

On-line Continuous Potentiometric Measurement of Potassium Concentration in Whole Blood During Open-Heart Surgery

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We describe a flow-through system with an ion-selective electrode for measurement of blood potassium ion concentration, continuously and on-line off the extracorporeal blood circulation in an operating theater during human open-heart surgery. Comparison measurements were made with the SMA flame photometer (blood plasma) and an Orion SS-30 sodium/potassium analyzer (whole blood). The potassium concentration values obtained with the flow-through system agree well with the ones determined with the flame photometer. The time delay of the measurement with the flow-through system was relatively long (2 min) but delays of only 10-20 s seem feasible. Short time delays can deepen insight and simplify rational treatment under surgery conditions.

Additional Keyphrases: *analytical systems · electrolytes · ion-selective electrode · on-site measurements*

The potassium ion plays an important role in body fluids. Normal functioning of body cells hinges on maintainance of the cell membrane potential, which is largely controlled by a concentration gradient of potassium ions across the cell membrane. The intracellular potassium concentration is about 40-fold the extracellular value. This polarization is of special importance in the heart muscle and in nerve tissues. Several factors can disturb this delicate balance. Defects of kidney function are followed by either loss or severe retention of potassium. Systemic acidosis (1, 2) or diabetes mellitus (3) depress the uptake of potassium into cells. Alkalosis (1, 2) and insulin (3) favor potassium uptake. Because less than 1% of all body potassium is in the plasma, these changes in the distribution of potassium result in hyper- or hypokalemia. In critically ill patients the compensatory mechanisms are depleted. Hypokalemia has dangerous effects on cardiac rhythm, while hyperkalemia leads to cardiac arrest.

In open-heart surgery with extracorporeal blood circulation, potassium measurement is of special importance. Potassium concentration varies with body temperature, kidney function, respiration, infusions, and several other functions during surgery (4). Before reactivation of the heart the potassium concentration should be within the physiological range or

slightly higher, so that normal heart function can be expected.

Usually the potassium concentration is determined off-line by use of flame photometers or ion-selective electrodes. With ion-selective electrodes, single measurements can be performed with whole blood within 1 or 2 min. Comparison of over 300 measurements performed under routine conditions in the course of several months at the university hospital in Zurich, with use of two different flame photometers, showed commercially available ion-selective electrode systems to possess less-than-satisfactory reproducibilities. On the other hand, systems based on ion-selective electrodes have been described that give reproducibilities for the measurement in whole blood that are at least comparable to those obtained by flame photometry on the corresponding sera (5-8). The disadvantage of flame photometers in this context is the time-consuming centrifugation step necessary to obtain blood plasma (6-8 min). Therefore, the advent of near-instantaneous (delays of less than 20 s are possible) continuous measurement of potassium promises to deepen insight and simplify rational treatment during surgery.

Only recently, continuous measurement of potassium in veins of a greyhound was reported (8). In the present contribution, we describe the continuous on-line determination of potassium of whole blood during human surgery. We compare the results of our flow-through electrode system and values determined on the same sample set with a flame photometer and with an Orion SS-30 sodium/potassium analyzer.

Materials and Methods

Apparatus

The continuous potentiometric measurement of potassium concentration was performed with a flow-through system (Figure 1). The electrode modules are machined from polymethylmethacrylate blocks and are interconnected by means of polytetrafluoroethylene cones. In order to prevent electrostatic field and short-term temperature interferences, the module assembly was mounted inside a grounded aluminum block. The liquid-membrane selective for potassium ion was composed of (per 100 g) 1.0 g of valinomycin, 32.9 g of polyvinylchloride (high molecular PVC, SDP; Lonza AG, Visp, Switzerland) and 66.1 g of di-(2-ethylhexyl)-sebacate (Fluka AG, Buchs, Switzerland; pract. grade). A chlorinated silver wire in combination with a reference electrolyte (1 mol/L KNO_3 + 0.01 mol/L KCl) was used as reference electrode. This electrolyte was forced through an open channel and a screw-restriction by a peristaltic pump (Perpex Model A; H. J. Guldener, Zurich, Switzerland); this set-up eliminates con-

