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Contributors

Webb, Gerald B. 1871-1948.
Williams, William Whitridge.
Bulloch, William, 1868-1941
Royal College of Surgeons of England

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G. B. WEBB, T

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Dr William Bulloch
The London Hospital
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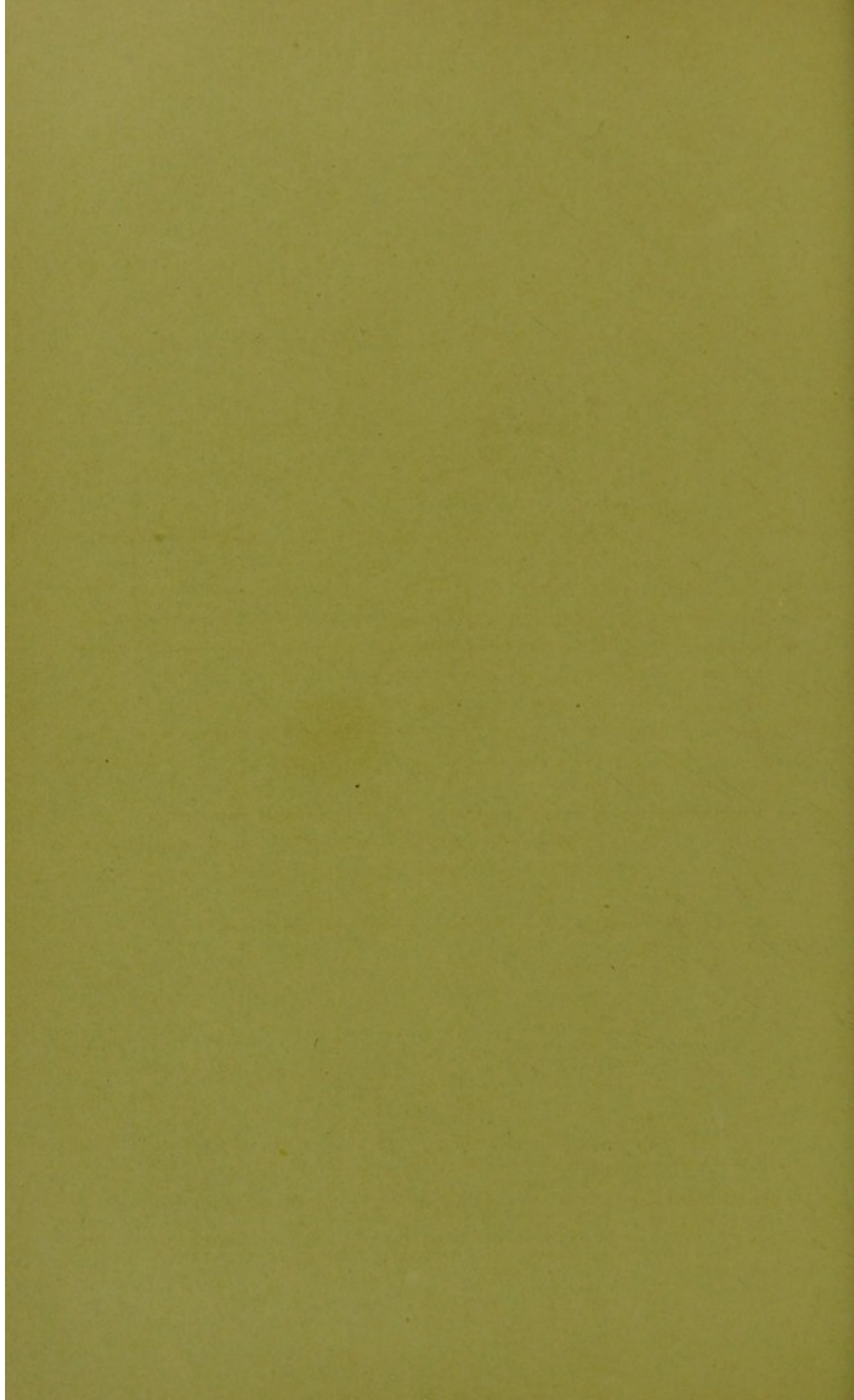
With kindest regards from Gerald B. Webb
who visited his laboratory and lunched
with him in the summer of 1906.

