The discussion is very complicated and not complete, but we report progress. Lie's theorem refers to the single inclination of the curve; but in space we have to introduce two slopes, or three direction angles of the surface. We find that these slopes or angles obey a fundamental set of three partial differential equations of second order. (In Lie's case, he found a single equation of second order which was identical in form with Laplace's equation). Our new equations are not of the Laplace form.

It is well known that the only transformations which convert (1) into itself form the conformal group. This is obvious from the theory of functions of a complex variable. Therefore isothermal families are converted into isothermal families by conformal transformations. The authors have proved that no other point transformations are legitimate. This is difficult because we can no longer take advantage of the isothermal parameter, and therefore we have to use an equation of third order, related to the Laplace equation, but not identical with it.

Now in three dimensions it is shown that the only legitimate point transformations which send (2) into itself are those of the similitude seven-parameter group. Thus we have merely arbitrary constants but no arbitrary functions. For isothermal families of surfaces, our discussion yields the same group.

If, instead of point transformations, we use the larger body of contact transformations, no new autotransformations are possible. However, by using general element transformations, we have discovered a larger set of possibilities in the plane. Studying the analogous situation in space, we prove that no larger group can exist.

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THE RATE OF DEVELOPMENT OF RED CELL PRECURSORS

SEVERAL attempts have recently been made to answer the question as to whether there are sufficient cells in the early developmental categories to maintain the number of mature red cells in the circulating blood. The solution of the general problem is simple when one approaches it from the standpoint of the steady state, and in the adult rat there are figures of sufficient accuracy to enable one to carry out the calculations.

Assuming that the cells of the red cell series develop irreversibly from hemocytoblasts to mature erythrocytes by passing through the successive stages of erythroblast, normoblast and reticulocyte, the number of cells N in any one class per unit volume at any one time will depend on P, the number of cells which enter the class per unit time, and Q, the number which leave it in unit time to enter the next class of the consecutive development. In the steady state in which N for the class remains constant, being fed by cells from the class before it as it delivers cells into the class beyond it,

$$t = N/Q,$$

where t is the average duration of the life of the cell in the class. When there is no cell division, $P = Q$, and the P for any class is the Q for the class before it.[1] If some of the cells in the class undergo mitotic division, the fractional number of cells which divide is

$$f = mt/d$$

where m is the number of the cells in the class observed in mitosis at any one time and expressed as a fraction of unity, and d is the duration of a mitosis in the same units of time as used to express t. For such a class in which a fraction of the cells divide, P is smaller than Q, and is

$$P = Q(1 - f/2).$$

The values assumed for the adult rat are shown in Table 1.

TABLE 1

Class	N per mm³	Explanation
Mature red cell	18.8×10^6	$9.0 \times 10^6 \times 6.27/3.02$*
Reticulocyte	11.6×10^6	$5.4 \times 10^6 \times 6.27/3.02$
Normoblast	7.2×10^5	36 p.c. of 2×10^6†
Erythroblast	8.0×10^4	4 p.c. of 2×10^6
Hemocytoblast	5.0×10^4	2.5 p.c. of 2×10^6; 50 p.c. of all hemocytoblasts present.

* Ratio of circulating blood to active marrow, Fairman and Corner.[7] The multiplication makes 1 mm³ of marrow equivalent to 1 mm³ of blood.
† Total number of cells per mm³ of marrow, Kindred,[5] Farrar.[8]

Starting the calculations with $t = 60$ days for the mature red cell, and assuming (a) that the fraction of cells observed in mitosis in the normoblast, erythroblast and hemocytoblast classes is $m = 0.005$,[2] and (b) that d is 0.5 hour, we get the values shown in Table 2.

The number of cells which must be produced by the cells of the erythrogenic capillaries or other cells of origin in order to maintain the steady state is accordingly 2.12×10^5 per mm³ of marrow per day. This is not a remarkable rate of production; if, for

[1] E. Ponder, *Quart. Jour. Exp. Physiol.*, 16: 241, 1926.
[2] Kindred,[5] Table 2. The value 0.005 is applied to all three classes as an approximation, but the number of mitoses is small, and even considerable variation in the value would not affect the final result much. No account is taken of amitotic divisions.

