seem to be prerequisites for the maintenance of cell shape and polarity of cell movement in relation to the substratum[31]. Endocytotic vesicles exist, mainly in the cytoplasm luminal part. It is known that the plasminogen activator is associated with vascular endothelium[32] and is released from these cells into the surrounding medium[33]. It is now generally accepted that this is the mechanism by which intravascular fibrin is lysed, so it can be thought that re-endothelialization of venous patch graft may be necessary for lysis of deposited fibrin in the vascular graft wall. Recently[34] endothelial cells have been shown to produce a growth factor in vivo which may play a part in the induction of smooth muscle cell movement and differentiation. Our recent work confirmed such a role of endothelium[2], for the formation of a new endothelium is immediatly followed by the appearance of smooth muscle cells in the venous patch wall.

Present findings do not indicate that the endothelial cells which cover the venous patch after the 2nd postoperative week originate from the smooth muscle cells of the patch, since the thrombus formed on the luminal part of the patch prevents cell migration from the medial layer of the patch wall, although a hematogenous re-endothelialization may occur at the level of the suture line[25]. Our results indicate that secondary endothelial cells originate mainly in the adjacent arterial endothelium. Future studies using radioactive labelling should clarify this postulate.

1 Supported by a grant from Banco Urquijo, Madrid, Spain.

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Action of group A streptococcus extracellular product(s) on the connective tissue of the human heart valve

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Summary. The cultivation of a 'rheumatogenic' strain of group A streptococcus in presence of human heart valve connective tissues leads to the release of substance(s) reacting with antistreptococcal polysaccharide and antihuman glycoprotein antibodies.

We have previously reported[1] that when certain group A streptococcus strains, isolated from rheumatic patients, were grown in the presence of bovine heart valves, the culture supernatants contained substance(s) showing immunological cross reactions with rabbit antisera to both group A streptococcal polysaccharide and a structural glycoprotein isolated from the connective tissue of bovine heart valves. This observation supports the hypothesis that an immunological mechanism may be involved in cardiac lesion pathogenesis in rheumatic fever. However, to uphold this view, it was necessary to show that similar results could be obtained with human heart valves; the present study reports on these complementary experiments.

Material and methods. Materials, methods and techniques were described in detail in a previous publication[1]. Strain A 5205, type 5, was cultivated in phytone-yeast medium, as specified. Human heart valves were obtained during necropsy on patients deceased with no known cardiac disease. Approximately 4 g of valves were dissected free of cardiac muscle, cut into small pieces, sterilized with β-propiolactone[2] and divided equally between 2 diffusion chambers, prepared as described previously[1]. Four 250-ml vials of phytone-yeast medium were prepared and inoculated as shown in the table. The vials were incubated at 37 °C for 62 h. The cultures were centrifuged and the supernatants precipitated by acetone[3]. Human urea-soluble glycoprotein was prepared as previously described by Goldstein et al.[1], using human, instead of bovine, heart valves. Rabbit antisera to group A streptococcal polysaccharide (a/PS) and to human glycoprotein (a/GP)

Setting of the experiment

Vial	Inoculated[a]	Diffusion chamber[b]	Control cultures[c] of the vials	of the chamber contents
CM: control, medium	No	No	Negative	
CV: control, valves	No	Yes	Negative	Negative
CB: control, bacteria	Yes	No	Group A streptococcus	
T: test	Yes	Yes	Group A streptococcus	Negative

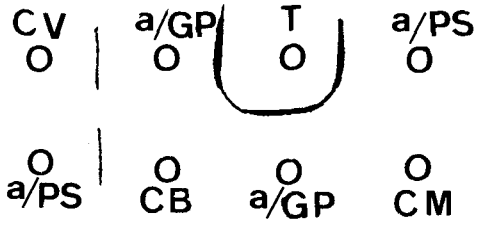
[a] Group A streptococcus, strain A 5205; [b] containing approximately 2 g of human heart valves; [c] on blood agar, after 62 h of incubation of the vials.

were prepared as described[1,3]. Amino acids, amino sugars and sugars in acetone precipitates were identified and estimated as outlined previously.

Results and discussion. The results of immunodiffusion analysis of the acetone precipitates are shown in the figure. No immunoprecipitation was observed with CM precipitates. CB precipitates traced a weak, uneven line with undiluted antipolysaccharide antisera; no line was obtained with 1:2 or 1:4 dilutions of the serum. T precipitates showed strong, forward and constant lines with both antisera, with an identity reaction. These precipitation lines were still present with 1:20 dilutions of the antisera. Results of chromatographic evaluation of amino acids, amino sugars and sugars showed that T extracts, as compared to all other controls, had a marked increase in glucosamine, glycine, proline and hydroxyproline, and a moderate increase in glutamic acid.

These results are in agreement with the preceding observations made on bovine heart valves. The identity reaction of the immunologically active substance(s) is however more complete than with bovine material. The present results do not definitely prove that the immunologically active fraction was extracted from the valve connective tissue, but the results of the chemical determinations favour this hypothesis. CB precipitates showed an increase in cell wall amino acids such as alanine and lysine, which was probably due to spontaneous lysis of some bacteria. In the T precipitate, however, we observed a marked increase in amino acids present only in small amounts in the streptococcal wall and cytoplasm, e.g. glycine, proline, or hydroxyproline[4,5]. On the other hand, these amino acids are components of the connective tissue glycoproteins not extractable by ionic buffers[6] and are found in urea-soluble glycoprotein[3].

These results confirm that the observations previously reported for bovine tissues can provide a basis for hypothesis in human pathology. It is worthy of notice that, although direct immunofluorescence with antistreptococcal antisera was not observed on cardiac tissue sections, it was detected after a prior treatment of the same sections with a proteolytic enzyme[7]. Thus, the unmasking of a 'hidden' tissue determinant by bacterial enzyme(s), leading to an immunological cross-reaction, seems a feasible proposition, specially if one recalls that the original specific lesion of the Aschoff bodies is a peculiar response to a primary injury of the connective tissue[8].



Immunoprecipitation of the acetone-precipitates. CM: control, medium; CB: control, bacteria; CV: control valves; T: test (see table); a/PS: anti-streptococcal polysaccharide anti-serum; a/GP: anti-human glycoprotein anti-serum. Immunodiffusion gel: 1% agarose in 0.17 M NaCl, buffered at pH 6.0 with 0.01 M phosphate buffer 0.01% cadmium acetate.

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Allogeneic effect on induction of thyroglobulin antibodies and thyroid lesions in mice[1]

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Summary. All previous attempts failed to induce thyroglobulin antibodies or thyroid infiltrates in mice immunized with homologous thyroglobulin without adjuvants. However, an allogeneic effect obviated the need of adjuvants for triggering thyroglobulin-reactive lymphocytes to produce thyroglobulin antibodies or thyroid lesions.

Immunization of mice with homologous thyroglobulin emulsified in Freund's complete adjuvant usually induces autoimmune thyroiditis characterized by circulating thyroglobulin antibodies and infiltration of the thyroid gland predominantly with mononuclear cells. This experimental model of autoimmune disease is particularly interesting because the cellular events of the immune response are better established in the mouse and genetic influence on