20

Some Hematological Studies in Tuberculosis

G. B. WEBB, M.D., AND W. W. WILLIAMS, M.D.
COLORADO SPRINGS

Reprinted from the Transactions of the Fifth Annual Meeting of the
National Association for the Study and Prevention of Tuberculosis



SOME HEMATOLOGICAL STUDIES IN TUBERCULOSIS

BY G. B. WEBB, M.D., AND W. W. WILLIAMS, M.D.

COLORADO SPRINGS

DURING an epidemic of whooping-cough in the fall of 1908 we attempted to diagnose this disease from an epidemic of catarrhal bronchitis by means of differential leucocyte counts.

Barach¹ in July, 1908, had recalled attention to the increased percentage of lymphocytes which characterized pertussis, and showed the value of differential counts in establishing a diagnosis.

He found both a leucocytosis and a lymphocytosis. The smaller lymphocytes first increased, and the large lymphocytes followed the course of the small ones, reaching their greatest numbers, however, after the small lymphocytes had reached theirs.

After investigating several patients who presented high lymphocyte counts, and yet who clinically we felt certain had only micrococcus catarrhalis infection, we were led to examine the blood of normal children of ages from six to twelve.

Thirty-one counts made on fifteen children resulted as follows:*

CHILDREN

	POLY-MORPHO-NUCLEARS	MONONUCLEARS			EOSINO-PHILES	MAST-CELLS
		Average.	Mean.	Extremes.		
Colorado Springs.....	37.3	60.3	55.0	45-71	2.0	0.4
Sea-level For comparison.....	53.0	46.0	1.0	0.0

It happened that at the same time some experimental work was undertaken

*In all tables the entire non-granular mononuclear cells, comprising small and large lymphocytes, large mononuclears, and transitionals, are grouped under the one heading of mononuclears.

on rabbits to ascertain what blood changes, if any, could be brought about by inoculations of mercury, and in the light of the growing importance placed upon lymphocytes in the problem of immunity to tuberculosis, especial attention was paid to see if these elements could be increased.

The result of differential counts on normal rabbits showed that they too had a higher percentage of non-granular mononuclear cells than sea-level rabbits, as the following figures indicate:

RABBITS

	AMPHOPHILES	MONONUCLEARS (NON-GRANULAR)	EOSINOPHILES	MAST-CELLS
Colorado Springs..... Sea-level, Brinkerhoff and Tyzzer.....	31	65	0	4
	43	52	0	5

These discrepancies between our counts and those of sea-level observers naturally led us to investigate normal adults and also guinea-pigs. The differential counts on the latter will first be stated.

GUINEA-PIGS

	POLYMORPHO- NUCLEARS	MONONUCLEARS	EOSINOPHILES	MAST-CELLS
Colorado Springs.....	19	81	0	0
Sea-level.....	60	40	0	0

The following table indicates the figures we obtained in ninety adults from 143 counts:

NORMAL ADULTS

	POLY- MORPHO- NUCLEARS	MONONUCLEARS			EOSINO- PHILES	MAST- CELLS
		Average	Mean	Extremes		
Colorado Springs.....	54.0	43.6	43.0	28-69	2.0	0.4
Sea-level*.....	61.7	37.4	0.9

* We have taken for comparison the highest sea-level mononuclear average we could find, that of Jolly. ("Handbuch der Technik und Methodik der Immunitätsforschung," 1909, p. 303.) Ehrlich's figures on page 304 give only, at highest, 29 per cent. of these cells.