TABLE 2

Class	t, days	Q, per mm³./ day	P, per mm³./ day	f
Mature red cell	60	3.13×10^5	3.13×10^5	0
Reticulocyte	3.6	3.13×10^5	3.13×10^5	0
Normoblast	2.3	3.13×10^5	2.27×10^5	0.55
Erythroblast	0.35	2.27×10^5	2.18×10^5	0.084
Hemocytoblast	0.23	2.18×10^5	2.12×10^5	0.055

example, the cells of the erythrogenic tissue were 5 per cent. of the total number in the marrow, only 2 mitoses per cell per day would be required. Whether or not this development occurs in erythrogenic capillaries involves the recognition at any one time of the presence (Sabin[3]), or absence (Jordan,[4] Kindred[5]), of cell division in about one capillary endothelial cell out of 25. Such a marrow would regenerate from the depleted state in about 10 days. The difficulty which Jordan, Kindred, Duran-Jorda[6] and other investigators have experienced in finding a sufficient number of precursors to maintain the red cell population in the steady state is thus considerably reduced when the precursors are regarded as *becoming* the cells of the subsequent classes by maturation instead of as *giving rise* to the cells of subsequent classes by mitosis; it should be understood, however, that my purpose is not to try to settle the question, but to call attention to this way of approaching the problem.

The same type of calculation is applicable to the steady state of the granulocytes, but here the difficulty is to assign a value to N for the class of the polymorph, because this cell is present not only intravascularly but also extravascularly. Reasonable values, however, point to the duration of life of the various white cell precursors being longer than that of the red cell precursors.

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FLUORESCENT MICROSCOPIC STUDY OF THE PHYSIOLOGICAL DISTRIBUTION OF ATABRINE

STUDY of the pharmacology of atabrine has led to a more rational use of the drug and increased its efficiency as an anti-malarial agent. Chemical determinations have demonstrated that atabrine is localized chiefly in leucocytes, liver, spleen and kidney.[1] The study here reported has been undertaken to determine where, within the tissues, atabrine is localized, in an attempt to better understand its action on the infectious organism.

The fluorescent property of atabrine, with its maximum wave-length at 365 mμ, is utilized in its chemical determination in plasma.[2,3] The same principle is used in the microscopic study. The source of illumination is from an H-4 bulb mounted in an ordinary microscope lamp attached to the appropriate transformer. A Corning No. 5984 filter is interposed in front of the lamp and a Corning No. 3894 filter, ground down to fit the ocular, is used as the selective filter.

Fluorescent microscopy has been utilized for some time. Dempsey[4] and Dempsey and Wislocki[5] have recently used it extensively. However, these authors use ultra-violet light and quartz lenses throughout and therefore could detect true fluorescence of tissue. The fluorescence used in this study is at a wave-length of 365 mμ, which is within the range of visible light, and therefore glass lenses can be used.

Frozen sections are made from fresh tissue, or after fixation in neutral or slightly alkaline formalin, and mounted in saline or 0.2 M Na_2HPO_4. (Atabrine shows its greatest fluorescence at pH 9.5 in aqueous solutions.) No method has been perfected for making permanent mounts of these sections. The above technique is a modification of the method of Popper.[6]

Adult male and female mice were injected intraperitoneally with a 2 per cent. solution of atabrine hydrochloride, the daily dosage being 2 mg and the total dosage 4–12 mg. Uninjected mice were sacrificed and studied simultaneously with each test animal. Control tissue shows a slight amount of yellowish fluorescence which is diffuse throughout the entire section, although under the high power (440X) it is barely visible. However, the fluorescence of atabrine is of an entirely different color, being yellowish green, and has an intensity so much greater that the diffuse yellowish background is completely lost. With this method the absence of fluorescence manifests itself as a black background.

Preliminary studies revealed the greatest concentration in the liver, spleen and kidney, as has been demonstrated quantitatively by Shannon *et al.* In the liver fluorescence appeared diffusely distributed throughout the parenchymal cells. The nuclei showed no greater concentration than the cytoplasm. The sinusoids appeared black and there was no evidence of any great concentration within the Küpffer cells. In the spleen, the fluorescence appeared to be con-

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