tory). Thus, the conjugate discussed by O'Brien *et al.*[1] and Kuhnert *et al.* may simply be N-acetyl CABA, and that no discrepancy really exists. On the other hand there may also exist additional conjugates, though we failed to find significant amounts of the glycine conjugate.

We agree that the urine sampling period in our experiment is short (3 h) compared to that of Kuhnert *et al.* (72 h). However, O'Brien *et al.*[1] reported a very rapid elimination of CABA and CABA conjugate following a 30-min intravenous infusion of chloroprocaine. In fact, 65 per cent of the administered dose was recovered within 90 min from the onset of the infusion. Thus, it was felt that a three-hour collection period would suffice.

In conclusion, therefore, we feel that only minor conflicting results exist, that N-acetyl CABA is the major metabolite (or conjugate), and that the last sentence in letter of Kuhnert *et al.* is not justified.

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Pharmacogenetics and Halothane Hepatitis

To the Editor:—There is now published evidence in humans that pharmacogenetics may be a factor in human halothane hepatitis.[1] In addition to our recent report of differences in halothane hepatotoxicity among three different strains of rats,[2] we now have evidence within one rat strain (Fischer 344) of considerable variability in hepatic damage following halothane.[3] In a study of the time course of changes in liver function and structure following halothane, maximum values for serum alanine amino-transferase (ALT) varied from 143 IU/l to over 28,000 IU/l. Although mean peak serum ALT was 5,180 IU/l, three of 128 animals studied had values of 28,925; 18,550; 7,650 IU/l, respectively. These high serum ALT values in three animals were accompanied by massive hepatic necrosis, whereas animals with moderate increases in serum ALT had focal necrosis.[3] This provides further evidence of a genetic influence in halothane hepatitis, since the conditions of anaesthesia and oxygenation were identical for all animals.

Clinical studies of repeated halothane anaesthesia report that mild liver injury occurs with a frequency as high as 24–40 per cent of patients; yet severe liver injury is rare. It now seems that pharmacogenetics may provide a key that predisposes a small number of individuals to severe liver injury. Even in such individuals it seems likely that a complex set of factors, such as high rate of reductive bio-transformation and low oxygen concentration in the liver, may be conditional to the development of massive hepatic necrosis. This is entirely in keeping with a multifactorial etiology of halothane hepatitis as discussed by commentators in both the field of anesthesiology[4,5] and general medicine.[6,7]

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CO_2 Monitoring during Cardiopulmonary Bypass

To the Editor:—Pa_{CO_2} may fluctuate widely during cardiopulmonary bypass. Variations in Pa_{CO_2} reflect changes in production of CO_2 occurring secondary to changes in temperature. CO_2 removal is proportional to gas flow into the pump oxygenator. CO_2 is added as either a fixed or variable percentage of the gas flowing into the oxygenator. Variability in Pa_{CO_2} can be reduced through frequent monitoring of arterial blood gases and subsequent adjustment of either total gas flow, per cent CO_2 in the gas flow or both. We have devised a simple method for rapid adjustment of Pa_{CO_2} based upon use of a portable end-tidal CO_2 analyzer (Puritan-Bennett®, etc).

One end of the sampling port of the CO_2 analyzer is fitted to a 3-mm endotracheal tube adapter. The other end is occluded to prevent sample contamination. The endotracheal tube adapter is then attached at the quick priming port of the oxygenator (Shiley S-100A) and gas is continuously sampled (See fig. 1).

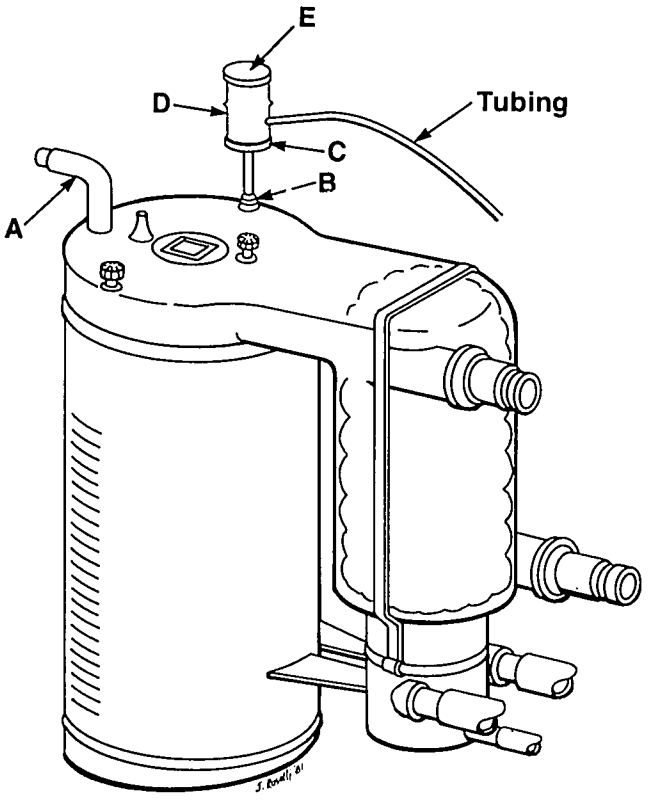

FIG. 1. Puritan-Bennett CO_2® Analyzer attached to Shiley S-100 A oxygenater. Gas exhaust port, A; quick prime port, B; 3-mm endotracheal adaptor, C; CO_2 sampling attachment, D; occlusive cap, E.

TABLE 1. Analysis of End-tidal CO_2 and Respective Blood Pa_{CO_2}

End-tidal CO_2 (mmHg)	Blood Pa_{CO_2} (mmHg)	Error/mmHg
35.5	36.6	0.9
40.0	39.7	0.7
39.5	39.7	0.2
29.5	30.7	1.2
34.0	34.6	0.6
40.0	41.0	1.0
41.0	41.5	0.5
41.5	41.0	0.5
41.5	40.7	0.8
35.0	34.1	0.9
29.5	29.3	0.2
34.0	33.6	0.4
35.0	33.8	1.2
40.0	39.7	0.3
44.0	43.1	0.9
38.0	36.8	1.2
39.5	39.0	0.5
48.0	47.3	0.7
42.0	40.0	2.0
40.5	42.3	1.8
Mean 38.4	38.2	0.8 (Range $^{-}$1.8 to $^{+}$2.0)

We compared twenty temperature-corrected, arterial blood gas determinations (IL 813 Blood Gas Analyzer®) to comparably timed readings from the CO_2 analyzer. In no case did the two measurements differ by more than two mmHg (See table 1).

We present this as a simple method of monitoring Pa_{CO_2} suitable for rapid adjustment of CO_2 addition or removal during cardiopulmonary bypass and as a means of reducing the necessary number of blood-gas determinations.

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