

THE SIGNIFICANCE OF HAEMIC PLASMA CELLS IN VARIOUS INFECTIVE CONDITIONS.

BY R. A. HICKLING.

*(From the Institute of Pathology, Charing Cross Hospital
Medical School, London.)*

THE investigation of infective maladies from the haematological aspect has always presented numerous difficulties, which have deterred all those other than professed haematologists from employing a method capable of supplying valuable information. It is essential first to emphasise that no single constituent of the blood picture can alone be regarded as being of diagnostic significance: the whole aspect of the morphological change in the blood must be considered.

The plasma cell, as seen in the blood, has many of the characters of the lymphocyte, but possesses an intensely basophilic cytoplasm: cells of this type with a central nucleus are commonly referred to as "Türk cells," while the term plasma cell is reserved for similar elements with eccentric nuclei surrounded by fine vacuolation of the cytoplasm. Cells with these characters are almost entirely absent from normal blood, but, in many infections, appear in considerable numbers: their significance can be deduced only after consideration of anomalies in other types of leucocyte.

The complete examination of blood should include enumeration of erythrocytes and leucocytes, calculation of colour index, and a "differential" count of the white cells in stained films; in many cases the last method is sufficient for diagnostic purposes if a suitable technique be employed. Fine details of leucocytic structure can best be elucidated by the modified panoptic method (Piney): Films are made on cover slips, and placed face downwards in a watch-glass: Jenner's stain (1 c.c.) is run in under it and allowed to act for three minutes, then, being diluted with an equal amount of distilled water, is left for another minute. The film is not washed but is directly transferred, face downwards, to the Piney neutrophile stain (obtainable from Gurr, New King's Road, London) for seven to ten minutes: it is then washed with distilled water, dried without heat and mounted in Canada balsam (preferably neutral, if permanent preparations are required).

The diseases to which most of the present investigation has been devoted are rubella, scarlatina and measles; the results of the quantitative examinations are seen in the table.

It will be noted that, in rubella, there is always a considerable percentage of plasma cells and allied forms, but that this is not a specific change because, in measles and in scarlatina, they may also be present, but much less frequently.

Leucocytosis is the rule in scarlet fever but a rarity in measles and in rubella.

Eosinophile leucocytes are scanty in measles and rubella but persist, often in increased numbers, in scarlatina: nevertheless, the variations in number are too great to enable a definite conclusion to be drawn with certainty.

There is a difference between scarlatina on the one hand and measles and rubella on the other in that, in the first disease, the majority of the leucocytes are neutrophile polymorphonuclear, while in the other two lymphocytes predominate.

It is obvious that, if any practical deductions are to be drawn from haematological examination in these diseases, it is necessary to make a series of

Rubella.

Case	Leucos	P.	E.	B.	Hy.	Ly.	Plasma	Türk	Day of disease
I.	9,500	46.4	8.4	0.6	5.2	34.0	2.8	2.6	2
	7,400	41.8	5.6	0.2	3.8	38.2	3.6	6.8	5
II.	7,600	54.3	1.0	0.5	5.8	31.2	2.0	5.2	3
III.	7,100	53.5	2.5	0.2	9.2	27.3	4.0	3.3	?
IV.	11,200	54.6	0.6	0.6	4.4	37.2	1.0	1.6	?
	13,700	52.4	0.6	0.6	11.0	34.4	1.0	—	? plus 3
V.	9,400	39.2	3.8	0.2	16.4	29.6	8.8	2.0	3
VI.	12,700	53.0	1.6	0.4	9.2	29.2	3.8	2.8	2
VII.	6,900	52.5	2.0	0.5	9.0	22.5	13.0	0.5	3
VIII.	7,600	57.3	2.0	—	7.3	31.6	1.3	0.3	2
IX.	?	46.0	1.0	—	13.0	31.0	8.0	1.0	?
X.	?	70.0	—	—	7.0	19.0	3.0	1.0	?
	?	29.0	1.0	—	12.0	49.0	5.0	4.0	? plus 2
XI.	?	50.0	—	—	7.0	32.0	8.0	3.0	?

