RED CELL MEMBRANE CHANGES IN ACQUIRED HAEMOLYTIC ANAEMIAS

ESSAY

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ABBREVIATIONS

AA	Amino acid.
Ab	Antibody.
ACHE	Acetyl choline esterase.
Ag	Antigen.
AHA	Acquired hemolytic anaemia.
ALA	Aminolevulinic acid.
Ank	Ankyrin.
ATPase	Adenosine triphosphatase.
Ca	Calcium.
cAMP	Cyclic adenosine monophosphate.
Fl	Fento liter.
G6PD	Glucose 6-phosphate dehydrogenase.
GAPD	Glyceraldehyde phosphate dehydrogenase.
GL	Glycolipid.
GP	Glycophorin.
GSL	Glycosphingolipid.
HA	Hemolytic anaemia.
Hb	Hemoglobin.
Ig	Immunoglobulin.
IHA	Immunohemolytic anaemia.
IL-1	Interleukin-1

K	Potassium.
LCAT	Lecithin cholesterol acyl-transferase.
Mg	Magnesium.
MoABs	Monoclonal antibodies.
MW	Molecular weight.
Na	Sodium.
PC	Phosphatidyl choline.
PE	Phosphatidyl ethanolamine.
PI	Phosphatidyl inositol.
PNH	Paroxysmal nocturnal hemoglobinuria.
PS	Phosphatidyl serine.
RBC	Red blood cell.
RES	Reticulo-endothelial system.
Rh	Rhesus.
RNA	Ribonucleic acid.
SM	Sphingomyelin.

CONTENTS

INTRODUCTION

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AIM OF THE WORK

Three major changes can take place that lead to premature destruction of the *RBC*. Firstly, immunological process in the form of circulating antibodies; these can be produced in response to foreign *RBC* antigens (allo-antibody), to self-antigens (auto-antibody) or to drugs bound to *RBC* membrane or plasmaproteins (**Zupanski et al., 1987**).

Secondly, alteration of the environment leads to change of *RBC* surface characteristics. Thirdly, alteration of the circulating system in such a way that leads to inability for *RBC* to be circulated (**Baca and Gibbons, 1988**).

AIM OF THE WORK:

This work aims to provide updated changes of the red cell membranes in acquired hemolytic anaemias.

REVIEW OF LITERATURE

RED CELL MEMBRANE BIOLOGY

The mature adult human *RBC* has a diameter of 7-8 μm, a surface area of 140 μm^2 and a volume of 90 Fento Litre *[FL]*. The red cell membrane serves as a barrier to help maintaining a concentration of various ions and metabolites in the interior of the cell which differs markedly from the concentrations found in the exterior. It contains pumps and channels for the movement of sodium *[Na]*, potassium *[K]* and calcium *[Ca]* ions and facilitate transport of glucose and other small molecules (**Palek et al. 1981**).

The red cell membrane is responsible for the biconcave shape as the *RBC* is a discocyte with an excess surface area. This important factor allows the 7-8 μm *RBC* disc to traverse 3 μm capillaries and sinusoids. It is tough enough to resist fragmentation under pressure in arterioles and across the heart valves and has advantage to recoil to resume its stable discocytic shape after deformation (**Schrier, 1985**). The red blood cell membrane is composed of 52% proteins, 40% lipids, 8% carbohydrates attached to both proteins called glycoproteins and lipids called glyolipids (**Brain, 1978**).

Components Of The Red Cell Membrane:

Membrane lipids:

They are partially responsible for many of membrane physical characters, as the passive cation permeability and the mechanical flexibility of the *RBC* can be influenced by modifying the lipid composition of its membrane (**Corrocher et al., 1987**).

All of the *RBC* lipids is in the membrane, half is phospholipid and half is free cholesterol and there is no esterified cholesterol. The cholesterol in the membrane of a mature *RBC* is in equilibrium with plasma cholesterol, small amounts of glycolipids, glycerids and free fatty acids are also present (**Allan et al., 1980**).

Membrane phospholipids:

There are four major classes of phospholipids. Their relative concentration is tabulated in table [1]. Phospholipids containing only one fatty acid have lipophilic and hydrophilic characters and they tend to accumulate at phase interfaces. This change in relative solubility increase both their detergent qualities and their rate of exchange between the cell membrane and plasma. Lysophosphatides in low concentration can cause lysis of the cell membrane. In even smaller concentrations, they can produce the profound, irreversible shape changes "echinocytogenesis" in the membrane (**Delaunay et al., 1991**).