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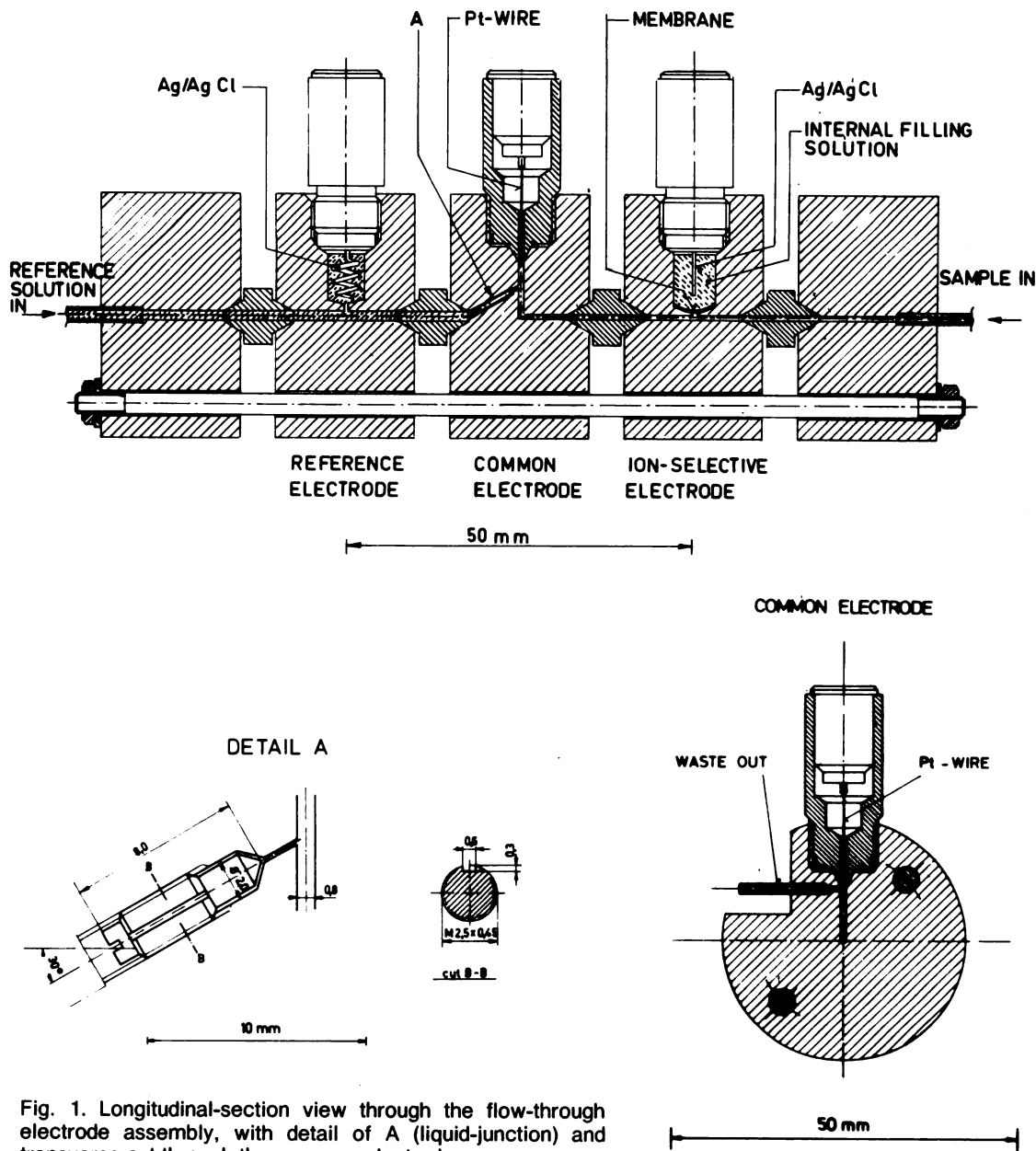


Fig. 1. Longitudinal-section view through the flow-through electrode assembly, with detail of A (liquid-junction) and transverse cut through the common electrode

tamination of the reference junction by proteins. A second peristaltic pump (Perpex Vario) with a flow rate of 18 mL/h was used downstream of the common electrode to aspirate all liquids.