In addition the following differential leucocyte counts were made as indicated on tuberculous patients:

POLY- MOR- PHONUCLEARS	MONONUCLEARS			EOSINO- PHILES	MAST-CELLS
	Average	Mean	Extremes		
	CURED CASES OF PULMONARY TUBERCULOSIS				
	57 CASES; 100 COUNTS				
55.5	41.7	41	25-63	2.3	0.5
	IMPROVING CASES				
	43 CASES; 114 COUNTS				
5.49	38.5	37	18-54	1.7	0.4
	STATIONARY CASES				
	44 CASES; 125 COUNTS				
63.6	34.4	33	18-50	1.6	0.4
	CASES PROGRESSING UNFAVORABLY				
	43 CASES; 159 COUNTS				
70.8	27.5	27	14-46	1.3	0.4

Through the kindness of Mr. Carl Hedblom blood slides were obtained from eighteen Harvard students and sent to us to be counted. The results were compared with those of eighteen students of Colorado College, Colorado Springs.

POLY- MOR- PHONUCLEARS	MONONUCLEARS			EOSINO- PHILES	MAST-CELLS
	Average	Mean	Extremes		
	STUDENTS, HARVARD				
	18 CASES; 18 COUNTS				
59.5	38	37	27-56	2	0.5
	STUDENTS, COLORADO COLLEGE				
	18 CASES; 18 COUNTS				
48.5	49.5	52	37-66	1.7	0.3

Next it was attempted to ascertain if the increase in the non-granular mononuclear blood-cells was only relative, as the figures given indicate, or absolute, as a total count of these per cubic millimeter of the blood would show.

In estimating the leucocytes per cubic millimeter, the method of Kjer-Petersen² was employed. This method was several times checked by the usual

Thoma-Zeiss apparatus, and gave similar results. Total leucocytes were counted, and simultaneously differential slides made, in thirty-three normals, resulting as follows:

Leucocytes per cubic millimeter:	
Average.....	5589
Extremes.....	3300-9000
Percentage of mononuclears:	
Average.....	47.4
Extremes.....	35-68.5
Mononuclears per cubic millimeter:	
Average.....	2660
Extremes.....	1236-4347

Kjer-Petersen² gives the average leucocyte count per cubic millimeter at sea-level as 4000 to 5000. These figures, however, are not agreed to by Cabot and others, and are stated to be too low.

Most observers agree to 6000 to 7000 as the sea-level average, so that it will be observed our figure at 5589 is not an increase. Huggard³ and Tissier⁴ state also that the number of leucocytes is not increased by altitude.

We now undertook to attempt to find the reason for the increase in the mononuclear element as evidenced by the counts which had been made on rabbits, guinea-pigs, children, and adults.

It was natural to expect altitude to be the factor, as in the increase of erythrocytes.

The following chart (I) is prepared from observations made on a healthy adult male, aged twenty-five, and represents the percentage of mononuclear elements.

The first part of the chart illustrates from December 20, 1908, to January 1, 1909, the changes from the percentage estimated immediately on arrival in Colorado Springs to his departure for New York.

The observations on February 25, 1909, and March 6, 1909, were made during his residence in New York by Dr. T. W. Hastings.

On his return to Colorado Springs, June 19, 1909, will be noticed that the percentage lies in the shaded area which represents the sea-level average.

It will be seen that from eight to eleven days were necessary to obtain the highest change.

Chart II represents graphically the increase in mononuclears in the blood of a doctor from Boston during the dates indicated. The first observation was not made, as in Chart I, immediately on arrival, but after the doctor had been walking and going around some five or six hours.

An initial rise in erythrocytes is seen at times in the first hours of residence

at an altitude, and it might be that the mononuclear count here recorded could be compared to this.

Chart III records observations on three patients—an adult female, a child aged six, and a Yale student.

