Hamilton G, Canadian Association of Radiologists Journal, 1994; 45: 331

Controversy over ionic and nonionic radiopaque contrast media

Adverse reactions to ionic and nonionic radiographic contrast media are a subject of concern. However, unsuspected sources of such reactions may have led to bias in comparisons between ionic and nonionic media.

Disposable syringes with rubber plunger seals started being used to replace glass syringes in the 1950s. 2-mercaptobenzothiazole (MBT), used in rubber manufacturing, (Ref. 1) is a known IgE-mediated skin allergen, and asthma may be caused by inhalation of MBT-contaminated dusting powder.[1] MBT from seals for syringes and contrast agent ampoules has been linked to reactions that occurred when ionic urographic contrast media were being injected (Ref. 1, 3). 2-(2-Hydroxyethylmercapto)benzothiazole, formed during gas sterilization of MBT, can be metabolized into carboxymethyl-mercaptobenzothiazole, more than half of which becomes protein-bound (Ref. 4), forming a hapten-protein complex, a feature of allergenicity.

Allergy to latex has been implicated in contact dermatitis, asthma and anaphylaxis (Ref. 5). Rubber particles have been found in injectable fluids in contact with pharmaceutical rubber (Ref. 6). Rubber-related anaphylactic reactions to barium enema have raised the possibility of reactions to MBT, sulfites and latex (Ref. 3).

From 1976 to 1981, deaths of cells in cultures maintained around the world were linked to disposable plastic syringes (Ref. 7,8). In 1981, these cell deaths were specifically linked to MBT compounds (Ref. 9). In the same year, MBT leached from syringe rubber was determined to be a "common contaminant" in North America (Ref. 10). A Japanese manufacturer implicated in the Australian study (Ref. 9) announced that, beginning inn July 1981, the plunger seals for its syringes would be free of MBT and suggested that other manufacturers would follow its example (Ref. 11).

The ampoules for nonionic radiopaque contrast agents use MBT-free seals, and in Japan nonionic agents have been injected with MBT-free seal since 1982. In a Japanese series of 337,647 cases studied from 1986 to 1988 (Ref. 12)(when MBT-free syringes were used) no deaths could be attributed to either ionic or nonionic agents (the series included roughly equal numbers of each type). Given these results, can the findings of other series be valid, if they compare reactions to ionic and nonionic agents without considering the possible impact of rubber contaminants?

Since 1971, I have performed intravenous pyelography more than 10,000 times, injecting 40 to 50 mL of contrast each time (Ref. 13***). Nonionic agents cost 7 times more than ionic agents and are almost free from minor side effects, but because of the cost factor, I would use ionic agents almost exclusively. I do not do***

so because of the medicolegal opinion, according to the Canadian Medical Protective Association, that the nonionic agents are safer. With this information, is this opinion really warranted?

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References

1) Hamilton G, "Controversy over ionic and nonionic radiopaque contrast media," Canadian Association of Radi- ologists Journal, 1994, Volume 4, 331.
2) Fisher AA: Management of dermatitis due to surgical gloves. J. Dermatol Surg Oncol 1985; 11:628=631
3) Hamilton G, Medical rubber anaphylaxis. Lancet 1990; 336: 1453-1454
4) J.Meek JH, Pettit BR, "Avoidable accumulation of potentially toxic levels of benzothiazoles in babies receiving intravenous therapy," Lancet, 1985, Volume 2, 1090–1092.
5) SpanerD, Dolovich J et al, Hypersensitivity to natural latex. J Allergy Clin Immunol 1989; 83: 1135-1137
6) Blais P, The impact of of medical devices on quality of pharmaceuticals. In: Warbick-Cercone A, Johson LG (editors): Quality Assurance of Pharmaceuticals manufactured in the Hospitals.Pergammonon, New York 1985: 83-93
7) Garver KL, Marchese SL, Boas EG, Amniotic cell failure: possible role of syringes. (Letter) New Engl J Med 1976; 295: 286
8) Purvis-Smith SG, Jones MA, et al, Amniotic cell-culture failure and syringe toxicity. (Letter) Lancet 1978; 1: 993
9) Graham DT, Pomeroy AR, Chemical leaching from Terumo seals. (Letter) Aust NZ J Med 1982; 12: 305-306
10) Reepmeyer JJ, Juhl YH, "Contamination of injectable solutions with 2-mercaptobenzothiazole leached from rubber closures," The Journal of Pharmaceutical Sciences, 1983, Volume 72, 1302–1305
11) Terumo (Australia) Pty Ltg: Leaching of a contaminant into the contents of disposable syringes. (Letter) Aust NZ J Med 1981; 11:435
12) Katayama H, Yamaguchi K, Takashima T, Reactions to ionic and nonionic contrast media. Radiology 1990; 175: 621-628
13) Hamilton G, The vascular nephrogram phase of excretory urography and its implications. Radiology 1973; 102: 37-40