To obtain blood samples, we pierced the venous blood conducting tube of the heart-lung machine (for run I: TMO Membrane-Oxygenator, Travenol Lab. Inc., I, with Sarns pump; for runs II-IV: Venotherm-Bubble-Oxygenator, Polystan AS, Copenhagen, with in-house designed pump) with a syringe-needle attached to the sampling capillary (polytetrafluoroethylene; run I: length 100 cm, i.d. 1.1 mm, and 70 cm with i.d. 0.8 mm; runs II-IV: length 40 cm, i.d. 0.8 mm) by means of a Luer fitting. The other end of this capillary was connected to one input part of the sample-selection valve (Cheminert stream-sampling valve, Model SSVA 8031; Laboratory Data Control, Division of Milton Roy Co., Riviera Beach, FL). The second input part received standard solution. The output of the valve is coupled as closely as possible to the flow-through system by a polytetrafluoroethylene tube (length 20 cm, i.d. 0.8 mm) (see Figure 2).

To reduce mutual interference between sample and standard solution, we injected air-bubbles for 10 s, beginning 1 s

before switching the valve. The bubble-injection position was situated directly downstream of the valve.

The electric potential difference between the reference electrode and the ion-selective electrode was measured by a differential method relative to the common electrode (Pt-wire, Figure 1). The circuit diagram of this high-impedance difference amplifier was described earlier (9, see also 10). The analog signal of the difference amplifier was simultaneously processed by a digital voltmeter (Solartron LM 1604 DC; Solartron Electronic Group Ltd., Farnborough, Hampshire, England; operating sensitivity, ± 0.01 mV) and recorded with a Recorder 1100 (W+W Electronic AG, Basel-Münchenstein, Switzerland). The BCD-output of the digital voltmeter was fed to a printer (Print Swiss DT 21 MK II; Wenger Datentechnik, Basel, Switzerland).

The four runs were performed with two specimens of K^+ -selective electrodes and with use of the same membrane composition. The electrode used in run I had a slope of voltage vs. $\log K^+$ activity of 59.59 ± 0.08 mV at 25 °C in the concentration range 1-10 mmol of K^+ per liter (background 140 mmol/L NaCl + 1.1 mmol/L $CaCl_2$). The electrodes used for runs 2 to 4 had a slope of 57.33 ± 0.15 mV. Both electrodes had

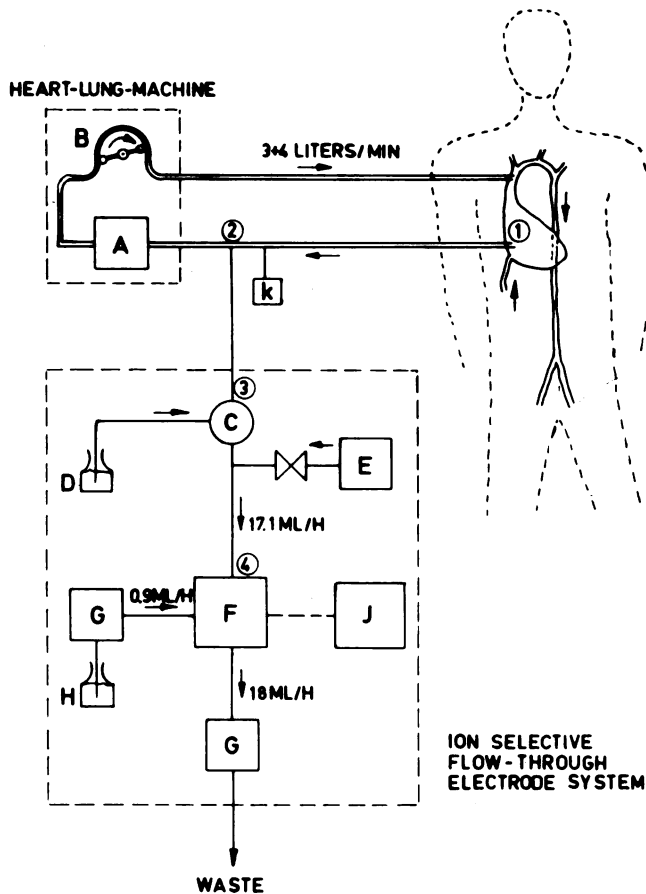


Fig. 2. Scheme of extracorporeal blood circulation

A, oxygenator; B, pump; C, sample-selection valve; D, standard solution; E, air-pump; F, K^+ -flow-through electrodes; G, peristaltic pump; H, reference electrolyte; J, signal acquisition and data output; K, sampling syringe for off-line potassium determination. Distance ① → ②: ~100 cm; time < 2 s. Distance ② → ③: run I: 170 cm; time ~5 min; runs II-IV: 40 cm; time ~100 s. Distance ③ → ④: 20 cm; time ~25 s. Due to laminar-flow effects operative in the small-diameter capillary used here, sharp signals are somewhat smeared; in clinical context this is immaterial, though