The latter was an especially interesting case. His mother had died of

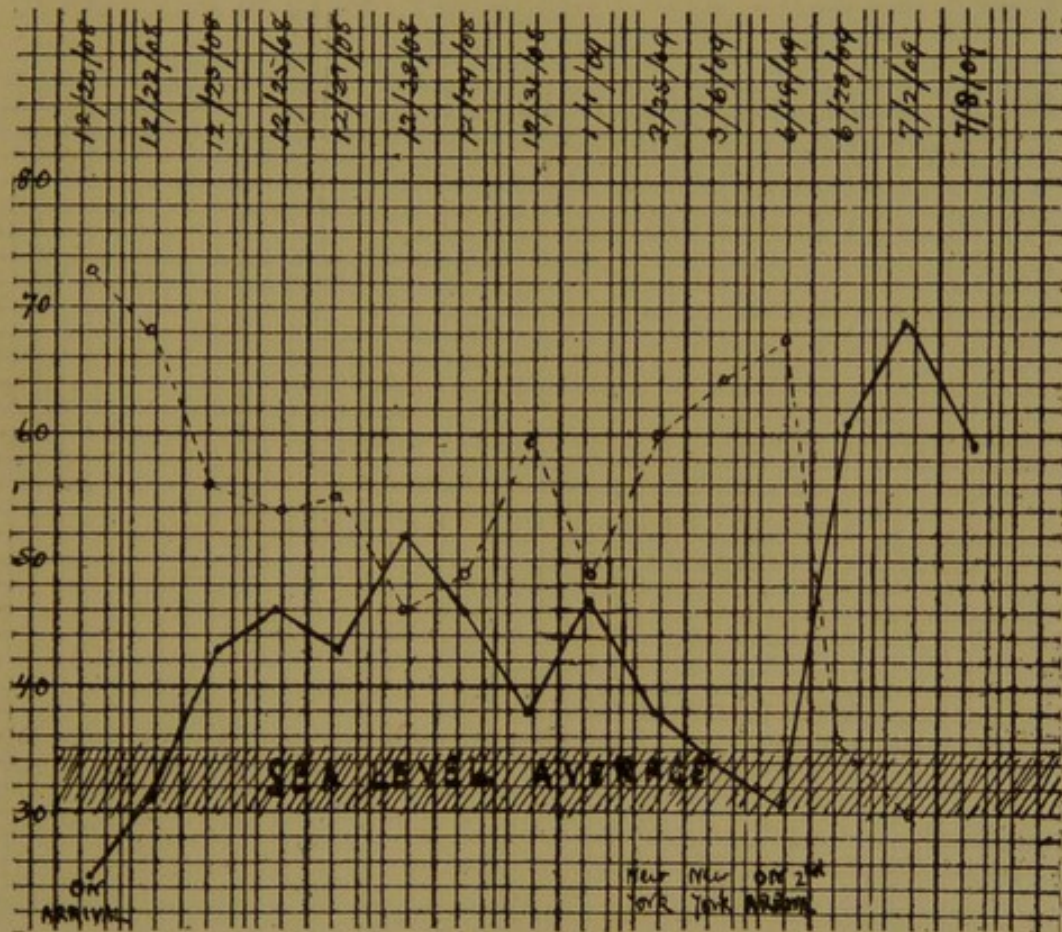


CHART I*

pulmonary tuberculosis soon after his birth, and some three years ago his father had been advised not to send the lad away from Colorado to college. Running down and losing weight at Yale, he returned home, when we found suspicion of pulmonary lesions beginning and tubercle bacilli in the urine.

The observation recorded February 25, 1909, coincided with a complete return to health.

*In the accompanying charts the dotted lines represent the percentages of the poly-morphonuclear cells; the black lines represent the percentages of the non-granular mononuclear cells.

Observations made on other normal cases following their arrival in Colorado Springs without exception yielded similar results, as also happened in tuberculous cases which improved.

The above cases illustrating the fact that the altitude of 6000 feet induced increase in the percentage of mononuclears, it was then attempted to show if descent to sea-level would be accompanied by the reverse, as partly suggested in Chart I.