Disease	Case	Leucos	P.	E.	B.	Hy.	Ly.	Pl. C.	Türk	Myelos	Day
Scarlatina	I	26,100	92.0	1.5	—	1.5	4.8	0.2	—	—	2
	II	18,400	77.3	2.3	—	4.2	15.5	0.5	—	0.2	3
	III	16,700	89.8	2.5	0.2	4.0	3.5	—	—	—	?
	IV	19,700	93.3	1.0	—	3.2	2.5	—	—	—	?
	V	?	43.4	3.6	—	6.4	23.8	1.4	—	21.4	?
		25,200	53.0	2.0	—	10.0	29.0	—	—	6.0	? plus 3
	VI	?	80.0	—	0.5	7.5	12.0	—	—	—	?
Measles	I	9,500	40.0	—	0.2	6.8	48.6	4.4	—	—	3
	II	16,400	71.5	—	—	7.0	20.0	1.5	—	—	4
	III	8,000	58.0	—	—	3.0	38.0	1.0	—	—	?
And pertussis	IV	28,200	44.0	1.0	0.4	5.0	46.4	3.2	—	—	?
ditto	V	22,600	57.4	1.0	—	14.4	25.2	2.0	—	—	?
Serum rash	I	14,100	85.0	2.0	—	2.0	11.0	—	—	—	?

finer observations on the structure of the individual cell types. In almost all maladies associated with toxæmia there are well-marked changes in the polymorphonuclear neutrophile leucocytes. These cells normally present a very faintly acidophile (pink-staining) cytoplasm which is regularly filled with very minute granules: the nucleus has a more or less contorted form, in which dark blue staining areas of basi-chromatin are sharply separable from pale pink oxy-chromatic portions so that a sort of "scaly" appearance of the nucleus is typical. In diseases in which there is alteration of these cells by "toxic" substances, changes occur both in cytoplasm and in nucleus. The cytoplasmic changes are similar but usually less intense than those seen in leucocytes in pus: the granules are collected into small aggregations, *i.e.* are

clumped, so that some areas of the cytoplasm are free from granulation. In more severe stages, it is common to find one or more small vacuoles. The nucleus first shows disappearance of the demarcation between basi- and oxy-chromatin so that no pink areas can be seen in it: the result seems to depend upon abnormal processes of diffusion between the two nuclear substances. This condition is a transient one, and the more distinctive stage is one in which almost all structure has been obliterated and *pari passu* with this change there is usually decrease both in the size and the complication of the nucleus (pyknosis).

In rubella such "toxic" changes of the neutrophile polymorphonuclear leucocytes do not occur, but in scarlatina they are invariable and severe, while in measles, although invariable, they are often less well marked.

It will be seen that, in any case presenting a large number of plasma cells in the blood, it is necessary to suspect the possibility of rubella, but that detailed cytological examination is essential in order to exclude the other two diseases.

The number and arrangement of the nuclear lobes of the polymorphonuclear leucocyte is very variable, and has served as the basis of the "Arneth index," but it will be noted that apparent simplicity of the nucleus may be the result of pyknosis as described above, so that it is possible to use the structure of these cells only as a criterion of the amount of "toxic" injury.

SUMMARY.

The blood picture in *rubella* is characterised by the presence of numerous plasma and Türk cells and by the absence of toxic changes in the neutrophilic leucocytes.

Plasma cells occur also in *scarlatina* and in *measles* but with less regularity and, as a rule, in smaller numbers, but these diseases are always associated with "toxic" changes in the neutrophilic cells.

Such haematological features must be considered in relation with the clinical findings because plasma cells and toxic changes in the neutrophiles may occur in entirely different conditions, *e.g.* in association with the lymphocytosis following almost any acute infective malady.

The haematological method would probably find its greatest application in those cases in which the characters of the rash are not sufficiently well developed to enable a diagnosis to be made in the usual way.

Acknowledgments. My investigations were carried out at the Institute of Pathology of Charing Cross Hospital Medical School, and I am much indebted to the Director, Dr Piney, for assistance and advice, and to Dr Whittaker of the Metropolitan Asylums Board for access to clinical material. Moreover, financial assistance has been afforded by The Virol Research Scholarship which I hold.

(*MS. received for publication 22. v. 1925.—Ed.*)