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The Retention by the Body of ^{131}I-Polyvinylpyrrolidone and its Effect on Radiation Dose

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Polyvinylpyrrolidone (PVP) labeled with iodine 131 was introduced by Gordon (1) as an agent for studying gastrointestinal protein loss (2). More recently it has been added to the long list of radioactive compounds used for brain scanning, Tauxe *et al* (3), Pitlyk *et al* (4,5). In this connection it has an advantage over radioiodinated human serum albumin in being cleared relatively rapidly from plasma. Forty-eight hours after injection there is no appreciable interference from blood radioactivity, so that enhanced contrast is obtained from concentrations in tumour tissue. This advantage also pertains to another compound used extensively for brain scanning—'Neohydrin' (3-chloromercuri-2-methoxypropyl urea) labeled with ^{203}Hg. It has been pointed out by Greenlaw and Quaiffe (6), Blau and Bender (7), and Spencer (8) that the use of the latter compound results in a dose to the kidneys of 12-50 rads, and this is thought by Spencer to be unjustifiably high. Tauxe and his colleagues claim that the use of PVP-^{131}I avoids radiation doses of this magnitude, owing to its short biological half-life. In this paper, evidence is presented that demonstrates that the biological half-life is not a sufficient criterion for the assessment of radiation dose, and that use of this criterion may grossly underestimate the dose received by the patient.

MATERIALS

The PVP-^{131}I was supplied by the Radiochemical Centre, Amersham, Buckinghamshire, England, and had a nominal molecular weight range of 30-40,000. However, studies to be reported subsequently suggest that a considerable fraction of the material was of a higher molecular weight.

SUBJECTS

The full range of measurements was carried out on only one subject, a normal adult male (subject 1). Studies of limited duration, primarily performed for diagnostic purposes, were made on six patients, who were subsequently shown to be free from disorders which might affect the fate of intravenously administered PVP-^{131}I. In all cases, thyroidal uptake of any free iodide ^{131}I was blocked

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by administration of potassium iodide before injection and for a period after. The ampoule supplied by the Radiochemical Centre contained a sachet of ion exchange resin to absorb any iodide released by decomposition during autoclaving or storage.

MEASUREMENTS

Plasma, urine and faeces were collected for varying periods after intravenous administration of PVP- ^{131}I. Aliquots of plasma and urine were assayed by well scintillation counting. Stool radioactivity was determined by placing the carton in front of a collimated 3-inch crystal scintillation counter in such a geometry that results were relatively independent of distribution of radioactivity.

Whole body counting was performed with a single crystal, either 3 × 3 inch or 5 × 3½ inch with some local shielding. The subject sat in a reclining chair, with the crystal approximately 30 cm from the sternum. This geometry gives high sensitivity, but leads to errors due to redistribution of radioisotope within the body. Consequently, body retention was assessed from the cumulative excretion for the first two days, after which the distribution was virtually constant.

Sites of concentration of radioactivity were surveyed by surface counting with a 2-inch crystal in a simple shield.

RESULTS

Total Retention

The retention of radioactivity in subject 1, derived as described from excretion measurements and whole body counting, is shown in Fig. 1. In the other subjects the pattern was similar over the limited times of the investigations,

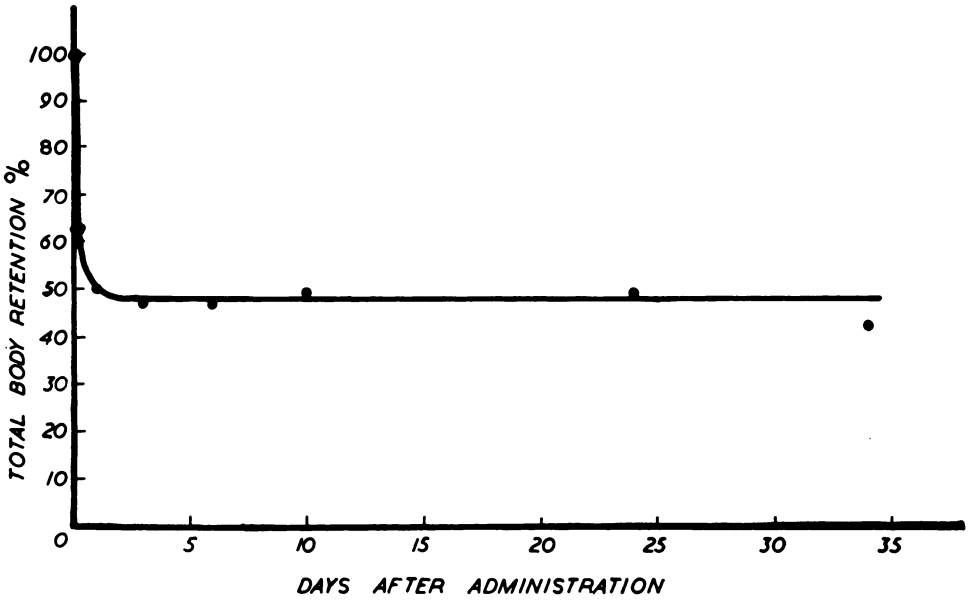

Fig. 1. Total body retention of radioactivity in Subject 1 at various times after administration of PVP-^{131}I.

the 48-hour retention of radioactivity varying from 48 to 63 per cent of the administered dose.