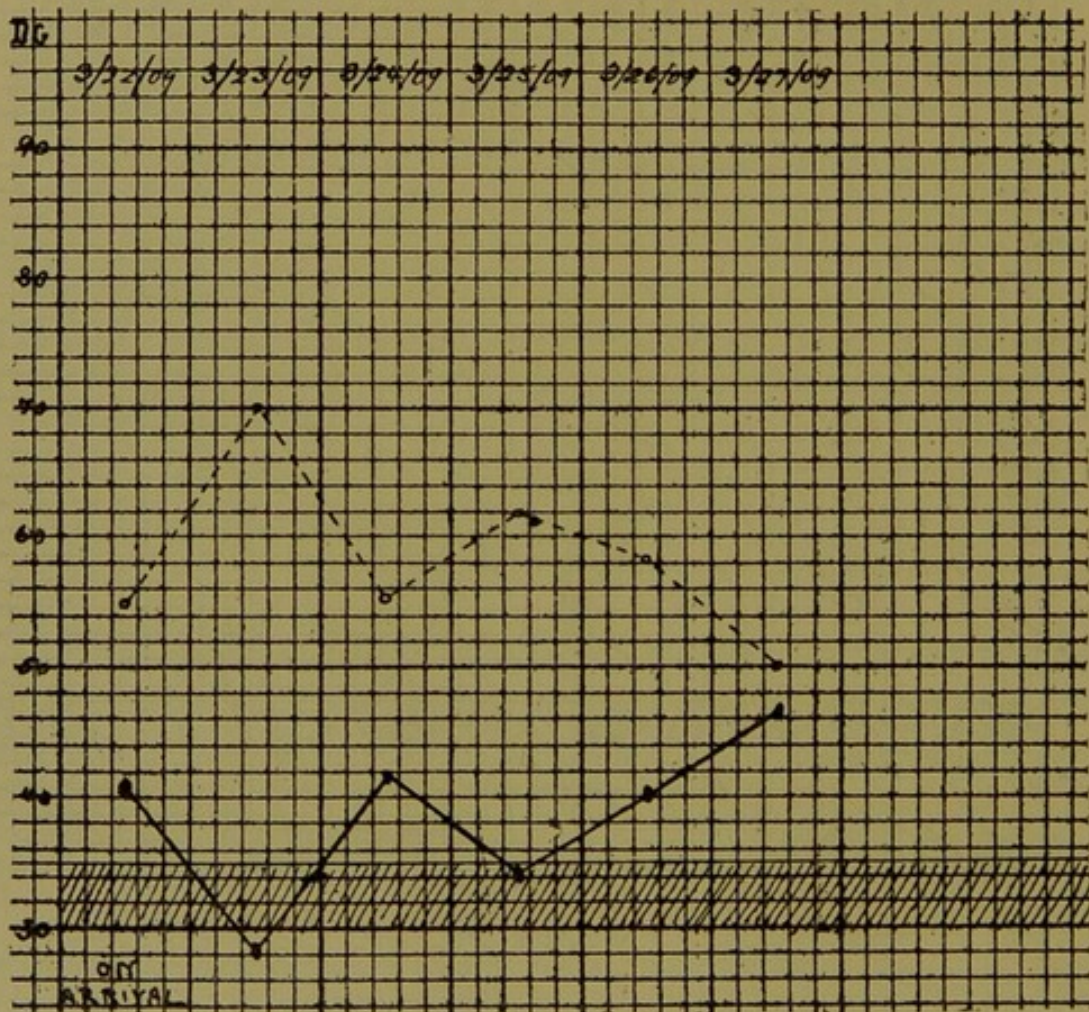


CHART II

In Chart IV are depicted the changes in mononuclear percentage of a patient cured of pulmonary tuberculosis.

The drop on February 23, 1909, coincided with an influenza attack taken just before leaving.

Observations on March 14 and March 24, 1909, were made on slides prepared by the patient during his stay in Boston.

The observation on March 29, 1909, was made on his return, and on April 12, 1909, twelve days later.

