meristem, which form the separation between *adami* and one of the variants, there must occur transitory cells, which, could they be independently developed and cultivated into new individuals, would produce such derivated hybrids. Perhaps the "supplanting" of these transitory cells by the completely varied cells, may be compared to the rarity (discussed in the preceding paper on the variants of microbes) of the sub-variants as compared to the normal form and the main variants, by which it seems possible to explain, on the one hand the existence of distinctly marked bounds between the species, on the other hand, the not less marked bounds between the different organs and tissues of the higher organisms.

Physiology. — "*On the permeability of the red bloodcorpuscles for NO_3- and SO_4-ions*". By Dr. H. J. HAMBURGER.

The question whether cells are permeable for certain substances and if so, to what extent, is not only important for our knowledge about metabolic and other vital processes, but is also of great importance from a pharmacological point of view. Here again the red bloodcorpuscles are found to be the favourable test-objects to study this question accurately. It is only natural that these cells are in this case equally serviceable as in many other problems of a general scope. In the first place they are met with in the isolated condition (in contrast with most other cells) and they can therefore be procured without being injured; in the second place the influence of different agencies can in them be better traced than in other cells, thanks to their change of form and dimension as well as to the extrusion of red colouring matter, and in the third place the reciprocal influence between the contents of the cell and its natural surroundings can be studied in detail by chemical analysis.

It is through the study of the laws of the isotonic coëfficients (HUGO DE VRIES) of the red blood-corpuscles that the problem of permeability was first brought into the foreground [1]).

I will not here enlarge on what has hitherto been investigated and written on this subject. I only wish to point out that it has been agreed that there are: 1°. substances which penetrate through the bloodcorpuscles and destroy them (for instance NH_4Cl); 2° sub-

[1]) HAMBURGER, De permeabiliteit der roode bloedlichaampjes in verband met de isotonische coëfficienten. Versl. en Meded. d. Kon. Akad. v. Wetensch., 1890, bl. 15.

stances which permeate them, but are harmless (for instance urea); whereas there is a great number of substances, amongst others salts as $NaCl$, Na_2SO_4 etc., which are likewise harmless, but concerning whose permeating capacities opinions differ.

Some assert that alkali-salts as such can penetrate into the bloodcorpuscles, others say that they are absolutely impenetrable to these salts.

Formerly I agreed with the former opinion; now I am convinced, considering the theory of the electrolytic dissociation, that the truth lies half-ways and that the bloodcorpuscle is not permeable for the alkali-salt as such, nor for the metal-ion either, but for the acid-ion.

When CO_2 is mixed with blood the following symptoms will be observed: the bloodcorpuscle becomes richer in chlorine, richer in water and poorer in alkali. The serum undergoes just the reverse change, an exchange of substances has thus taken place.

The *kalium-* and *natrium*-contents of blood-corpuscle and serum have nothing to do with this, these are unchanged (GURBER).

There is now no difficulty in explaining these symptoms.

Through the influence of CO_2 carbonate appears in the bloodcorpuscles. A part of the bivalent electronegative CO''_3-ions leaves the bloodcorpuscle and is replaced by the double number of electronegative Cl'-ions. Therefore increase of the Cl-contents of the bloodcorpuscles and increase of the alkali-contents of the serum.

As two Cl'-ions are needed to replace one CO_3''-ion and every ion, be it mono- or bivalent, represents the same power to attract water (osmotic pressure), the power of water-attraction in the bloodcorpuscle-contents must increase more than that of the serum and the bloodcorpuscle attracts water, it swells.

The following experiment confirms this proposal.

The serum is removed as thoroughly as possible from defibrinated blood and the bloodcorpuscles are then washed with a solution of glucose, until all the serum has been removed. The intracellular liquid now reacts neutrally. The passing of CO_2 through the fluid suspension of the bloodcorpuscles in glucose does not make the liquid alkaline, although the bloodcorpuscles have taken in CO_2, and K_2CO_3 has been formed; *but as such it does not extrude.* CO_3 however can leave the bloodcorpuscle, provided an equivalent quantity of another ion of the same name takes its place. Thus, when the glucose-solution is substituted by a $NaCl$-solution isotonic with the bloodcorpuscles, the latter becomes immediately alkaline and the bloodcorpuscles swell. The reason is this that CO_3''-ions have left the bloodcorpuscles and the double number of Cl'-ions have taken their place. The

kalium and natrium of the bloodcorpuscles and surrounding have in the meantime remained unchanged.

