Section I

RED CELL SHAPES. AN ILLUSTRATED CLASSIFICATION AND ITS RATIONALE

By M. BESSIS.

THE various shapes that the red cell can assume are just beginning to be analysed in a critical fashion. It is now possible to assign names to most of the cells which have been anonymously designated as poikilocytes. Thus, the erythrocyte may become the first living cell permitting us to assess its internal molecular structure on the basis of its external configuration.

SCANNING ELECTRON MICROSCOPY

Correct appreciation of the fine details of is cell shape can provide information of great importance. Until recently, red cell shape could only be appreciated with the optical microscope, i.e. with a limiting resolution of 0.2 micron. The situation has changed completely with the advent of the scanning electron microscope (SEM), since we are now able to see the details of cell shape with a tenfold improvement in resolution and a depth of field that permits an appreciation of the three-dimensional shape of the cells. This has provided a major stimulus for several investigators to examine normal and pathologic erythrocytes with SEM. Great excitement was generated by the initial publications, and the almost seductive beauty of the three-dimensional images. As further publications have appeared it

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has become apparent to hematologists that at least some of the cells depicted were not those which they were accustomed to seeing in the circulation or between slide and coverslip. It must be asked whether some of the phenomena reported may represent artifacts arising either during preparative handling of the cell or during fixation. Contrary to what might be expected intuitively, red cells are more difficult to fix without inducing artifactual alterations than white blood cells or blood platelets, which might be considered more fragile or sensitive to environmental influences. Because of the importance of red cell shape, it would be desirable to know all the potential factors which result in artifacts. Although at the present time we cannot identify all of these, we can at least monitor the characteristics of the washing medium, the conditions of fixation and drying; checking each step with the optical microscope with the hope of minimizing potential misinterpretations. Many of these artifacts have been illustrated in a recent review of this problem (BESSIS and WEED, 1972).

Hematologists normally will not require a scanning electron microscope or need to spend a lot of time making detailed studies of living cells. It is hoped this article will help them interpret the various appearances of red cells as they are seen flattened on blood smears. Bearing, these ideas the hematologist may find the information available from a simple examination of a blood smear may take on a that new significance.

THE REVERSIBLE DISCOCYTE-ECHINOCYTE TRANSFORMATION

If a red cell is washed with isotonic sodium chloride and then examined between glass slide and coverslip, its shape changes from a biconcave disc to a sphere covered with crenations or spicules (echinocyte, from the Greek word meaning *sea urchin*). If these cells are re-introduced into fresh plasma they will reassume their discoid shape. This reversible transformation without change in cell volume or viability, is the phenomenon which PONDER (1955) described as the « disc-sphere » transformation. As he pointed out, there are several recognizable stages between the extremes of a discocyte and that of, a prelytic sphere. Five stages can be recognized : echinocyte I, an irregularly contoured disc; echinocyte II, a flat cell with spicules; echinocyte III, an ovoid or spherical cell with 10 to 30 spicules evenly distributed over its surface and sphero-echinocytes, distinctly sperical cells whose spicules have become fine, needle-like projections. If the cells are exposed to high concentrations of certain chemical agents or very high pH (10.0) they become sphero-echinocytes I and then a spherocyte-echinocyte II with very tiny spicules.

The echinocyte transformation can be produced by, 1) washing cells free of plasma and examining them between a glass slide and coverslip (it does not occur with a plastic slide and coverslip), 2) extrinsic factors, and 3) intrinsic factors. The echinocytes are reversible in certain conditions by bathing them in fresh normal plasma. This subject has been reviewed by BRECHER and BESSIS (1972).

THE REVERSIBLE DISCOCYTE-STOMATOCYTE TRANSFORMATION

Certain chemical agents (e.g. phenothiazine, chlorpromazine) will produce a cup-shaped change in erythrocyte shape (different from the bell-shaped change). As these cells, have the appearance of a stomatocyte in blood smears, we shall refer to them by this name rather than cup-shaped cells. The stomatocytic shape change in red cells is also readily produced by low pH, just as the echinocytic change is produced by a high pH. If the cells are exposed to high concentrations of these chemicals or very low pH (3.0), they become sphero-stomatocytes and finally spherocytes with a small discrete hilum. The stomatocytes are reversible up to a point by washing in fresh normal plasma. The discocyte-stomatocyte transformation has been reviewed recently by WEED and BESSIS (1973).

NEW TERMS

There are only five new terms; but, what seems really important to me is that these terms, can be combined with each other and with all other older terms describing red cell shape (see table II). This particularly applies to the words echinocyte and stomatocyte, as all pathological cells, normal cells like are able to undergo the echinocytic and stomatocytic transformations.

Codocytes (from the Greek word meaning *bell*). Hypochromic erythrocytes which are bell-shaped if examined fresh, may be found in many hypochromic anemias particularly in thalassemias. These bell-shaped forms are thin cells and should not be confused with cup-shaped forms.

When a smear is prepared the bell-shaped, hypochromic erythrocytes will often appear of « *target cells* » when they come to rest flat on the slide. (It should be noted that the as target cell appearance can also arise from other causes.) If the bell-shaped, hypochromic cells settle on their side, they will look like « *helmet cells* » on a Giemsa-stained smear.

Keratocytes (from the Greek word meaning *horn*). These are erythrocytes which are deformed in a distinctive fashion with one or more pointed projections, though their volume is normal. Their origin, as described by BELL (1963), is specific.

Recent studies have been done to characterize the keratocytes and the schizocytes which are seen in microangiopathic hemolytic anemias. BULL et al. (1968) and BULL and KUHN (1970) pointed out that these fragments can result from fracture of normal erythrocytes by fibrin filaments which result from the intravascular coagulation which is a feature of this disease. They were able to experimentally reproduce the formation of these cell fragments by passing blood through a glass or nylon fiber mesh. They also observed the formation of the *vacuoles* which have been described in keratocytes. It appears that each time the two internal surfaces of the red cell membrane come into contact, they can fuse. This contact

may be brought about by a variety of mechanisms. However, the most frequent seems to be passage through a fibrin network. It appears that contact with heart valve prostheses *per se* will not capable of crushing or fracture red cells.

Some authors have called the keratocyte a *burr cell,* a name which does not seem appropriate, others have used the term *spur cell.* Moreover, the different techniques for observing cells make critical comparison of the various cells that have been described difficult, if not impossible.

Torocytes (from the Greek word meaning *torus*). These have a thickened peripheral rim (« doughnut-cell »), and may arise from desiccation of the thick portion at the beginning of a smear. This artifact can also be seen after fixation with glutaraldehyde for scanning microscopy when the preparation is dried slowly.

Knizocytes (from the Greek word meaning *pinch*). This appearance, although frequently encountered, is nevertheless of interest for study of red cell structure. They may be seen in a variety of circumstances. In fresh blood it may be observed in certain hemolytic anemias, e.g. hereditary spherocytosis. In addition, if a suspension of cells is examined between slide and coverslip and an erythrocyte permitted to adhere to the slide, gentle deformation of the cell by a current of liquid in the preparation may produce this appearance (BULL, 1972).

Dacryocyte (from the Greek word meaning *tear drop*). This cell is a common feature of many severe anemias and especially of thalassemia major. Its mechanism of formation is controversial.

RED CELL FRAGMENTATION

Fragmentation of a red blood cell has been defined (WEED, 1968) as loss from the cell of a piece of membrane which may or may not contain hemoglobin. The « piece » may be large enough to be seen easily with the light or phase microscope, somewhat smaller and visible only with electron microscopy or even so small as to only be detectable biochemically. Such loss does not necessarily imply immediate hemolysis. However, it results in a decrease in the surface area-to-volume ratio of the cell, i.e. the cell becomes more spherical (JENSEN, 1969). Fragmentation occurs *in vitro* and *in vivo* in response to alterations in the cellular micro-environment and it may also occur because of intrinsic changes in the cell itself (or a combination of the two).

Fragmentation may result in loss of different sized pieces of membrane. The phenomenon of erythrophagocytosis (POLICARD and BESSIS, 1953) in which antibody-injured cells are bisected by a phagocyte without loss of hemoglobin, results in the loss of very large fragments. The non-phagocytized portion of the cell becomes spherical. This fragment will have a decreased survival. Intermediate sized fragments can be produced by thermal injury (BROWN, 1946) and high concentrations of urea (PONDER, 1955) which induce budding. Fragmentation and « microspherulation » occur frequently in sickle-cell anemia (JENSEN, 1969).