It is of interest to note that during the stay in Boston a slight attack of pleurisy developed.

Again it was necessary to discover if the relative increase indicated by the

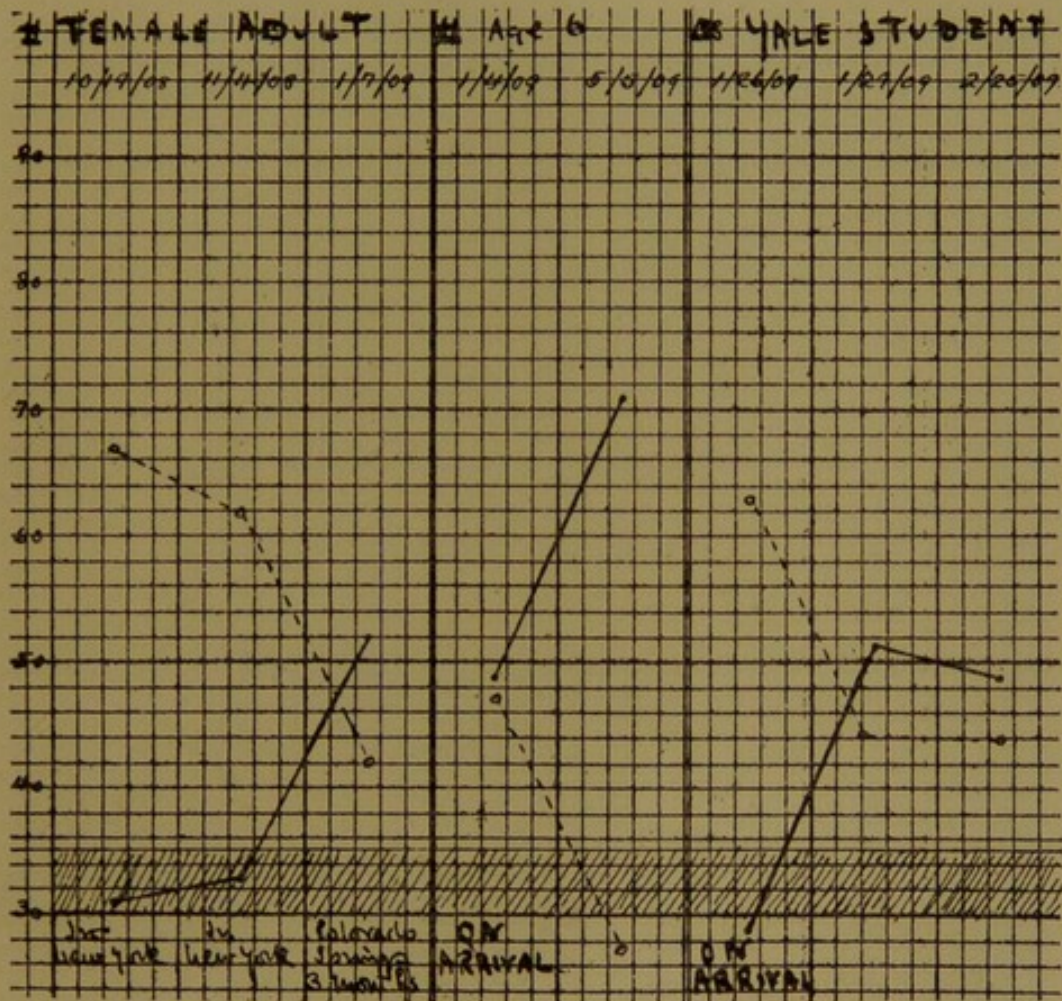


CHART III

differential counts coincided with an absolute increase. The two following charts indicate that this is so.

In Charts V and VI the black figures and lines represent the total mononuclears, the red figures and lines represent the percentage of mononuclears.

An observation made in New York three months previously, of the case represented in Chart VI, gave mononuclear percentage 34. Total number of mononuclears per cubic millimeter, 2400.

