrence, a large-scale clinical trial appears warranted to establish or refute definitively a protective effect of autotransplantation. Such a trial could never be accomplished in a single institution. A multicenter cooperative effort will be required to answer this critical question. Because this involves a procedure that all general and trauma surgeons can easily perform, the results of such a study would have broad applicability in the management of patients with complex nonsalvageable splenic injuries.

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