TABLE I

Names	Meaning in Greek	Comments
Discocyte	Disc.	Normal biconcave erythrocyte.
Echinocyte (I, II, III)	Sea urchin.	Different stages of crenation.
Stomatocyte (I, II, III)	Mouth.	Different stages of cup shapes.
Acanthocyte	Spike.	a-betalipoproteinemia and acquired syndromes.
Codocyte	Bell.	Thin bell-shaped erythrocyte (target cell = codocyte flattened on a surface, or a cell with a single spicule in the dimple).
Dacryocyte	Tear drop.	Frequent in thalassemia.
Drepanocyte	Sikle.	S. hemoglobin.
Elliptocyte	Oval.	Congenital or acquired.
Keratocyte	Horn.	Results of one or more incomplete cuts.
Knizocyte	Pinch.	Triconcave erythrocyte.
Leptocyte	Thin.	Flattened cell.
Megalocyte	Giant.	Oval macrocyte in megaloblastic states.
Schizocyte	Cut.	Result of a complete cut.
Spherocyte	Sphere.	Spherical shape without change in volume (macro = swollen sphere : micro = reduced volume).
Torocyte	Torus.	Thinned dimple (center) with redistribution of Hb to periphery.

Nomenclature of red cell shapes.

TABLE II

Compound names (*)	Comments
Sphero-echinocyte I	Fine spicules.
Sphero-echinocyte II	Few small spicules.
Sphero-stomatocyte I	Small hilum remaining.
Sphero-stomatocyte II	Irregularities at site of hilum.
Sphero-schizocyte	Sphered schizocyte.
Echino-schizocyte	Crenated schizocyte.
Drepano-echinocyte	Echinocyte which undergoes sickling.
Drepano-stomatocyte	Stomatocyte which undergoes sickling.
Echino-acanthocyte	Echinocytic change in an acanthocyte.
Stomato-acanthocyte	Stomatocytic change in an acanthocyte.

(*) Any name (examples : Drepanocyte, Elliptocytes, etc.) combined with a prefix (macro, micro, lepto, etc.).

Nomenclature of red cell shapes.

Finally, cells which have become depleted of ATP, either through incubation *in vitro* without a nutrient substrate for 36 hours, through storage at 4° C for several days under suboptimal conditions (BESSIS and MANDON, 1972) or prolonged storage under blood bank conditions (HARADIN, WEED and REED, 1969) will first undergo the echinocyte transformation and then begin to fragment by budding and losing microspherules from

TABLE III

Fragmentation	process by which schizocytes are produced.
Microspherulation	as in preserved blood or sickle cell anemia or burns or by urea.
Myelin forms	or preferably : membrane strands.
Annulus ..... *Dimple* ..... *Spike or spicule*	surface topography of the red cell.
Red cell membrane ..... *Red cell ghosts*	their definition depends on the investigator, his point of view and method of investigation.

Special Terminology for Red cell Structure.

their surface. The biochemical counterpart of the loss of myelin forms from the red cell surface is a measurable loss of all membrane lipids from the cell (e.g. cells stored under blood bank conditions for 8 weeks lose 30 % of their membrane lipid).

Microspherules are limited by membranes and usually contain some hemoglobin. Intermediate stages between these microspherules and myelin forms may be seen. Section of these cells also reveals internal myelin forms (BESSIS and MANDON, 1972).

DISCOCYTE-ECHINOCYTE TRANSFORMATION

FIG. 1. — *Discocyte.* Normal biconcave red cell.

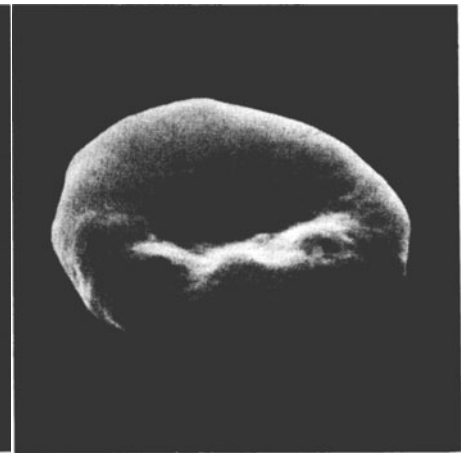

FIG. 2. — *Echinocyte I.* An irregularlay countoured discocyte.

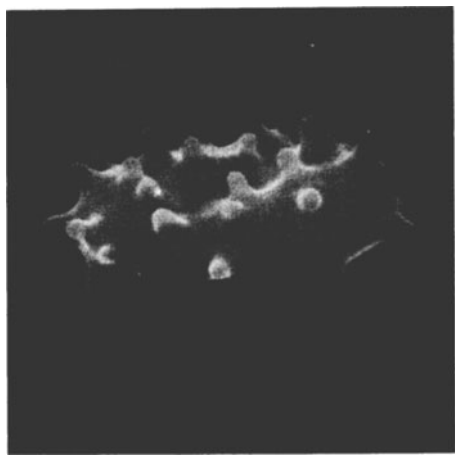

FIG. 3. — *Echinocyte II.* A flat red cell with spicules.

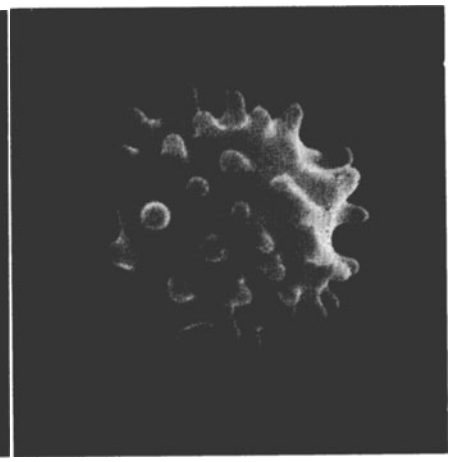

FIG. 4. — *Echinocyte III.* An ovoid or spherical cell with 30 to 50 spicules evenly distributed over its surface (see BRECHER and BESSIS, 1972).

SPHERO-ECHINOCYTES

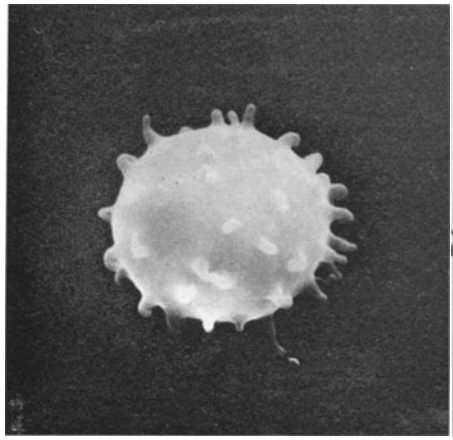

FIG. 5. — *Sphero-echinocyte I.* A sphere with short spicules.

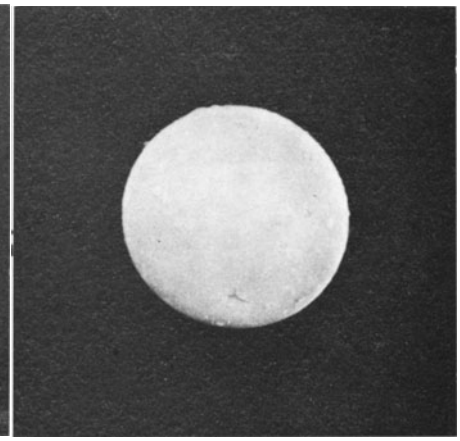

FIG. 6. — *Sphero-echinocyte II.* A sphere with spicules which can only be clearly seen with the scanning electron microscope (too small to be visible with the optical microscope).

DISCOCYTE-STOMATOCYTE TRANSFORMATION

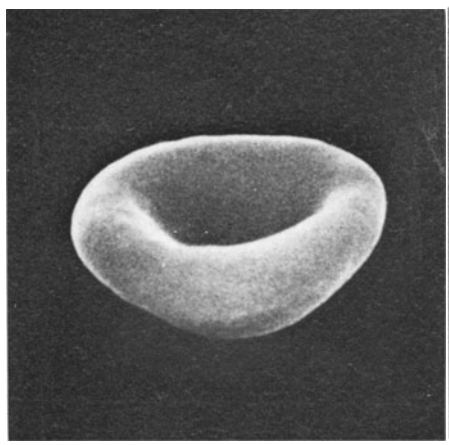

FIG. 7. — *Stomatocyte I.* This shape may be seen in certain hereditary and acquired hemolytic disease states (fig. 50). The stomatocytic this appearance may result from normal cells, being unadequately prepared for examination with SEM.