In all subjects, surface counter surveys revealed after 24 hours significant concentration in the liver area, but no other organ concentrations.

Plasma Concentration

The variation with time of concentration of radioactivity in the plasma in subject 1 is plotted in Fig. 2. Again, results of the other investigations were similar.

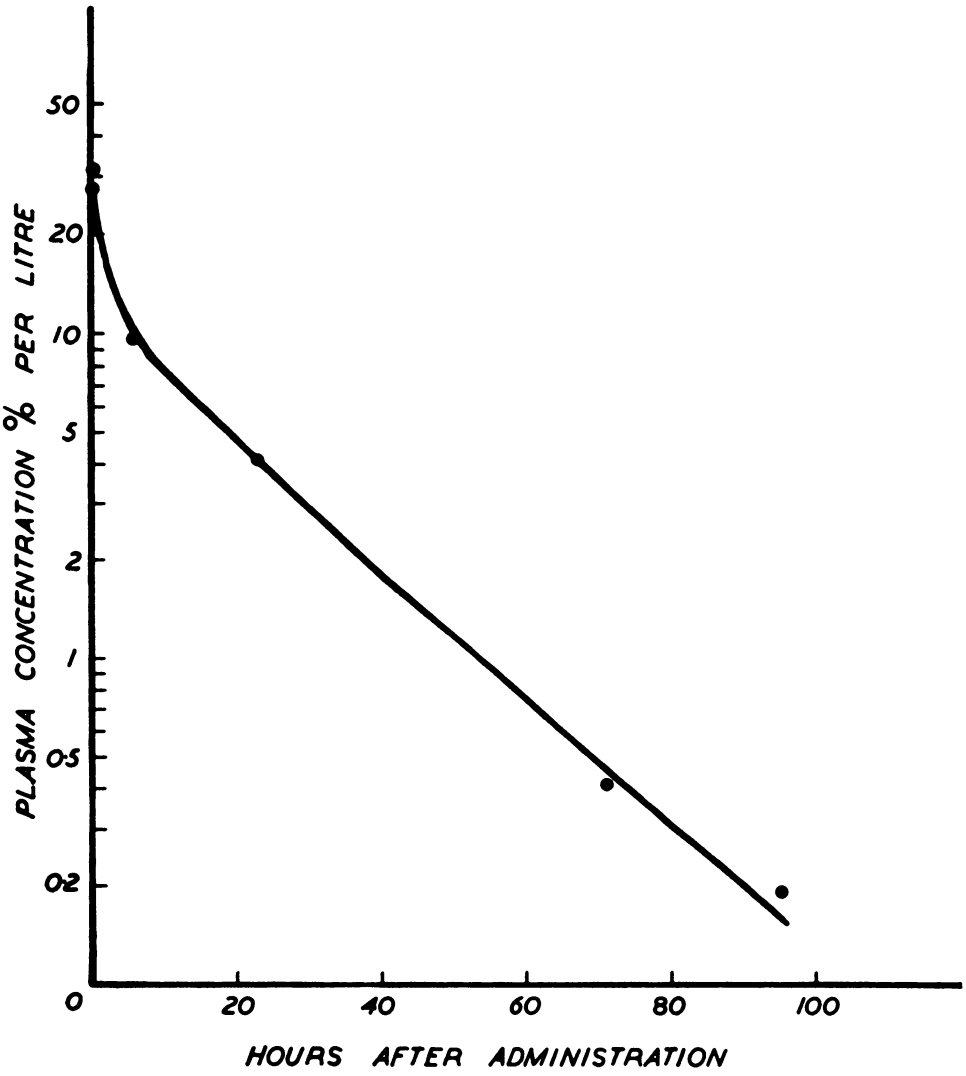

Fig. 2. Variation with time after administration of concentration of radioactivity in plasma.

Excretion Measurements

The cumulative urine content is plotted in Fig. 3. In no case did the total faecal excretion of radioactivity over a period of three days exceed 1 per cent of the administered dose.

DISCUSSION

The retention figures show that approximately half the activity was retained in the body for a very long time. This means that for radiation dosimetry purposes the effective half-life after the first 24 hours was equal to the physical half-life, 8 days. The results of this investigation indicate that most of this activity was in the liver. No significant concentrations were detected elsewhere, and by 48 hours the activity in the plasma was too low for generally distributed PVP to contribute much to the body content. It may be that other organs in the reticuloendothelial system concentrated some activity that could not be detected with the doses used here, but such concentrations would not materially affect the discussion.

