

immersing the cellophane bag containing the serum in a vessel of distilled water or physiological saline solution, water dialyzing into the bag. Since bacteria will not pass through the intact cellophane membrane the redissolved serum will remain sterile even though the water in which the bag is immersed is not sterile. The residue of a small amount of serum, 10-20 cc., will redissolve under these conditions in from 1-2 hours.

9673 P

**Experimental Exchange Transfusions for Reducing Azotemia.
Use of Artificial Kidney for This Purpose.**

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Howell¹ first isolated heparin, which retards the coagulation of blood whether added *in vitro* or *in vivo*. Purified, non-toxic heparin was prepared by Charles and Scott.^{2, 3, 4} This preparation has been demonstrated by Best^{5, 6, 7} and his co-workers to be non-toxic when injected intravenously into humans.

A new type of transfusion, called for the time being, an "exchange transfusion," has been carried out experimentally by using heparin* as a non-coagulant.

After removing both kidneys from a dog the animal's blood urea increases rapidly. The morning after bilateral nephrectomy this animal and a donor animal are anesthetized by nembutal† injected intravenously. Cannulae are inserted into the femoral artery and vein of one leg of each animal. At this time a small amount of heparin was injected intravenously into each animal. With a 50 cc. all-glass syringe 200 cc. of blood is transferred from the donor

¹ Howell, W. H., and Holt, E., *Am. J. Physiol.*, 1918, **47**, 328.

² Charles, A. F., and Scott, D. A., *J. Biol. Chem.*, 1933, **102**, 425.

³ Charles, A. F., and Scott, D. A., *J. Biol. Chem.*, 1933, **102**, 431.

⁴ Scott, D. A., and Charles, A. F., *J. Biol. Chem.*, 1933, **102**, 431.

⁵ Murray, D. W. G., Jaques, L. B., Perrett, T. S., and Best, C. H., *Canad. M. A. J.*, 1936, **85**, 621.

⁶ Best, C. H., Cowan, Campbell, and MacLean, D. L., *Science*, 1937, **85**, 338.

⁷ Murray, D. W. G., Jaques, L. B., Perrett, T. S., and Best, C. H., *Surgery*, 1937, **2**, 163.

* Heparin was generously furnished by Dr. C. H. Best, University of Toronto.

† Nembutal was generously furnished by Dr. J. F. Biehler, Abbott Laboratories.

animal into the azotemic one, and then from the azotemic animal to the donor animal. This exchange of blood is carried out 20-40 times. Samples of blood were obtained from each animal before the transfusion, after 20 exchanges of blood and after 40 exchanges. The azotemia of the nephrectomized animal was markedly reduced. Correspondingly, azotemia was produced in the donor animal.

In each of the 6 experiments (only one typical experiment is given in detail) the donor animal's condition was normal the morning after, and the blood urea, which had been elevated, also had returned to a normal level. When the donor animals were sacrificed from one to 3 weeks later their kidneys were found to be normal both grossly and microscopically.

TABLE I.
Experiment 4.

Nephrectomized Dog Weight 6.8 Kilos. Calculated Blood Vol. 566 cc. Blood Urea N in mg. per 100 cc.		Donor Dog (normal) Weight 10 Kilos. Calc. Blood Vol. 833 cc. Blood Urea N in mg. per 100 cc.	
8/18/37, 1 P.M. Before bilateral nephrectomy	16.8		
8/19/37, 10 A.M. 21 hours after nephrectomy	75	Before 1st exchange transfusion	22.5
	61.3	After 1st exchange transfusion	30.5
	54	After 2nd exchange transfusion	36.6
Decrease in blood urea N per 100 cc.	21	Increase in blood urea N per 100 cc.	14.1
Total decrease blood urea N in 566 cc. (Blood Vol.)— 21×5.66	118.8	Total increase in blood urea N in 833 cc. (Blood Vol.)— 14.1×8.33	117.4

Experiments also were carried out using an artificial kidney made of tubes of cellophane immersed in physiological saline similar to the celloidin tubes used by Abel^{8, 9, 10} years ago.

In the experiments so far, from 1 to 4 of these cellophane tubes[‡] were used, each 2 cm. in diameter and 30 cm. in length. Through

⁸ Abel, John J., Rowntree, L. G., and Turner, B. B., *Trans. Assn. Am. Phys.*, 1913, **28**, 51.

⁹ Abel, John J., Rowntree, L. G., and Turner, B. B., *J. Pharm. and Exp. Therap.*, 1914, **5**, 275.

¹⁰ Abel, John J., Rowntree, L. G., and Turner, B. B., *J. Pharm. and Exp. Therap.*, 1914, **5**, 611.

[‡] Cellophane sausage casings were generously furnished by Visking Casing Corp.

a 2-hole rubber stopper tied into one end of the cellophane tube a glass tube was introduced to the bottom of the tube, the bottom end of the cellophane tube having been tied off with twine. Through the second hole in the stopper another glass tube, just long enough to penetrate the stopper leads the blood either back into the animal's vein or through the other cellophane tubes before returning it to the vein. The nephrectomized animal circulated his heparinized blood from his artery through the cellophane tube or tubes back into his vein. In from 3-5 hours 200-700 mg. of urea nitrogen passed from the blood through the cellophane membrane into the surrounding physiological salt solution.

These preliminary experiments suggest the possible use in humans, of either or both of these procedures, since apparently they are harmless. In humans only vein puncture would be necessary, the transfer or circulation of blood to be accomplished by means of a syringe or other mechanical device.

Conditions not infrequently arise in humans as a result of accident, operation or disease which cause previously competent kidneys to become incompetent, leading to azotemia and death. A number of situations of this sort suggest themselves: reflex anuria after an operation on one kidney, post-operative renal insufficiency, anuria in an old prostatic after insertion of an indwelling catheter or after a suprapubic cystotomy preparatory to prostatectomy, anuria in a child suffering a severe, accidental burn, etc.

However, this human application should not be made until further investigation, which is now under way in collaboration with Professor C. H. Best.*

* Since this report was written the work of others has been brought to my attention. Necheles^{11, 12} modified the artificial kidney of Abel successfully, and Haas¹³ used a modified artificial kidney, along with hirudin, successfully to combat temporarily uremia in humans. Nyiri¹⁴ carried out crossed experimental transfusions with paraffin cannulae and without the use of antieoagulants. Azotemia was produced either by bilateral nephrectomy or the injection of uranium nitrate. In some of his experiments thrombi occurred, but several were fairly successful.

¹¹ Necheles, H., *Klin. Wchnschr.*, 1923, 2, 1257, 1888.

¹² Lim, R. K. S., and Necheles, H., *Proc. Soc. Exp. Biol. and Med.*, 1926.

¹³ Haas, Georg, *Klin. Wchnschr.*, 1925, 4, 13; *Abderhalden's Handbuch der Biol. Arbeit.*, 1929, 5, 717.

¹⁴ Nyiri, Wilhelm, *Arch. f. Exp. Path. und Phar.*, 1926, 116, 117.