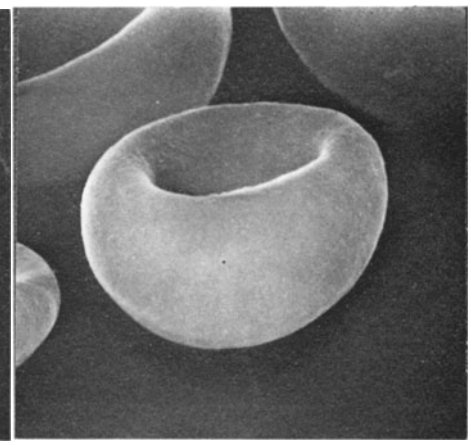

FIG. 8. — *Stomatocyte II.* If the pH is decreased, the cells assume a more profound cup shape and at very low pH, sometimes the ring shape tends to become triangular (WEED and BESSIS, 1973).

SPHERO-STOMATOCYTES

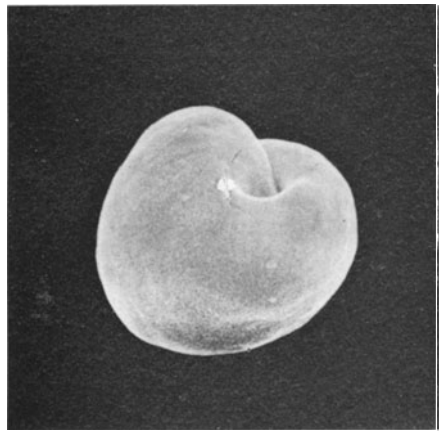

FIG. 9. — *Sphero-stomatocyte I.* Stomatocyte with a minimal central depression. At low pH (3.0) the cup-shaped cell is converted into a bean-shaped, nearly spherical configuration which still has a hilum-like structure.

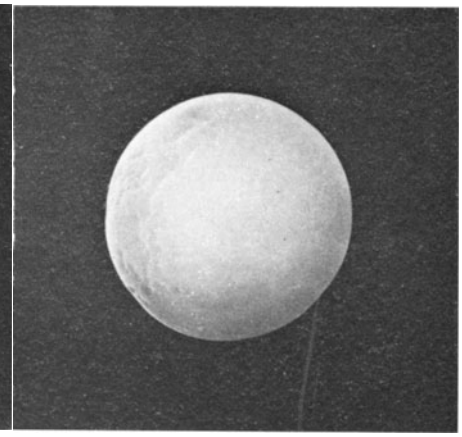

FIG. 10. — *Sphero-stomatocyte II.* A sphere with an irregular by contoured region on one side (which can only be clearly seen with the scanning electron microscope).

STOMATOCYTOSIS

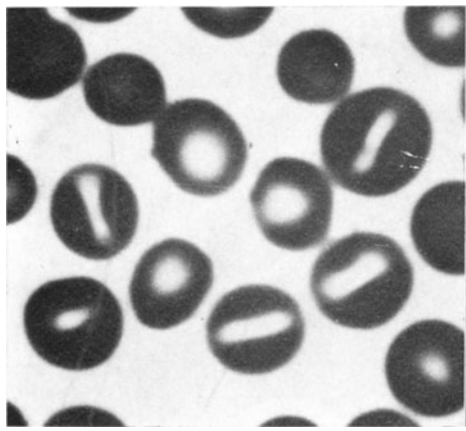

FIG. 11. — *Stomatocytes.* These are cells whose central portion appears elongated instead of circular on a smear. Stomatocytes are seen in certain hemolytic anemias for which this shape change appears to be characteristic (hereditary stomatocytosis).

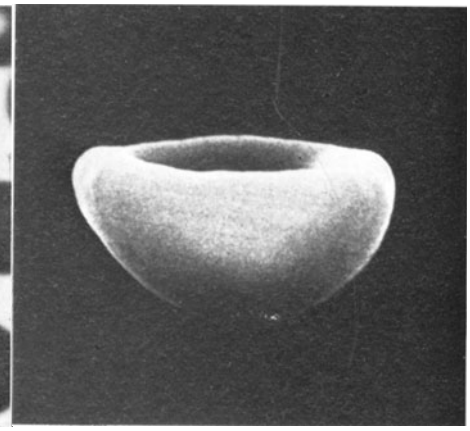

FIG. 12. — *Stomatocyte.* From a case of acquired stomatocytosis.

ACANTHOCYTOSIS

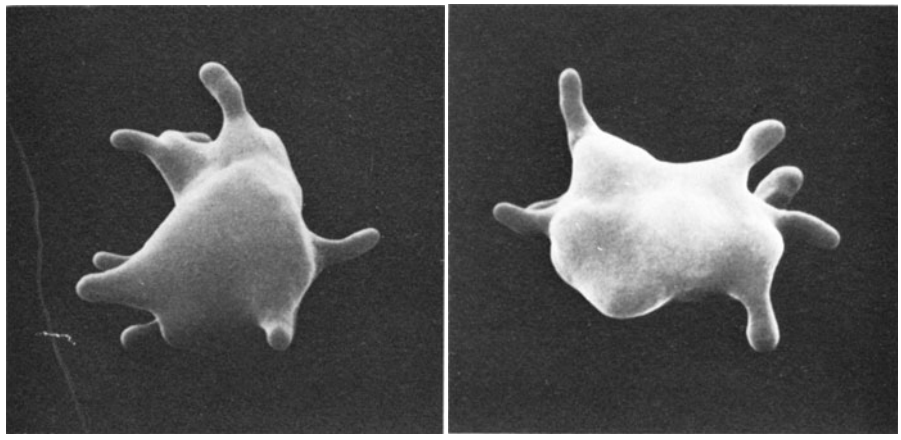

FIG. 13 and 14. — *Acanthocytes.* These cells have a characteristic shape and they bear only a superficial resemblance to echinocytes. They have much fewer spicules which are irregularly arranged and bent back at their tips.

ECHINO-ACANTHOCYTES

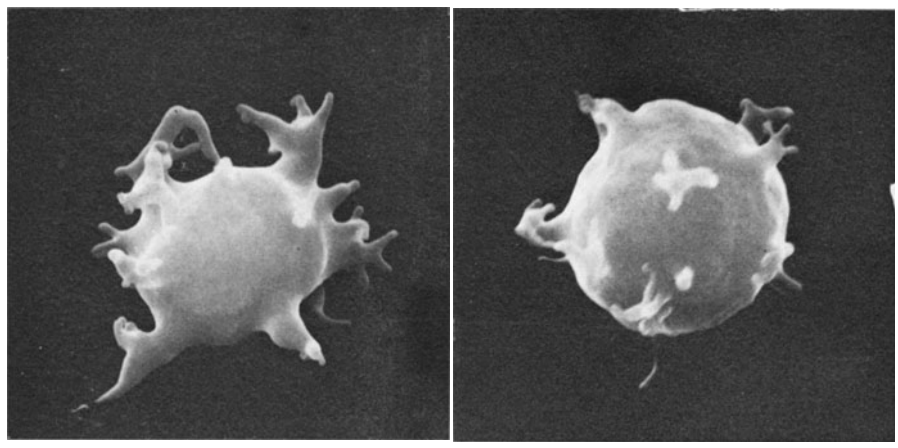

FIG. 15. — *Echino-acanthocyte.* When acanthocytes are exposed to echinocytogenic factors, new finer spicules appear, superimposed on the primary spicules (KAYDEN and BESSIS, 1970).

FIG. 16. — *Sphero-echino-acanthocyte.*

STOMATO-ACANTHOCYTES

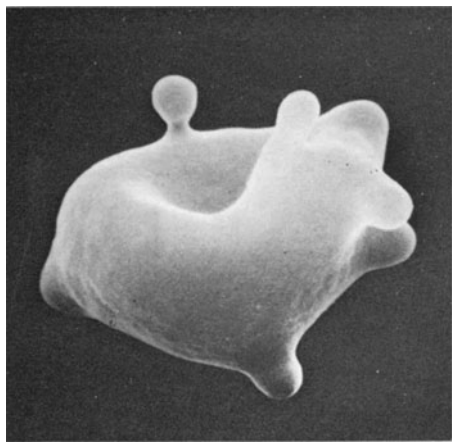

FIG. 17. — *Stomato I-acanthocyte.* These cells are produced by exposing acanthocytes to chloropromazine or low pH (4.0) to (WEED and BESSIS, 1973).