Table [1]: Membrane phospholipids and their relative concentrations. **After Cooper (1978).**

Phospholipid	**% of total phospholipi**
Phosphatidyl choline (lecithin) (PC)	30.5
Phosphatidyl ethanolamine (PE)	27.3
Sphingomyelin (SM)	26.0
Phosphatidyl serine & phosphatidyl inositol (PI)	13.2
Lysolecithin	1.3
Phosphatide & phosphatidic acid	1.7

Arrangement of lipids in the membrane:

The phospholipids in the *RBC* form a lipid bilayer (**Chasis and Shohet, 1987**). The polar head of each lipid layer face outward away from the center of the membrane into the hydrophilic environment of the cytoplasm and the plasma, while the fatty acid tails extend inward forming a central hydrophobic core of the membrane (**Bretscher, 1972**) [Figure 1].

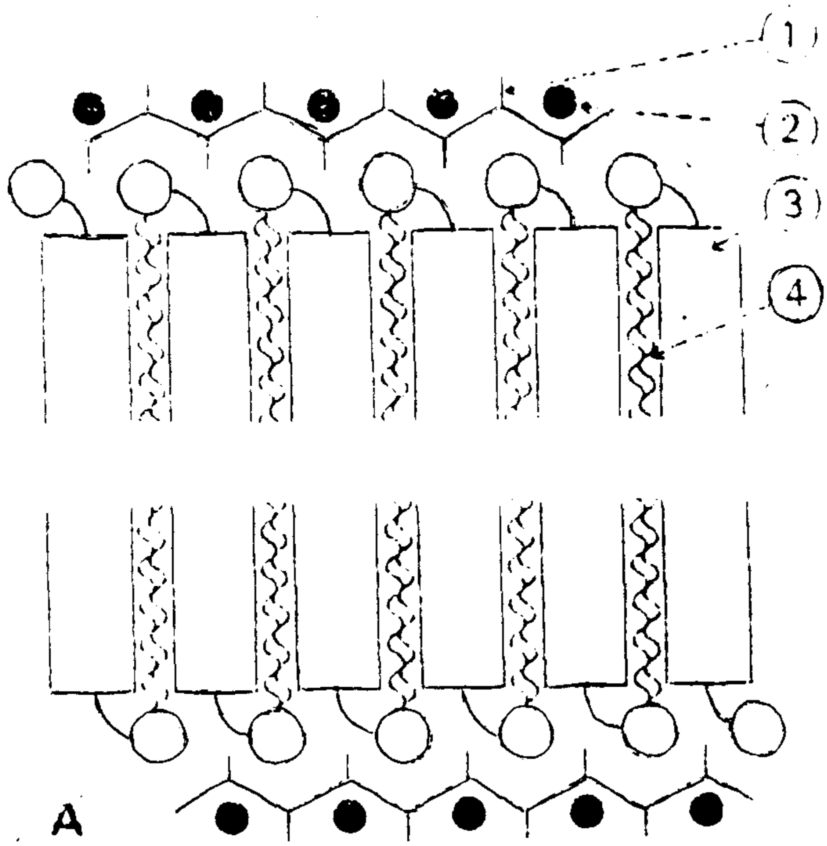

Figure [1]: Model of membrane membrane structure.

A = Lipid bilayer membrane model.

1 = Protein polypeptide chain.

2 = Mucopolysaccharide.

3 = Phospholipid: circles indicate the polar ends.

4 = Cholesterol.

Cited from Singer and Nicholson (1972).

The cationic phosphatidyl choline *[PC]* and sphingomyelin *[SM]* being found predominantly in the outer half of the bilayer, the anionic phosphatidyl ethanolamine *[PE]* and phosphatidyl serine *[PS]* are confined to the inner half of the bilayer. The phospholipid 'Flipase", an enzyme that translocates acid phosphatides from the outer to the inner half of the bilayer is likely to be involved in maintaining this asymmetry (**Zalhowski et al., 1988**). The maintenance of asymmetric distribution appears to be the result of slow and symmetric rate of phospholipid movement across the two lipid monolayers and the coupling of the membrane bilayer to the membrane skeleton which serves as a scaffolding for the lipid bilayer (**Tchernia et al., 1981**).

Cholesterol:

Cholesterol comprises 25% of the *RBC* membrane lipid and is present in a 1:1 molar ratio with phospholipids. Red blood cell membrane cholesterol is in continual exchange with plasma cholesterol and is therefore, affected by changes in body lipid transport (**Ronald and Pittiglio, 1981**). Cholesterol probably is equally distributed between the two lipid layers. It interacts with phospholipid to form "intermediate gel state". Thus as compared with pure phospholipid membranes, membranes containing cholesterol are less fluid and more viscous (**Bull and Brailsford, 1973**).