selectivities typical for valinomycin-based K^+ -electrodes (11, 12); e.g., the preference for K^+ over Na^+ was 16 000:1 for 0.1 mol/L solutions. The system responded to within 0.1 mV to the final voltage value in about 1 s, counting from the last air-bubble when changing from standard solution (2 mmol/L KCl + 140 mmol/L NaCl + 1.1 mmol/L $CaCl_2$) to a test serum (4–8 mmol/L K^+). The reproducibility of the reading 10 s after the last air-bubble was ± 0.060 mV (SD $n = 7$) as measured with different test sera by changing samples every 60 s. This corresponds to a coefficient of variation for the potassium concentration of 0.23%.

The blood samples for independent K^+ determinations were taken with a syringe from the venous blood-conducting tube of the heart-lung machine, very close to the sampling position of the flow-through system. One sample was brought to an Orion Model SS-30 sodium/potassium analyzer (Orion Biomedical, Inc., Cambridge, MA). The measurements were carried out with whole blood according to the Orion manual. The second sample was taken to the central chemical laboratory, centrifuged, and the plasma measured either (first run) with a flame photometer IL-343 (Instrumentation Laboratory Inc., Lexington, MA; recalibration after three plasma samples) or (other runs) with the flame photometer of a SMA 6/60 AutoAnalyzer (Technicon Instruments Corp., Tarrytown, NY; recalibration after seven plasma samples). The remains of the plasma samples were kept at room temperature in closed centrifuge cones for 2 to 5 h. Then a second measurement with these samples was made with the flame photometer IL-343

calibrated with the same standards as the flow-through system.

Chemicals

The chemicals used for the calibration solutions were from Merck, Darmstadt, West-Germany; grade "pro analysi." The composition of the "Ringer-glucose" was (in mmol/L): 65 Na^+ , 2.7 K^+ , 0.5 Mg^{2+} , 0.45 Ca^{2+} , 13.5 lactate, 56.1 Cl^- , and 139 glucose. The cardioplegic solution contained (in mmol/L): 82.5 NaCl, 30 KCl, 0.5 $CaCl_2$, 26.8 $NaHCO_3$, 54.9 mannitol, and 2.78 glucose.

Procedure

The flow-through system was brought into the operating theatre and switched on 15–30 min before use. The heart-lung machine was filled with blood, and potassium measurement commenced. In the beginning, some recalibration was necessary because the flow-through system was still approaching thermal equilibrium (~1 h start-up time would be appropriate), causing a potential drift of 2–3 mV within the first 30 min. Later, the calibration points remained reproducible to within 0.2 mV. The effect of any drift was eliminated by using the potential difference (ΔV) between standard solution and blood to calculate the potassium concentration of the blood (linear interpolation between two calibration points during the drift phase). The slope s of the electrode function (V vs. $\log a_{K^+}$) was determined before and after the blood measurement with five solutions in the concentration range 1–10 mmol/L KCl, with 140 mmol/L NaCl and 1.1 mmol/L $CaCl_2$ as background. The two slopes did not differ significantly. The potassium activity a_{K^+} was calculated from the activity of the standard solution a_{std} using the potential difference measured and the experimental slope, both corrected for the liquid-junction potential (V_D) (12, 13).

$$a_{K^+} = a_{std} \cdot 10^{(\Delta V - \Delta V_D)/s}$$

$$c_{K^+} = a_{K^+} / \gamma_{K^+}$$

$$\gamma_{K^+} = 10^{(-0.509 \cdot \sqrt{I} + 0.328 \cdot 3.5 \cdot \sqrt{I}) + 0.018 \cdot I}$$

$$I = \frac{1}{2} \sum_n c_n \cdot z_n^2$$

where

I : ionic strength of solution

\sum_n : sum taken over all charged species in solution

c_n : concentration of the n th ion in solution

z_n : charge of the n th ion in solution (in units of the proton charge)

In order to ascertain the potassium concentration, c_{K^+} , the activity coefficient γ_{K^+} was determined by an iteration, assuming mean serum electrolyte background (140 mmol/L Na^+ , 1.1 mmol/L Ca^{2+} , 0.6 mmol/L Mg^{2+} , 24 mmol/L HCO_3^- , 119.4 mmol/L Cl^- , pH = 7.4) and Cl^- as the counter ion.