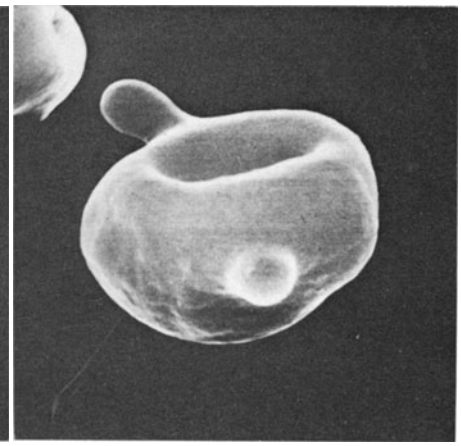

FIG. 18. — *Stomato II-acanthocyte.*

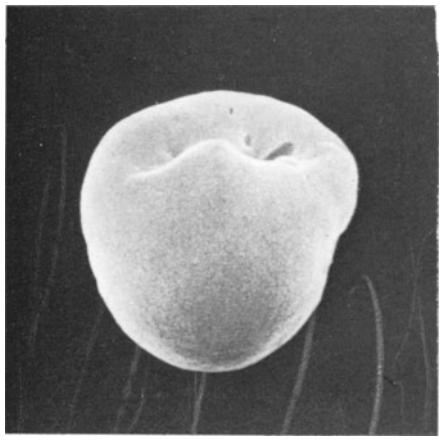

FIG. 19. — *Sphero-stomato I-acanthocyte.* The spicules tend to disappear. The cell is transformed into a sphere with a dimple and spicule remnants.

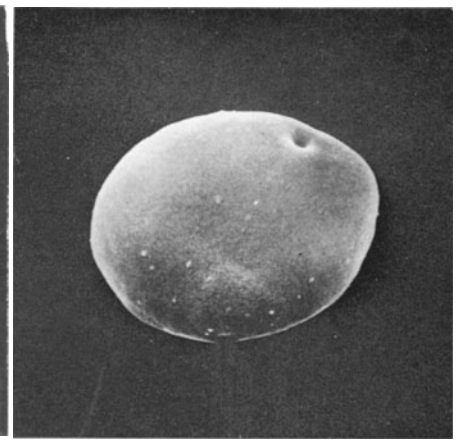

FIG. 20.

Sphero-stomato II-acanthocyte.

CODOCYTES

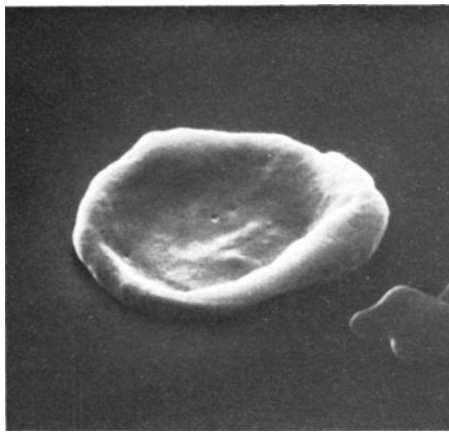

FIG. 21. — *Codocyte* I. Hypochromic erythrocyte (uni-concave discocyte).

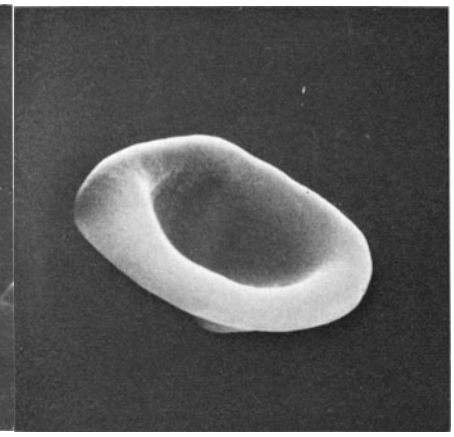

FIG. 22. — *Codocyte II.*

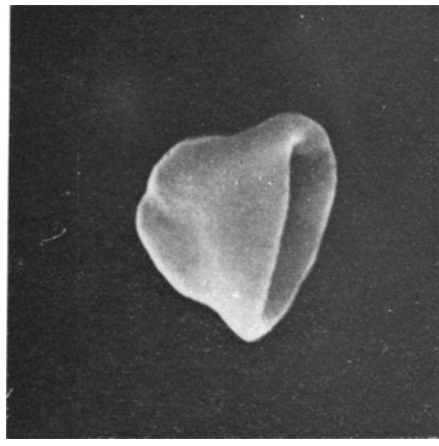

FIG. 23. — *Codocyte III.*

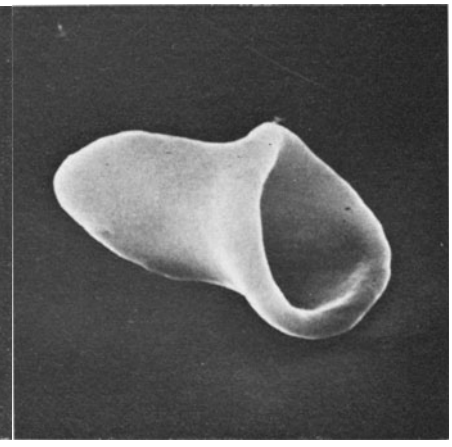

FIG. 24. — *Codocyte IV.*

CODOCYTES AND TARGET CELLS

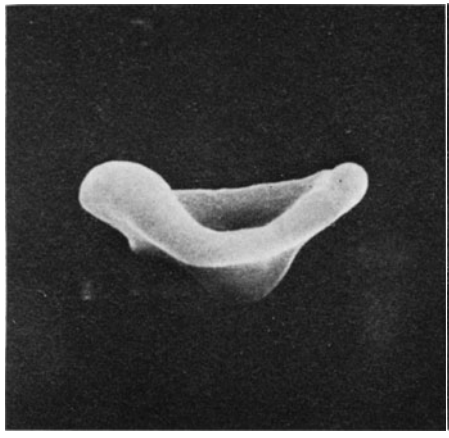

FIG. 25. — *Codocyte II.* Compare with figure 27.

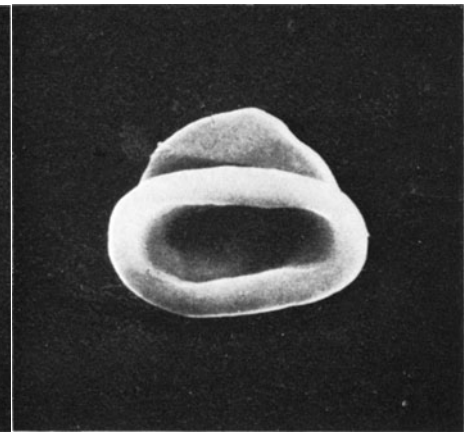

FIG. 26. — *Codocyte IV.* Compare with figure 28.

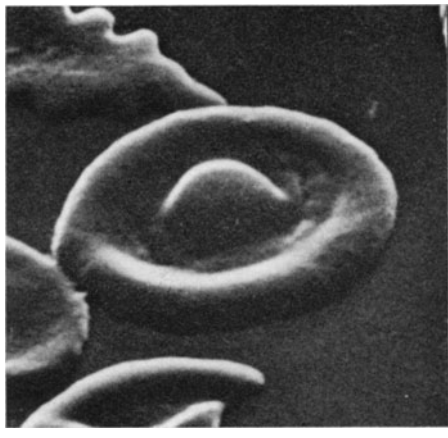

FIG. 27. — *Target cell.* When a smear is prepared, often these bell-shaped, hypochromic erythrocytes (codocytes I and II) will take the appearance of « target cells » when they come to rest flat on the slide (stained smear).

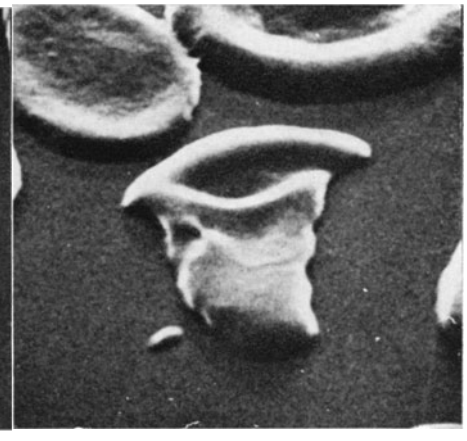

FIG. 28. — *Helmet cell.* When a smear is prepared, these codocytes III and IV often come to rest on their side and they will have the appearance of « helmet cells » (stained smear).

