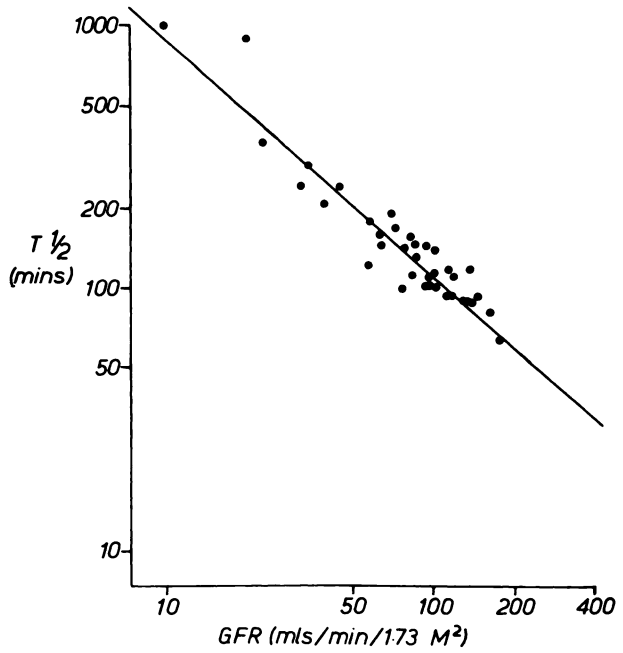

FIG. 1. Log-log plot of ^{51}Cr-EDTA biological half-life in minutes as a function of GFR/1.73 m^2.

relationship between these two parameters using a log-log plot. A high degree of correlation was obtained ($r = 0.945$).

We wish to suggest the use of the biological half-life of ^{51}Cr-EDTA, or of similar filterable substances, as an alternative to glomerular filtration rate for assessing renal function on two grounds: (A) this measurement is entirely independent of body size and thus no corrections are required on this accord; (B) the rapid increase in biological half-life at low glomerular filtration rates highlights important, albeit small, changes in GFR in subjects with poor renal function.

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CHEMICAL STATE OF TECHNETIUM

In a recent article, "Chemical state of ^{99m}Tc in biomedical products" (*J Nucl Med* 12: 596, 1971) the authors, Eckelman, Meinken, and Richards, conclude that "the technetium is probably reduced and chelated as a cationic species". They further conclude that "solutions of ^{99m}Tc compounds should be prepared oxygen free." Neither of these conclusions are supported by the experimental data presented in the paper. No evidence was presented to indicate a cationic species of technetium. The alleged primary supporting evidence of a reduced form of technetium was adsorption of a portion of the ^{99m}Tc activity from a ^{99m}Tc-Fe-citrate complex to Sephadex G-25. The authors did not perform a chemical analysis of the total Fe-citrate complex eluted from the column and compare it with the initial amount added to the column. Therefore it is possible that the column-bound ^{99m}Tc activity was bound to Sephadex as a complex and not as reduced technetium. Conrad and Schade have reported retention of iron-ascorbate complexes, pH 7.5, on Sephadex G-25 and reported increasing amounts of ferrous iron precipitated from ascorbate solutions between pH 6 and 9 (*Gastroenterology* 55: 35–45, 1968). It is conceivable that some of the bound complex or the precipitated iron retained by the column would also retain some ^{99m}Tc and account for the noneluted portion reported by Eckelman, et al. The fact that technetium becomes bound to Sephadex does not necessarily prove a reduced form. One might also question why, if a metal ion species is not necessary for efficient tagging as suggested by the authors, yields higher than 55% of tagged product were not achieved when the HCl/HI reducing agent was used alone (see Table 4). Yields in excess of 90% are achieved using metal ions under reducing conditions. It is apparent from the information in Table 4 that a reduced form of technetium alone does not produce high-yield complexing. Perhaps the authors have some unpublished information to support their statement that "This method of technetium incorporation argues against a metal pertechnetate complex."

The conclusion regarding the preparation of a product in the absence of oxygen is not justified by the data in Table 3. There is very little difference in either set of experiments. In some cases the products appear to get better with storage both in air

and under nitrogen. One might question the precision of the testing technique.

