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Reply to the Editor:

Annescis, mi fili, quantilla sapientia mundus regatur?

[Do you not know, my son, how little wisdom rules the world?]

We thank Dr Gabbay for his letter to the editor regarding our recent article, "Deleterious Outcome of No-React-Treated Stentless Valved Conduits after Aortic Root Replacement: Why Were Warnings Ignored?"¹ We understand that Dr Gabbay is under considerable pressure because he is not only chief scientific officer of Shelhigh Inc (Union, NJ) but also founder and therefore directly dependent on the economic well-being of the company. We believe it is human nature that Dr Gabbay is biased in his perception of the events surrounding the aortic conduit NR-2000C (Shelhigh Inc) and other products. We, as representatives of a medical institution, have no interest in accusing Dr Gabbay, but we merely worry about the outcome observed in some of our patients after having used products from Shelhigh Inc.

In our department within the Academic Center for Cardiac Surgery Berne-Basel (~1800 cardiac cases

per year), surgery of the thoracic aorta accounts for approximately 15% of the overall surgical volume. This is due to the high prevalence of aortic aneurysms in the region and a high rate of referrals. We perform approximately 200 to 220 thoracic aortic procedures per year. We most recently published our results after surgery on the thoracic aorta, and these are consistent with contemporary literature.²⁻⁴ All patients described in our article¹ were operated on by 3 senior staff surgeons (T.C., F.E., J.S.), each of whom has approximately 20 years experience in the field. None of them were ever faced with a pathology like the one observed with the NR-2000C aortic tube valved conduit.

As Dr Gabbay pointed out, a significant percentage of these patients were high risk: A few of them underwent repeat surgery because of endocarditis. We hesitated a long time to attribute these catastrophic findings to the Shelhigh device, but as the picture became more consistent, we were able to rule out other causes of failure, including surgical technique. Our suspicion that something was wrong with the device was emphasized by similar observations with other Shelhigh products (eg, the bovine internal thoracic artery used as peripheral bypass conduit or exceptionally as coronary bypass conduit).

We are concerned about the fact that Dr Gabbay refuses to acknowledge findings as demonstrated in our article.¹ We had several meetings with Dr Gabbay but it was never possible to bring our concerns to the point.

The fact that Dr Gabbay talks about salmonella and tomatoes when we report on patients who may unexpectedly die during follow-up or on the operating table supports our decision to not further discuss these matters with the company itself. We send all explanted material to our in-house certified pathology and microbiology department. Although we had severe concerns with the management of the company after several visits in Union, New Jersey, we were terrified after

reading the Food and Drug Administration (FDA) document: "Your firm's [Shelhigh] Medical Device Reporting Procedure (Document No. 020047) is deficient in that: (1) The procedure lacks a standardized review process for determining when an event meets the criteria for submitting an MDR report. (2) There are no procedures for documentation and record-keeping requirements to determine if information was evaluated to determine if an event was reportable and that all events and subsequent information are submitted within appropriate timeframes."⁵

Unlike Dr Gabbay, we were shocked to learn about additional, repeated warning letters issued by the FDA (April 26, 2000, December 14, 2005), because we were not informed by the company about ongoing problems and at the time they were brought to our attention, we had already implanted the NR-2000C in more than 100 patients. We assume that the majority of the readers of the *Journal* would be as worried as we are to learn about such a critical situation. Citation of the FDA: "The environmental controls and processes used to manufacture and test devices within your facility can compromise the sterility and safety of these products, and there is therefore a reasonable probability that use of such products will cause serious adverse health consequences or death."⁶

We can assure Dr Gabbay and the readership of the *Journal* that these patients receive the closest and most optimal follow-up possible. However, we are unable within this short letter to provide detailed in-hospital data and follow-up on these patients with more than 1500 single items per patient, including repeated imaging and extensive laboratory work. Dr Gabbay insists that the issue is site specific, and indeed that was one of the reasons we hesitated to issue a formal complaint. We do think at this point that the circumstances of a high aortic caseload together with an unusual follow-up of almost 100% may have helped to

recognize this specific problem. We are deeply worried that we are not the only ones to observe this sad experience: A case reported in Germany led to an unusual procedure and finally resulted in a transplant.^{7,8} Another similar observation was made in the United States after implantation of the device and led to correspondence with us: "I read with great interest your report of 7 patients with bad outcomes after placement of the Shelhigh stentless valve-conduit. We have had recent experience with a man who experienced valve failure 3 years after placement of one Shelhigh conduit. A false aneurysm and extensive inflammation were found at surgery (the surgeon said he thought there may be an abscess), and the entire prosthesis had to be removed and replaced with a homograft. Cultures for bacteria only were negative. The patient did well postoperatively and was discharged on day 17 postoperatively. Our pathologists also analyzed the tissue and found extensive acute and chronic inflammation. On special staining, the wall of the conduit was infiltrated with numerous acid fast bacteria. Unfortunately, we did not culture for acid fast organisms so we were not able to identify what it is." (P. O'Keefe, Loyola University Medical Center, personal communication).

We urge Dr Gabbay not to fight against reports regarding the NR-2000C but to encourage him to shed light on those cases and to recognize that we had made several attempts to warn him not only about the aortic valved conduit but also about several other devices that we found to give unsatisfactory results (e.g. the pulmonary conduit and the bovine IMA).

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SHELHIGH BIOPROSTHESIS IN ACTIVE INFECTIVE ENDOCARDITIS

To the Editor:

A recent article by Carrel and colleagues¹ deals with the deleterious outcome of patients who received No-React (Shelhigh, Inc, Union, NJ)-treated stentless valved conduits. Seven (6.1%) of 115 patients presented with sudden disastrous findings at the level of the aortic root, and 4 of them underwent emergency operations because of disintegration of the graft along with rupture of the aortic root. The authors reported that

retrospectively the main findings were persistent fever or subfebrility over months. They conclude that the use of the Shelhigh aortic stentless prosthesis can no longer be advocated. Is it possible that the authors have overlooked the patients' clinical condition of persisting postoperative fever, which can lead to the severe prosthetic endocarditis described in their article?

We previously reported very good clinical results from our center using the above products, especially in patients with severe active infective endocarditis. The device was tested with satisfactory results, and preliminary follow-up data were published in 2003 and 2005.^{2,3} Recent publications in 2006 and 2008 have shown satisfactory early and midterm results with a low reinfection rate in patients with native or prosthetic endocarditis complicated by paravalvular abscess, and the hemodynamic function of the implants in the aortic position was comparable with that of homografts.^{4,5} These articles have perhaps been overlooked by Carrel and colleagues.

From February 2000 until July 2008, 319 Shelhigh No-React-treated stentless valves have been implanted in 305 patients in our institution. Of these, 17 (5.5%) patients required reoperations because of reinfection. The 30-day and 1-, 3-, and 5-year rates for freedom from reoperation caused by reinfection were 100%, 94.4% $\pm$ 1.8%, 87.0% $\pm$ 3.2%, and 83.8% $\pm$ 4.4%, respectively.⁴

Analysis of reoperation because of valve-related complications showed 12 patients who underwent reoperations because of paravalvular leakage, which is mainly related to endocarditis. The freedom from reoperation because of valve-related complications is shown in Figure 1: the 30-day and 1- and 5-year freedom from reoperation rates were 98.9% $\pm$ 0.7%, 97.9% $\pm$ 8.4%, and 92.3% $\pm$ 2.3%, respectively.

Thus, in our series, there was no patient who required reoperation, as