DREPANOCYTES

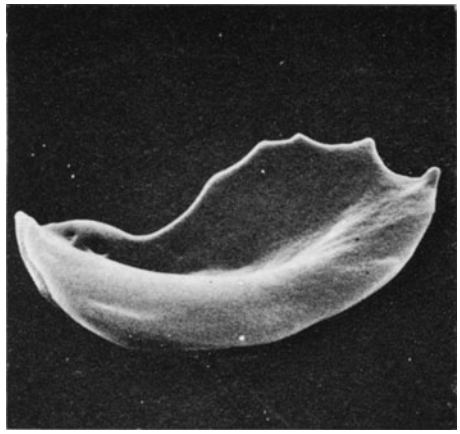

FIG. 29. — *Drepano-discocyte.* (Discocytic sickle cell). Note the development of deformation in a single plane.

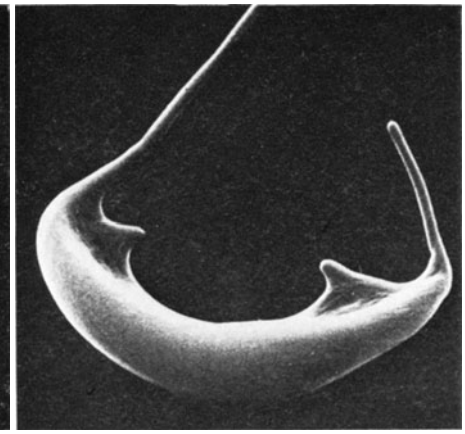

FIG. 30. — *Drepano-discocyte.* The spicules along the edge correspond to bulk of hemoglobin rods.

DREPANO-ECHINOCYTES I

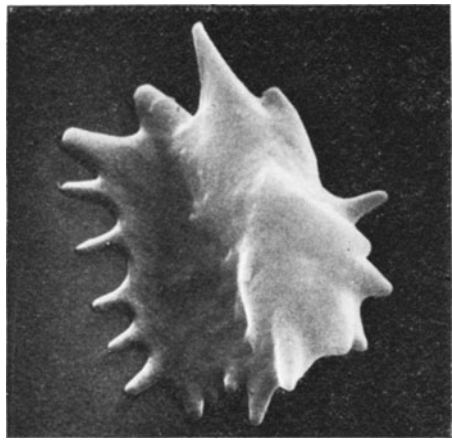

FIG. 31. — *Drepano-echinocyte I.* They are produced by making Echinocyte I from Hb S containing discocytes and then removing the oxygen.

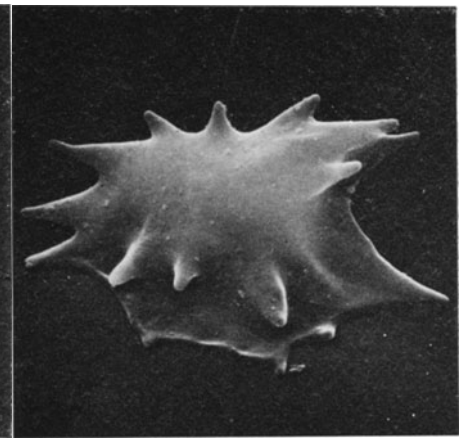

FIG. 32. — *Drepano-echinocyte I.* They produce the form frequently described as holly-leaf cell.

DREPANO-ECHINOCYTES III

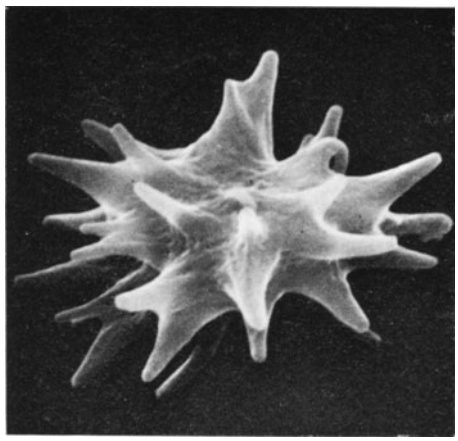

FIG. 33. — *Drepano-echinocyte III.* Note the three-dimensional development of spicules.

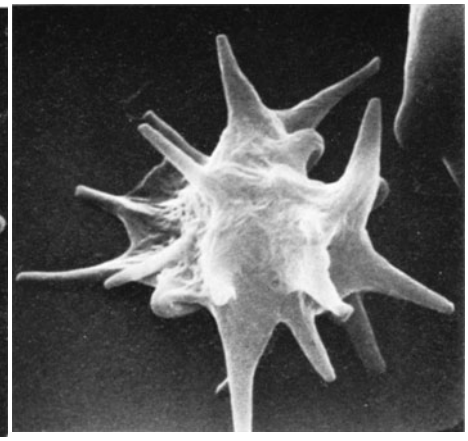

FIG. 34. — *Drepano-echinocyte III.* Note the « spicules » truncated tips and the folds in the membrane.

DREPANO-STOMATOCYTES

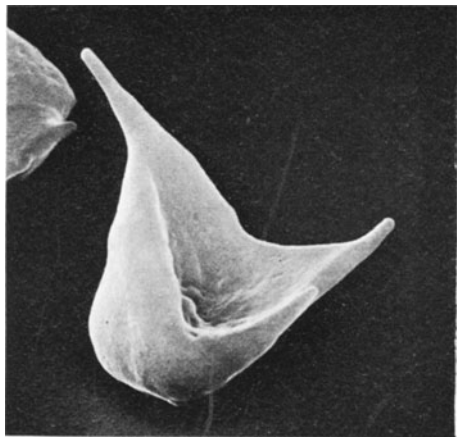

FIG. 35. — *Drepano - stomatocyte.* These cells are produced by making stomatocytes from Hb S-containing discocytes and then removing the oxygen.

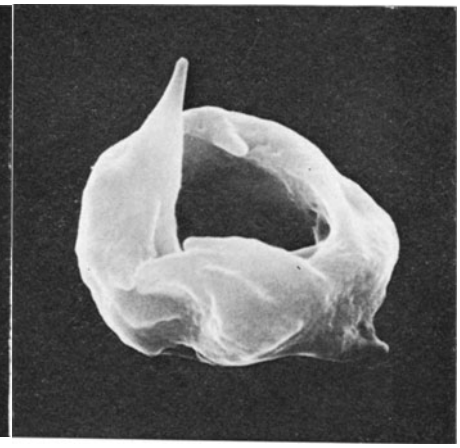

FIG. 36. — *Drepano - stomatocyte.* Note the combination of a cup-shaped cell and spicules due to the Hb rods.