The question may now be considered what the result will be, when in a suspension of bloodcorpuscles in glucose not a solution of Na Cl is added, but a solution of $NaNO_3$ isotonic with the bloodcorpuscles. Then the $NaNO_3$-solution also becomes *alkaline* through natrium-carbonate, very weak when no CO_2 was made to pass through the suspension, but pretty strong when this had been the case. And in accordance with what is observed in Na Cl, swelling is also found here after addition of the isotonic salt-solution to the CO_2-suspension of the bloodcorpuscles in glucose-solution. This is self-evident, for, when it is admitted that $(NO_3)'$-ions enter the bloodcorpuscles and CO_3''-ions extrude, then every CO_3''-ion which extrudes must be replaced by two $(NO_3)'$-ions, and as one $(NO_3)'$-ion represents the same osmotic pressure as one CO_3''-ion, the power of the bloodcorpuscle to attract water (osmotic pressure) must increase and the latter will swell.

If the experiment is performed with $NaSO_4$-solution, then this solution will likewise be seen to become alkaline, weak, when no CO_2 was mixed with the suspension of the bloodcorpuscles in glucose-solution, rather strong when this had been the case. The volume of the bloodcorpuscles did not increase however. This is evident; against one SO_4''-ion which enters the bloodcorpuscles, one CO''_3-ion extrudes; the power of water-attraction of the bloodcorpuscles-contents remains the same during this exchange.

From these experiments the conclusion may be drawn that the red bloodcorpuscles are permeable for NO_3'- and SO_4''-ions; which was hitherto not accepted even by those who did not doubt a permeation for chlorine, as based upon direct quantitative analysis.

Meanwhile our conclusions in regard to the permeability of the red bloodcorpuscles for SO_4- and NO_3-ions, also find their confirmation in direct quantitative chemical analysis of the added sulphate and nitrate before and after the mixture with the bloodcorpuscles.

Not for all acid-ions however quantitative chemical analysis can be performed with sufficient accuracy required for the purpose.

For such cases we now find in the described method a means which enables us to judge about the permeability of the bloodcorpuscles for such ions. It only requires to be noted whether alkaline reaction appears, or if already present, increases, in the bloodcorpuscles washed with glucose, after addition of the salt-solution containing the ion which must be examined. A preceding treatment of the suspension

of bloodcorpuscles in glucose-solution with CO_2 is much to be recommended, as the number of CO_3-ions in the bloodcorpuscles increases thereby and therefore a better opportunity offers itself for the acid-ions (anions), which are to be examined, to change places with CO''_3 and to enter. Consequently the alkaline reaction of the solution about to be examined will become stronger. That CO_2 is able to promote the entrance of ions into cells seems to me of great importance for the economy of the human body.

(November 21, 1900.)

E R R A T A.

p.	280	line	17	for	in plane	read	in a plane
		„	30	„	$\frac{a\psi}{dx}$	„	$\frac{d\psi}{dx}$
		„	31	„	in plane	„	in a plane
„	282	„	18	„	who	„	whom
„	283	„	24	„	aA, aB	„	aA', aB'
		„	29	„	aA'	„	aA''
		„	31	„	Aa	„	aA'
		„	31	„	qA'	„	aA''
		„	32	„	aB'	„	aB''
„	284	„	8	„	μ_b, μ_b	„	μ_a, μ_b
„	285	„	42	„	parobola	„	parabola
„	290	„	24	„	or	„	for
„	296	„	13	„	and of r	„	and v
„	297	„	9	„	$(1-x)\,lg\,1-x)$	„	$(1-x)\,lg\,(1-x)$
„	300	„	26	„	difference	„	differences
„	309	„	9	„	1.44	„	1.46
„	316	„	10, 12 and 16 for determination			read determinations	