In my opinion, the question of the chemical state of ^{99m}Tc in biomedical products remains unanswered and Benjamin's reduced pertechnetate-metal ion complex theory (*Int J Appl Radiat* 20: 187–194, 1969 and *J Nucl Med* 11: 147–154, 1970) might be correct.

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THE AUTHORS' REPLY

We wish to thank Dr. Hupf for taking the time to review our recent publication in detail. For determining the chemical state of a carrier-free substance physical measurements such as resonance and spectroscopy are difficult to carry out because of problems with impurities and sensitivity at the carrier-free level. We therefore felt that using collected chemical data might more easily suggest the chemical state of ^{99m}Tc; however, since this involves inferences from all the data, no single experiment would offer sufficient proof. Perhaps we did not emphasize this point enough. We wish to summarize here the collected chemical data which led to our conclusion that ^{99m}Tc is reduced in biomedical products and to answer Dr. Hupf's questions within this framework:

1. The electrolysis experiments: We believe that the data from the experiments described in the paper show that the dialysis tubing prohibits incorporation of technetium in chelates prepared from the cathode solution, and that this is not consistent with a zirconium pertechnetate complex since the cathode solution contained zirconium. In an unreported experiment, we could not chelate technetium by mixing pertechnetate with a strongly acidic solution of zirconyl chloride followed by chelate addition and pH adjustment to 7.

2. The gel chromatography data: Gel chromatography data indicate that a form of technetium is adsorbed to the Sephadex column. The key here is that both metallic and nonmetallic reducing agents can be used to prepare this form. This rules out coprecipitation of pertechnetate with a metal oxide. The data in Table 4 of our paper indicate that technetium can also be incorporated into chelates in the absence of metal. The chelate yield, as Dr. Hupf points out, is much lower than for metallic reducing agents, but the yield should be 0% if a metal is required. A subsequent paper (*1*) from this laboratory gives a likely explanation for the quantitative difference in yields, namely that the ability of different reducing agents to produce different oxidation states of technetium influences the chelate yield. Ferrous and stannous ion seem to produce high yields of the IV oxidation state, whereas the HCl-HI system produces lower but still significant yields of the IV state and consequently lower yields of the chelate. In addition, the molar amount of chelating agent was not maximal in this case.

The point made by Dr. Hupf concerning the work of Conrad and Schade is well taken, and it was one of the reasons we thought that the use of nonmetallic reducing agents would provide more definitive data by eliminating the possibility of coprecipitation. The systems used by Conrad and Schade are not completely analogous to ours: they use equimolar amounts of iron and ascorbic acid whereas we use large excesses of ascorbic acid and much smaller amounts of iron. Even with their unfavorable conditions the ferrous ascorbate system at pH 6.5 would yield 95% soluble iron according to Fig. 4 of their paper. Beyond that, comparison is difficult because of sparse experimental description. The ^{14}C ascorbic acid data published for a system comparable to ours (*2*) indicated little strong adsorption of ascorbic acid. Finally, hydrogen peroxide removes the adsorbed technetium from the column as pertechnetate, and it is difficult to see how peroxide would release pertechnetate from either a precipitated oxide or an adsorbed complex. Air also converts the adsorbed technetium to pertechnetate but at a much slower rate. We agree with Dr. Hupf that the chelate yield does not seem to be affected by air, but it does seem clear from the citrate data in Table 3 of our paper that the adsorbed species is not stable to air for the reasons given in the last paragraph on page 599.

3. The Redox potential data: The experiments in Table 2 of our paper involving the chelating agents DTPA and o-phenanthroline are identical except for the change in reduction potential of the iron. If a pertechnetate complex is being formed it should be formed in both cases because ferrous ion and pertechnetate concentrations and conditions are identical. However, if reduction is necessary, the iron-DTPA potential is sufficiently strong to reduce the technetium, but the iron o-phenanthroline potential is not. As the results show, only the DTPA system yields technetium-chelate. A control experiment in Table 4 of our paper shows that o-phenanthroline can form a chelate with technetium if a strong reducing agent is present.

We conclude from these three types of experiments that technetium is not present as pertechnetate. If the technetium is not bound to zirconium, it