ELLIPTOCYTES

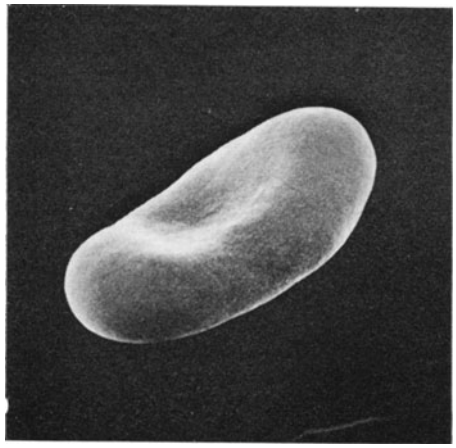

FIG. 37. — *Elliptocyte II.*

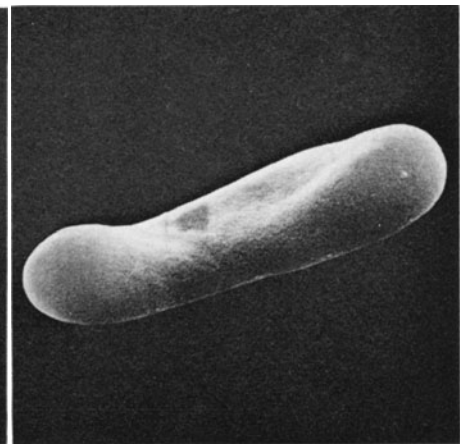

FIG. 38. — *Elliptocyte IV.*

ECHINO-ELLIPTOCYTES

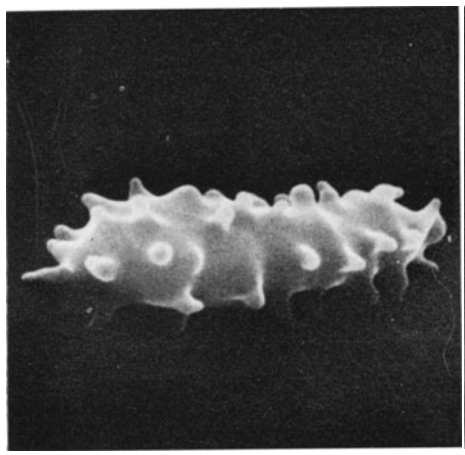

FIG. 39. — *Echino-elliptocyte.*

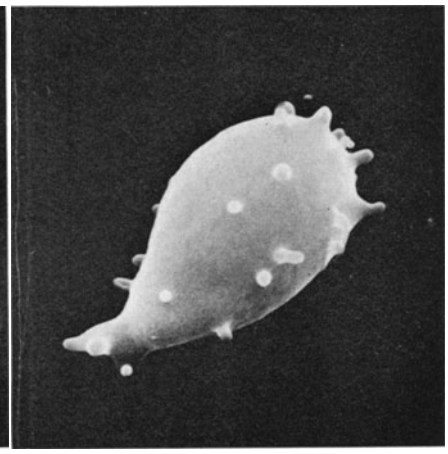

FIG. 40. — *Sphero-echino-elliptocyte.*

CODO-ELLIPTOCYTES

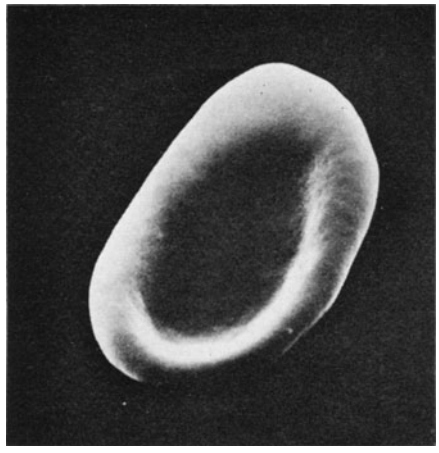

FIG. 41. — *Codo-elliptocyte III.* This combination is occasionally seen in some hypochromic anemias. It is the so called « ellipto-target cell » (AKSOY and ERDEM, 1968) when spread on a smear.

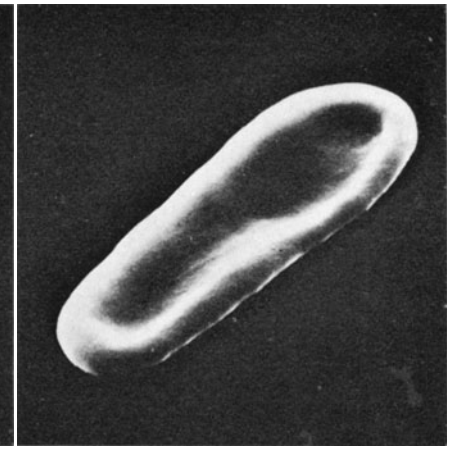

FIG. 42. — *Codo-elliptocyte IV.*

KERATOCYTES

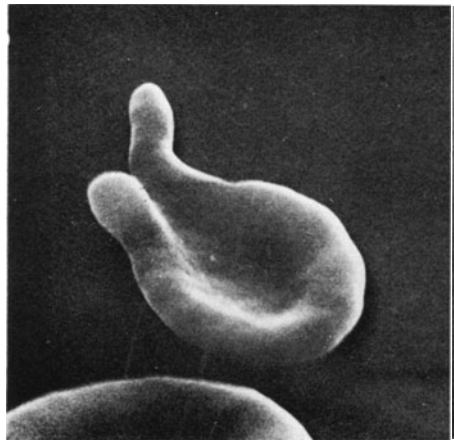

FIG. 43. — *Keratocyte.* Erythrocytes which are torn so as to have one or more pointed projections but whose volume is normal, distinguishing them from schizocytes.

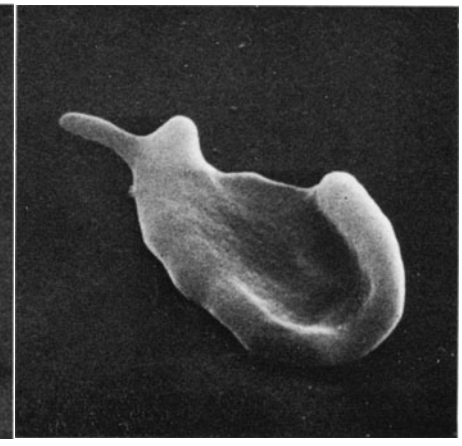

FIG. 44. — *Keratocyte.* In some cases, this form can be mistaken for other forms of spiculated red cells.

KERATOCYTES AND SCHIZOCYTES

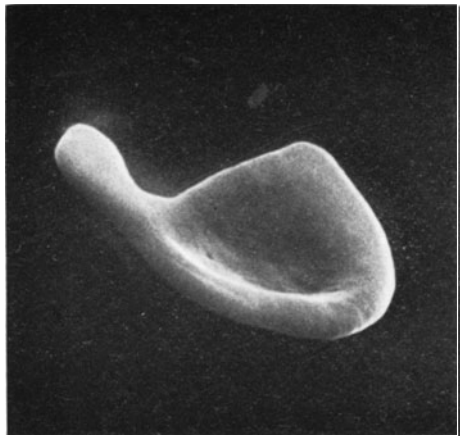

FIG. 45. — *Keratocyte.* Resulting from an almost comple cut. The damaged cells is are in the discocyte form.

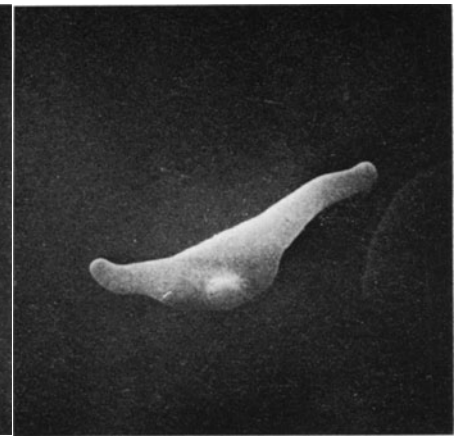

FIG. 46. — *Schizocyte.* BRAIN et al. (1962), BULL et al. (1968) and BULL and KUHN (1970) pointed out that these fragments can result from fracture of normal erythrocytes by fibrin filaments which result from intravascular coagulation.

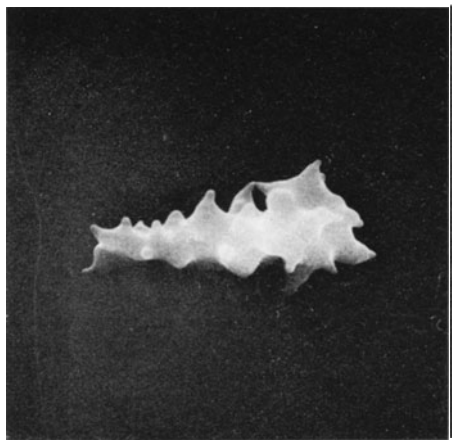

FIG. 47. — *Echino-schizocyte.*

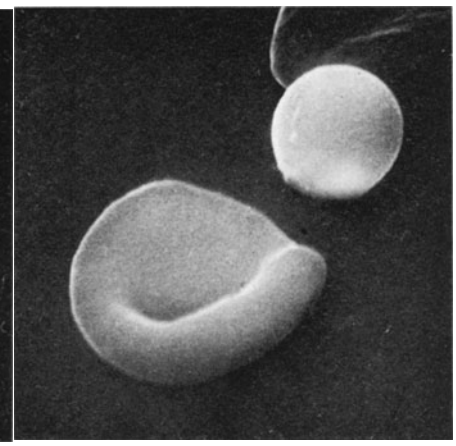

FIG. 48. — *Disco-and sphero-schizocytes.* Schizocytes become ultimately sphero-schizocytes before hemolysis. In some instances they assume this shape when a red cell is cut in two during phagocytosis.

SPHEROCYTES

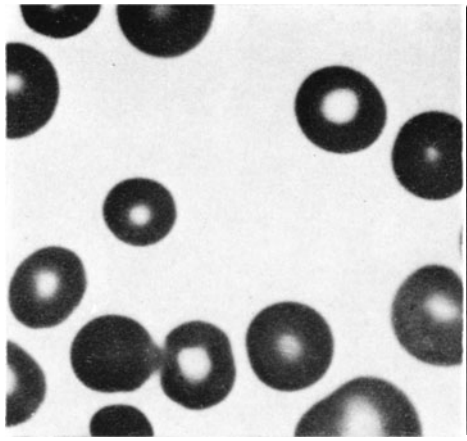

FIG. 49. — *Spherocytes.* On a smear, they appear hyperchromic and microcytic and, in fact, their volume is slightly decreased and the mean hemoglobin concentration slightly increased (hereditary spherocytosis).