Chart VII is from twins A and B, aged thirteen. B received a blow on

the left tibia in a hockey game, while east at school. Cold abscess resulted. Opened December 28, 1908, and Bier's hyperemia applied.

The mononuclear increase coincided with opsonic increase of from 0.7 (three observations) to 1.2 and 1.3.

Chart VIII was prepared from a tuberculous adult, two years in Colorado,

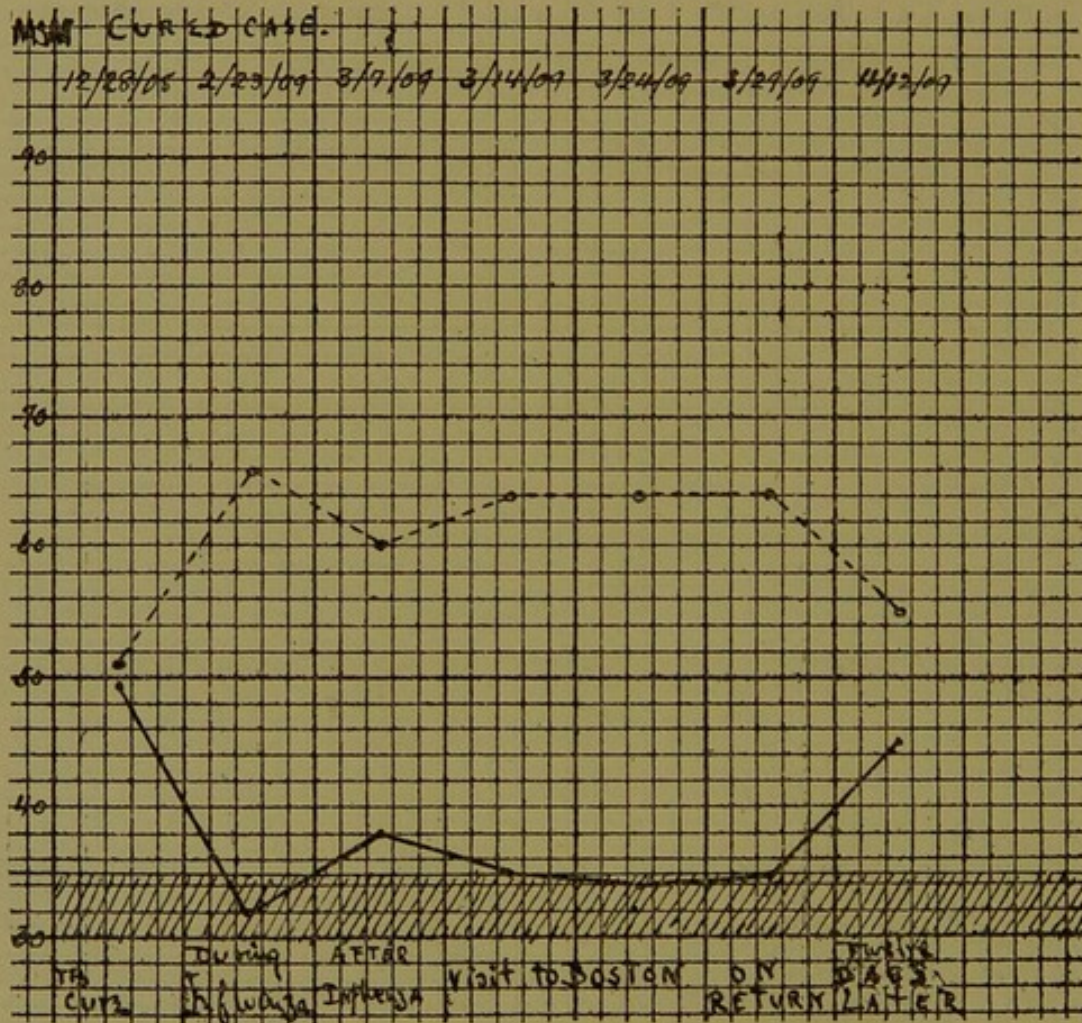


CHART IV

receiving inoculations of living tubercle bacilli, beginning with one on November 30, 1908, and increasing at weekly intervals to 1200 on June 24, 1909. Remarkable improvement was shown.