Results and Discussion

Table 1 shows results for potassium concentration obtained with four different methods. The mean and standard deviation of the difference between concentration values obtained with the flow-through electrode system and the SMA flame photometer are -0.05 and ± 0.11 mmol/L for $n = 25$ different samples. The mean difference is indistinguishable from zero (the ideal value). The difference in potassium concentrations found with the Orion SS-30 and the SMA flame photometer is 0.24 mmol/L (± 1 SD = ± 0.15 mmol/L, $n = 25$) according to Table 1. This standard deviation is indistinguishable from that obtained for the flow-through electrode system ($p \approx 0.1$), but the mean concentrations found are undeniably different

Table 1. Comparison of Potassium Concentrations as Obtained by Different Methods (in mmol/liter)

Run	Sample Identification	Flow-through system	SMA flame photometer (without delay)	IL-343 flame photometer (2-5 h later)	Orion SS-30
I	1	5.90	6.0 ^a	5.8	6.3
	2	5.77	5.8 ^a	5.8	6.0
	3	6.10	6.2 ^a	5.9	6.4
	4	6.17	6.1 ^a	5.9	6.4
	5	4.91	4.9 ^a	4.8	5.0
II	1	4.23	4.5	4.5	4.7
	2	3.97	3.9	4.0	4.3
	3	4.60	4.6	4.7	4.9
	4	6.36	6.1	6.2	6.6
	5	5.48	5.5	5.5	5.9
III	1	2.79	2.9	2.8	2.8
	2	3.38	3.4	3.4	3.5
	3	3.57	3.7	3.7	3.7
	4	3.33	3.4	3.5	3.4
	5	3.38	3.4	3.5	3.6
	6	5.65	5.5	5.6	5.9
IV	1	4.45	4.6	4.7	4.7
	2	4.42	4.5	4.6	4.7
	3	4.90	5.0	5.1	5.3
	4	5.65	5.8	5.9	6.2
	5	5.63	5.7	5.8	6.1
	6	5.25	5.3	5.5	5.6
	7	5.45	5.6	5.8	6.0
	8	4.67	4.7	4.8	5.0
	9	4.33	4.5	4.5	4.7

^a These measurements were done with the IL-343 instead of the SMA flame photometer, also without delay.

($p < 0.0001$). This shows the very good agreement of the potassium concentration as determined with the flow-through system and with a conventional flame photometer.

The potassium concentration difference between values determined on the same plasma sample immediately after centrifugation of the blood and 2 to 5 h later is 0.028 mmol/L (± 1 SD = ± 0.124 mmol/L, $n = 25$) according to Table 1. The mean is not significantly different from zero and therefore no change in plasma potassium concentration is detected after several hours of storage at room temperature.

The comparison of measurements made with ion-selective electrodes (whole blood) and with flame photometers (blood plasma) includes possible errors introduced by centrifugation (14) and delays of 15-20 min [there are metabolic mechanisms operative in blood that change the intracellular-to-extracellular concentration ratio of potassium, even while the sample is outside the patient's body (15)].

The time delay for the flow-through system was very long in run I owing to the particular arrangement of installations in the operating theater at that time. The volume of the present flow-through system—which, designed for the laboratory bench, was off-handedly mounted on a cart for the first trials under operating theater conditions—prevented a close approach to the heart-lung machine and thus had delays of less than 2 min. A radical redesign of component lay-out would reduce the necessary volume by about a factor of five and so make feasible delays of only 10-20 s.

Figure 3 shows four diagrams of the potassium concentration profiles. Measurement starts before the patient is put on extracorporeal circulation. In runs I and IV the perfusate (initial filling solution of the heart-lung machine) had a higher than physiological potassium concentration. On mixing the patient's blood with the perfusate (A in Figure 3) the potassium concentration is decreased in runs I and IV, while in runs II and III normal values are found. Thereupon blood perfusate mixture is cooled to diminish oxygen consumption by the body, especially the heart. Once the desired blood temperature is reached, the aorta is cross-clamped and cold cardioplegic solution is injected in excess (B, I, and J in Figure 3) into the coronary arteries to induce cardiac arrest and to ensure that all parts of the heart are perfused. The excess appears as a peak in all four diagrams. In runs II, III, and IV a rise in the potassium concentration is seen just after opening the aortic cross-clamp, when cardioplegic solution is washed out of the heart. The doses of insulin (C and L in Figure 3), given to reduce serum potassium by causing its re-uptake into cells, do not seem very effectual during hypothermia. In runs II and III the patient was given potassium (G in Figure 3) in the ordinary manner after a single potassium measurement (5 in run III and F in Figure 3) with the time delay typical for present-day clinical use. In both runs the potassium concentration increased just after the sample was taken for the separate potassium determination, because the aortic cross-clamp had been opened. These injections of potassium were super-