While hepatic uptake of PVP has been previously described (9,10) quantitative estimates of the accumulation of tracer amounts do not appear to have been published. Meijer (10) administered PVP of two different molecular weights to mice and assayed the amount remaining in the liver and spleen. He found it was only a small proportion of the administered dose, at the most 2 per

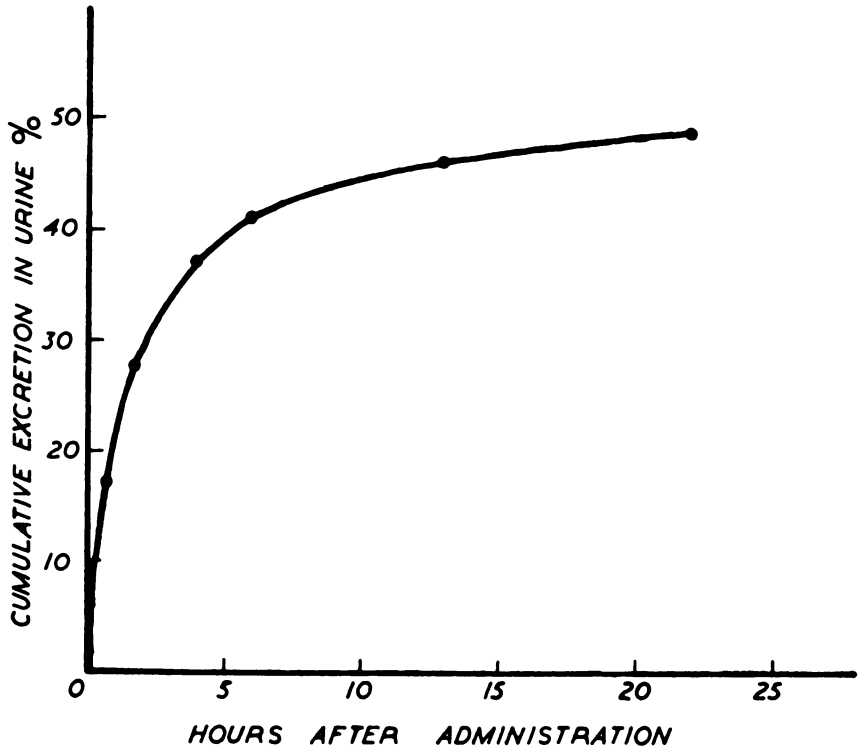

Fig. 3. Percentage of administered dose appearing in urine during first 24 hours.

cent. However, the quantities injected were relatively massive, and it is likely that tracer amounts would be treated differently.

For a liver of mass 1700g, an initial 1μC of ^{131}I uniformly distributed and retained with an effective half-life of 8 days leads to a total absorbed dose of approximately 0.1 rad. The commonly administered dose of PVP-^{131}I for brain scanning purposes is 500μC. The retention of half of this in the liver, as has been described, gives rise to a radiation dose of 25 rads. While this may be justifiable in investigating brain tumours, it is certainly not negligible, and is comparable with the kidney radiation dose arising from the injection of 500μC of 'Neohydrin'-^{203}Hg. Much smaller amounts of PVP-^{131}I are used for investigating protein-losing enteropathy, and in this case, the radiation dose may be quite acceptable.

The long-term retention by the liver of 50 per cent of injected PVP is not necessarily representative of all samples of the material, as the physiological behaviour is dependent on molecular weight. We have found that higher molecular weight fractions are cleared from the blood and retained by the liver to an even greater extent, while PVP of lower molecular weight is eliminated more efficiently by the kidneys. There would seem to be a good case for using lower molecular weight material for brain scanning, provided that localisation within the tumour is not affected. It may be that the PVP-^{131}I used by Tauxe *et al* (3) conforms to this requirement. These authors state that their material has a biological half-life of one day. The material used in this investigation has an equally short biological half-life, in that half the administered dose is excreted in 24 hours. However, this conception has little significance unless the reduction of retained radioactivity is exponential. Its use is particularly misleading when, as in the present case, long-term retention is accompanied by concentration in a relatively small volume. It is clear that there must be caution in the administration of relatively large doses of PVP-^{131}I unless hepatic uptake can be shown to be low.

SUMMARY

It is shown that following the intravenous injection of PVP-^{131}I, approximately half the material is excreted in the urine in the first 24 hours, while the remaining half is retained for a long time, mainly in the liver. The resulting radiation dose may be quite high when amounts required for brain scanning are administered. The use of the biological half-life to assess radiation dose is shown to be misleading under the circumstances described.

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