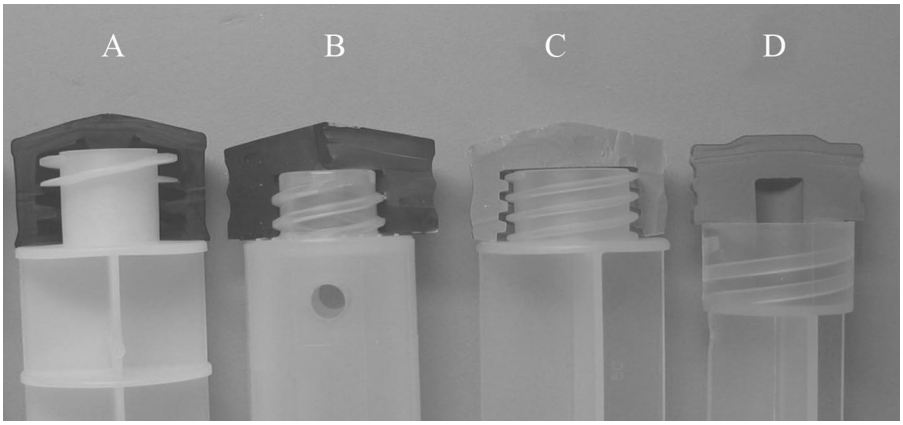

Fig. 2. The design of the plunger/piston assemblies in four prefilled syringes. The plunger head fits into the rubber piston that is sagittally sectioned. (*A*) Prefilled Inovan 0.3% injection syringe (Terumo Corp., Tokyo, Japan). (*B*) Iopamiron Injection 300 syringe (Bayer Healthcare, Bayer Schering Pharma, Osaka, Japan). (*C*) Nitrol injection for continuous infusion 25-mg syringe (Nipro Pharma Corporation, Osaka, Japan). (*D*) 1% Diprivan injection kit (AstraZeneca United Kingdom, Alderley Park, United Kingdom).

In the case of the 1% Diprivan injection kit (propofol; manufactured by AstraZeneca United Kingdom, Alderley Park, United Kingdom, imported and marketed by AstraZeneca K.K. Pharmaceuticals, Osaka, Japan), the piston has the thickest rubber wall among the four products and contortion hardly occurs, and the male screw threads of the piston engage with the female screw threads molded on the top portion of the plunger (fig. 2). A piston with a thick rubber wall is less likely to contort during use. However, the engineers of Kyowa Hakko Kirin and Terumo indicate that the thick wall may affect internal syringe compliance, influence the force needed to operate the plunger *via* a syringe pump, and may be associated with irregular drug delivery.[4]

We recommended that manufacturers provide a preassembled prefilled syringe with an integrated plunger/piston unit. However, the engineers indicated the following drawbacks of a preassembled prefilled syringe with an integrated plunger/piston: 1) Pressure may be exerted on the plunger during a fall or transportation of the syringe; 2) when the top film is peeled only partially during removal of the syringe, the finger grip may be caught by the film, resulting in tilting of the plunger with respect to the axial line of the barrel, which may cause plunger/piston misassembly; 3) the length of the whole unit becomes longer, posing problems in storage, transportation, and handling; 4) the manufacturers should apply to the Ministry of Health, Labor, and Welfare for changing a part of the original design, and approval will take more than 1 yr; and 5) the syringe pump structure may have to be modified to accommodate the newly arranged syringes. Based on these issues, Kyowa Hakko Kirin and Terumo are issuing appropriate warnings that the operator should not push the plunger into the rubber piston but should instead turn the plunger to engage the screw threads during assembly. They are also planning to modify the fundamental configuration of the plunger/piston assembly. We strongly recommend that the International Organization for Standardization, marketing companies, and manufacturers work together to supply prefilled syringes, particularly syringes with an integrated plunger/piston, that are safe and carefully designed to prevent plunger/piston misassembly by the operator.

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In Reply:

AstraZeneca would like to comment on the correspondence from Dr. Amagasa.

As pointed out in the article, the cause of the original failure is effectively down to poor assembly of the Prefilled INOVAN syringe. A key way to avoid this issue is for the users to always refer to the assembly instructions provided by the manufacturer. AstraZeneca provides clear and easy to follow assembly instructions on the 1% Diprivan Prefilled syringe exterior carton and interior tear-off lid on assembling the plunger rod to the rubber piston before use.

AstraZeneca also points out that the design of the thick wall impacting on the operation of the 1% Diprivan Prefilled

syringe is not a real concern. This is because the stopper/glass contact area, similar to any syringe design, is in the form of ribs, which will allow for a small size variation within the design tolerances. On top of this, the siliconization of our components lubricates the device in use, ensuring correct drug delivery.

The correspondence not only discusses the benefit of redesigning the plunger and stoppers on similar prefilled syringe products to what would effectively be a single piece but also comments that this might create a different suite of issues. AstraZeneca would agree with this latter point and comment that such a redesign would significantly reduce the viability of marketing such prefilled syringes, with the loss of the advantages in drug delivery these devices add to medical practice.

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Preoperative Electrocardiograms

To the Editor:

We read with interest the recent article by Correll *et al.*[1] about the use of preoperative electrocardiograms. The authors identified five clinical variables that constitute an independent risk factor for the presence of major electrocardiogram alterations. These variables could refine the criterion for preoperative electrocardiograms ordering.

We also believe that in patients with a family history of premature sudden death (< 35 yr of age at death), preoperative electrocardiogram should be considered. In fact, there is a familial cardiomyopathy, known as arrhythmogenic right ventricular dysplasia or cardiomyopathy, which is the major cause of sudden death in the young and athletes. Although arrhythmogenic right ventricular dysplasia or cardiomyopathy is quite a rare heart disease, it seems that it is also one of the main causes of sudden unexpected perioperative death.[2] In one series, among 50 forensic autopsies performed after perioperative death, arrhythmogenic right ventricular dysplasia or cardiomyopathy was detected in 18 patients.[3] All these patients were young (< 65 yr), with no previous cardiac history and underwent relative low-risk surgery. At least 50% of patients with arrhythmogenic right ventricular dysplasia or cardiomyopathy have an abnormal electrocardiograph at presentation, but within 6 yr of diagnosis, virtually all patients will have one or more of the following findings during sinus rhythm[4]: complete or incomplete right bundle branch block, QRS prolongation in the absence of right bundle branch block, epsilon wave in leads V1–V2, T-wave inversion in leads V1–V3, and delayed (*i.e.*, ≥ 55 ms) S-wave upstroke in leads V1–V3.

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The above letter was sent to the authors of the referenced report. The authors did not feel a response was required.—James C. Eisenach, Editor-in-Chief