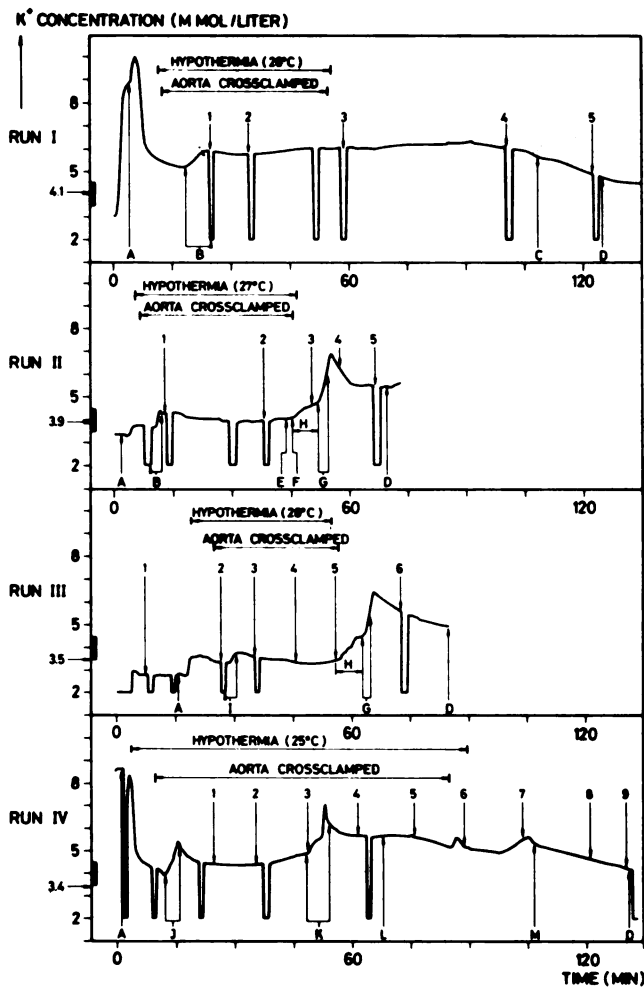


Fig. 3. Diagrams of potassium concentration as measured during four extracorporeal blood-circulation runs

The hatched bars on the left ordinate delineate the concentration range of potassium in blood plasma accepted as normal at the university hospital in Zurich and the horizontal arrows mark the potassium concentration of the patient's blood immediately before surgery. The concentration curves are corrected for the time delay of the measurement (run I: ~325 s, run II-IV: ~125 s). 1-9: sample identification number. A, start of extracorporeal blood circulation; B, addition of cardioplegic solution (addition of 25 mmol K^+); C, addition of insulin (40 units); D, end of extracorporeal blood circulation; E, addition of 45 mmol of $NaHCO_3$ (correction of acidosis); F, separate K^+ -determination, independent of this system; G, addition of 20 mmol of K^+ ; H, typical time delay (sampling- K^+ -determination—medical treatment) for separate K^+ determination with Orion SS-30; I, addition of cardioplegic solution (addition of 21 mmol of K^+); J, addition of cardioplegic solution (addition of 18 mmol of K^+); K, addition of cardioplegic solution (addition of 15 mmol of K^+); L, addition of insulin (20 units); M, addition of 50 mmol of $NaHCO_3$ (correction of acidosis)

fluous and would have been shunned if the anesthetist had had access to a continuously measured potassium concentration profile (the anesthetist did not know the results with the flow-through system presented here).

The time delay of the potassium determination has an im-

portant place in present-day open-heart surgery (4). The off-line measurements are often troublesome and time consuming. Therefore, an on-line continuous determination with ion-selective electrodes can speed results because time delay is determined only by the capillary volume and the flow rate in the flow-through system, so time delays of 10–20 s seem feasible.

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