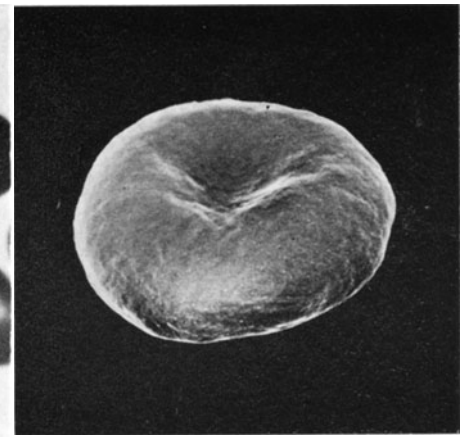

FIG. 50. — *Spherocyte I.* A classification of spherocytes has been proposed, based on their diameter-to-thickness ratio. The term spherocyte is used to describe a variety of appearances which are etiologically and morphologically dissimilar.

KNIZOCYTES

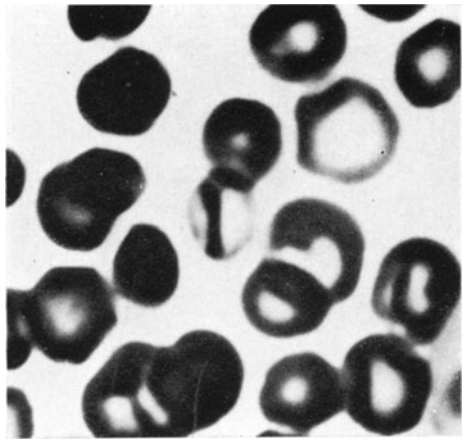

FIG. 51. — *Knizocyte* as seen on a smear. See commentary, figure 52.

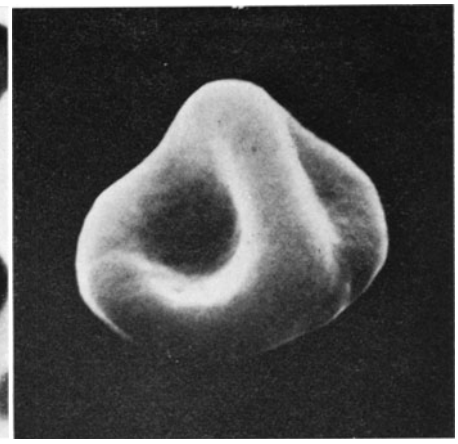

FIG. 52. — *Knizocyte :* triconcave red cell. This shape may be seen in several circumstances (see text). It may also occur as an artifact of desiccation, during preparation for scanning electron microscopy.

DACRYOCYTES

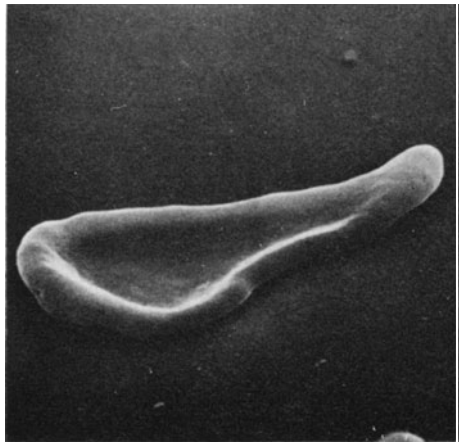

FIG. 53. — *Dacryocyte* (Thalassemia).

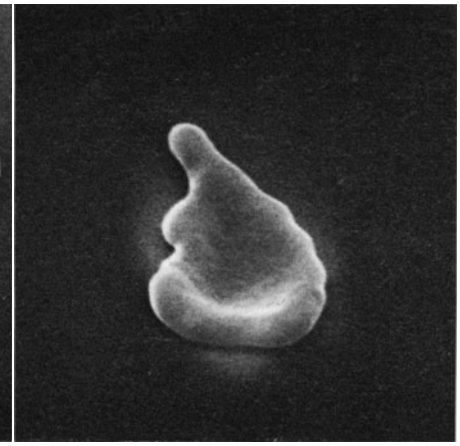

FIG. 54. — *Dacryocyte* (Thalassemia).

ECHINO-DACRYOCYTES

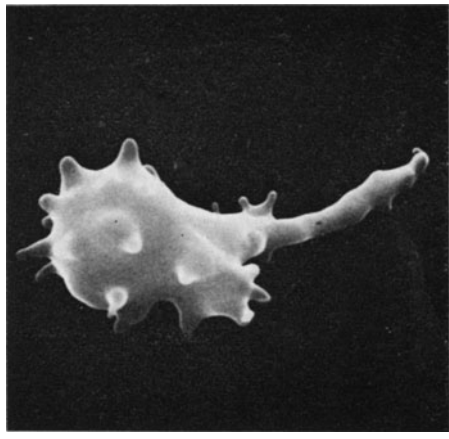

FIG. 55. — *Echino-dacryocyte produced* by treating fresh dacryocytes with sodium oleate (BESSIS and DE BOISFLEURY, 1970).

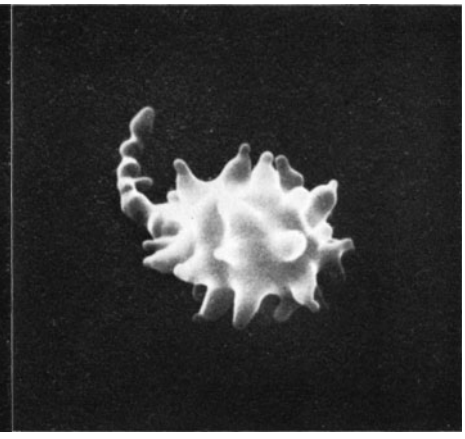

FIG. 56. — *Echino-dacryocyte* obtained by aging thalassemic blood (24 hours at 37° C).

TOROCYTES

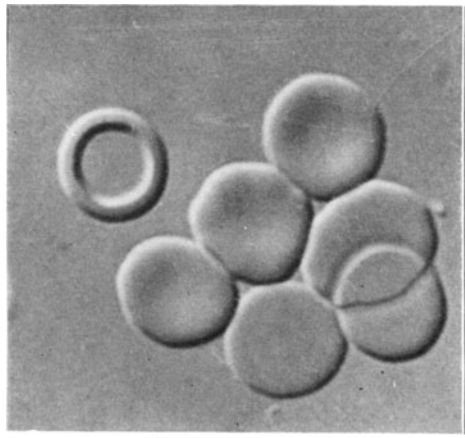

FIG. 57. — *Torocyte.* In some cells, between slide and coverslip, the hemoglobin may become redistributed to the cell periphery to give the cells a ring shape. This is an artifact that is potentially important.

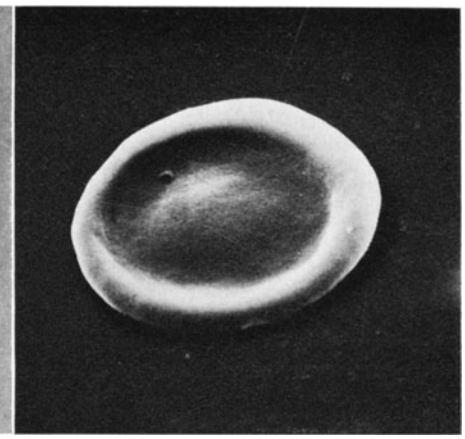

FIG. 58. — *Torocyte.* This cell is encountered in disorders in which the cellular hemoglobin concentration is decreased, such as iron deficiency or thalassemia.

TOROCYTES (ARTIFACTUAL)

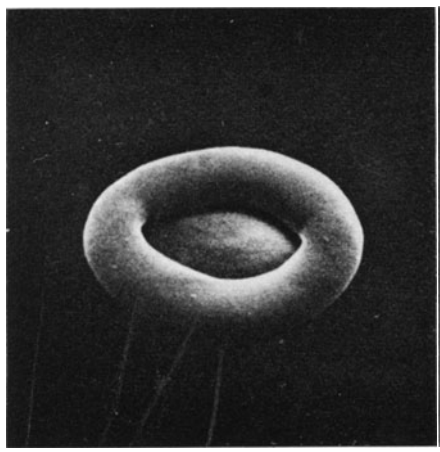

FIG. 59. — *Torocyte.* Cells with this appearance may be produced by desiccation of the thick portion at the beginning of the smear. Torocytes or « doughnut cells » have a thickned peripheral rim.

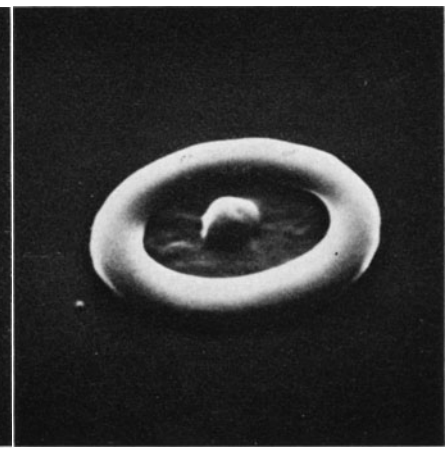

FIG. 60. — *Torocyte* with a « target cell » appearance. This artifact can be seen after fixation with glutaraldehyde for scanning microscopy when the preparation is dried slowly (BESSIS and WEED, 1972).

LEPTOCYTES

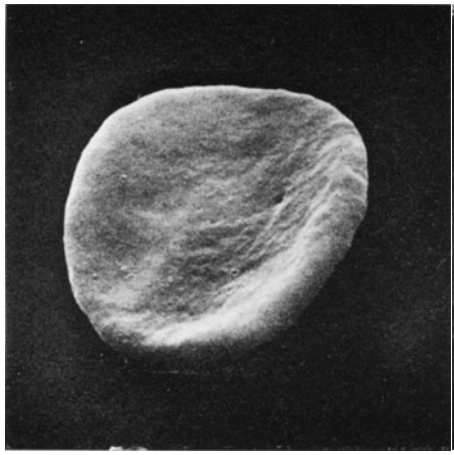

FIG. 61. — *Leptocyte* due to hypertonicity. If red cells are exposed to hypertonicity in a plasma containing medium the biconcave discocytes assume the appearance of a flattened cake.

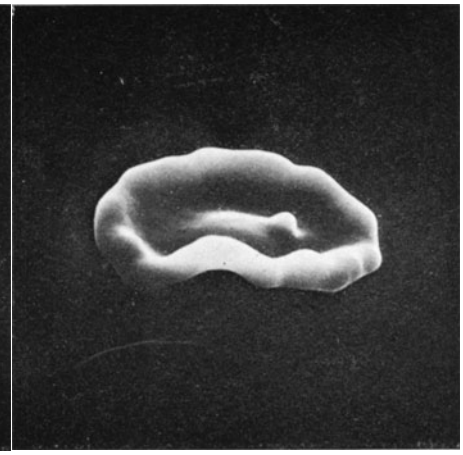

FIG. 62. — *Echino I-lepto-torocyte.* This combination gives the appearance of a « target cell ».

MICROSPHERULATION AND MYELIN FORMS

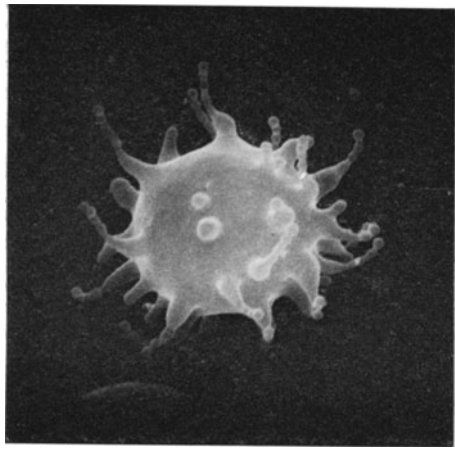

FIG. 63. — *Microspherulation.* Microspherulation is a form of red cell fragmentation frequently seen in preserved blood.

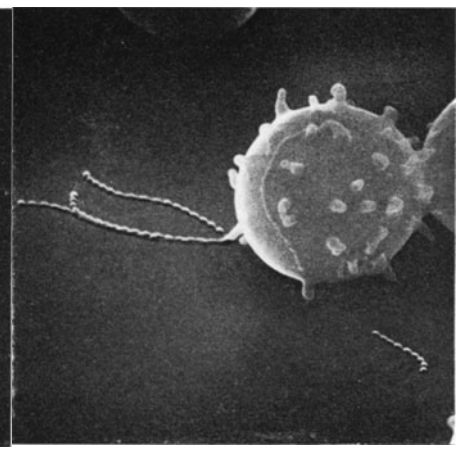

FIG. 64. — *Myelin forms.* This picture represents a red cell damaged by aging (BESSIS and MANDON, 1972).

RED CELL STRANDS

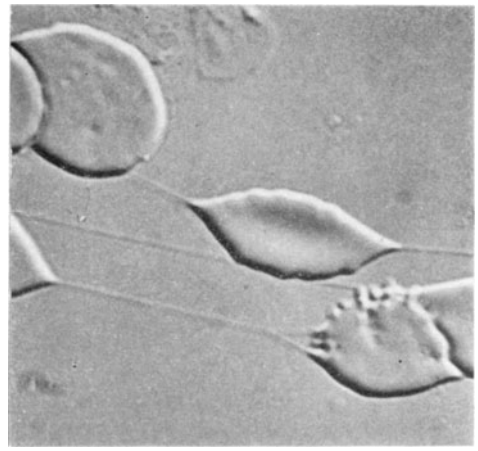

FIG. 65. — *Red cell strands.* When a force is applied to disrupt a clump of agglutinated red cells, the red cells can be seen to be adhering to one another. Often red cells which are stretched out between two clumps assume a fusiform appearance with the ends of the spindle shaped cells being attached to neighboring cells by thin filaments. These filaments are very elastic. When they break off they give rise to myelin forms (BESSIS and al., 1951).

ACKNOWLEDGEMENTS

The choice of this nomenclature has been the topic of many a discussion, especially with the participants of the round table on the shape and the structure of red cells, organized at the Institut de Pathologie Cellulaire, the 21st and 22nd of June, 1972.

It want to thank everyone who have offered suggestions and criticisms.

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GENERAL DISCUSSION

LESSIN : The introduction of five revolutionary terms is likely to meet with opposition of hematologists first, because this represents a complete reconstruction of existing terminology, second, because blood is usually examined by light microscopy and on stained smears, and hence three-dimensional shapes are not evident. Thirdly, the mode of formation of a given shape is not always implicit in the observed morphology.

BESSIS : To answer your first point, I think that when one observes new phenomena and understands the meaning of old ones it becomes necessary to use a new terminology in order to avoid confusion.

To your second argument, let me answer that the scanning electron microscope brings out new morphological details. Once they have been observed and interpreted, they permit a re-evaluation of whatever artifacts are present on blood smears, and I have shown many examples of this in the photographs you have just seen.

Finally, in answer to your last point, I agree that we do not know yet how all poikilocytes are formed, but we have made significant progress in this area and there is certainly more to come. One should remember that a given shape may result from different mechanisms; hence the necessity to search for new morphological details and a refinement of the nomenclature (e.g. sphero-echinocytes I and II).

HOFFMAN : What are the morphological stages characterizing the transition from an echinocyte to a smooth sphere ?

BESSIS : The cell becomes progressively more spherical and the spicules progressively smaller until they are no longer distinguishable with the scanning microscope. At this point I think the sphero-echinocyte is no more reversible.

HOFFMAN : Concerning the acanthocyte, I understood some years ago that someone had turned such cells back into disks by using detergents. What is your opinion Dr. BESSIS ?

BESSIS : It sounds hard to believe ! The only way we have been able to change acanthocytes (from a patient with abetalipoproteinemia) into something else is by using stomatocyte producing agents, like chorpromazine. In this case, what we obtained was a *stomato-acanthocyte.*

WEED : I think that if you look at a cup cell from the top you may easily be confused and take it for a disk. It is conceivable that this is what these people have seen ?

BESSIS : Cationic detergents will indeed produce cup cells. Were these cationic detergents to your knowledge, Dr. HOFFMAN ?

HOFFMAN : No, I would rather think they were anionic detergents.

BRECHER : I vaguely remember a report of someone having also reverted acanthocytes by using Tween-80. Would this substance by itself induce the cup shape, Dr. WEED ?

WEED : Yes, if you remember in my table, Tween-80 figures in the list of stomatocytic agents. Again, it is possible that there who described the effects of Tween-80 on acanthocytes, not being perfectly aware of the distinction between disk and cup, may have mistaken the two shapes. This, I think, is very pertinent and emphasizes the importance of fine morphological observation of red cells.