In consulting the literature regarding changes in the white corpuscles due to altitude, little has been found.

In a balloon ascent of one hour and twenty minutes by Jolly,⁴ November 21, 1901, observations showed that the white corpuscular elements remained the same.

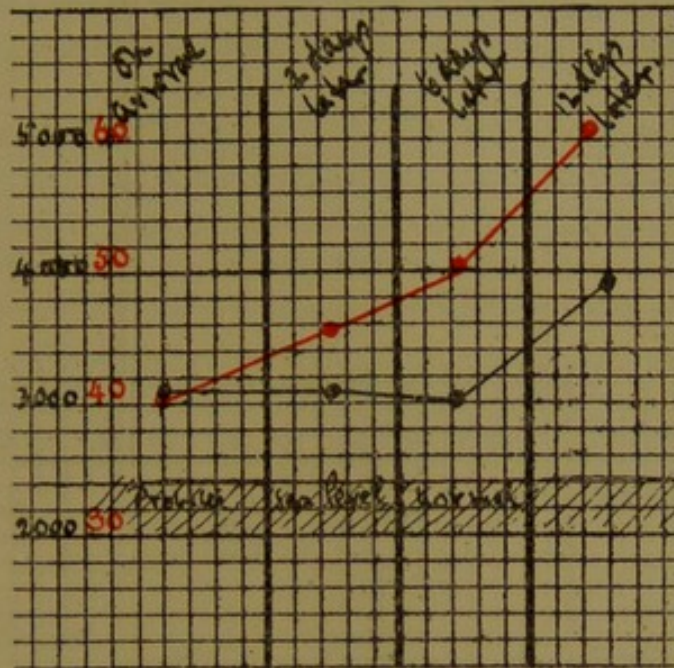


CHART V
HEALTHY MALE ADULT

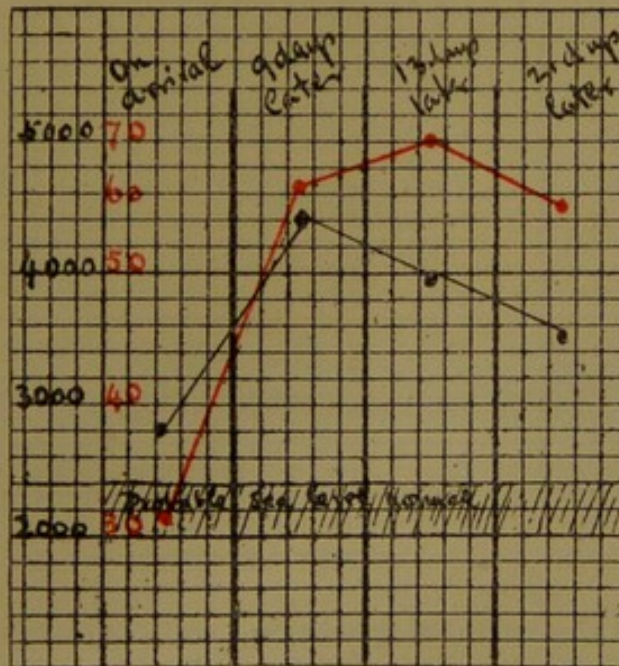


CHART VI
HEALTHY MALE ADULT

Bensaude,⁴ November 28, 1901, in an ascent of 4400 meters in two hours, observed the following, but did not seem to be struck by the change:

	ON GROUND	4400 METERS	ON RETURN TO GROUND
Polymorphonuclears.....	75.5	72.3	65.0
Mononuclears.....	23.7	26.9	34.8
Eosinophiles.....	0.8	0.8	0.2

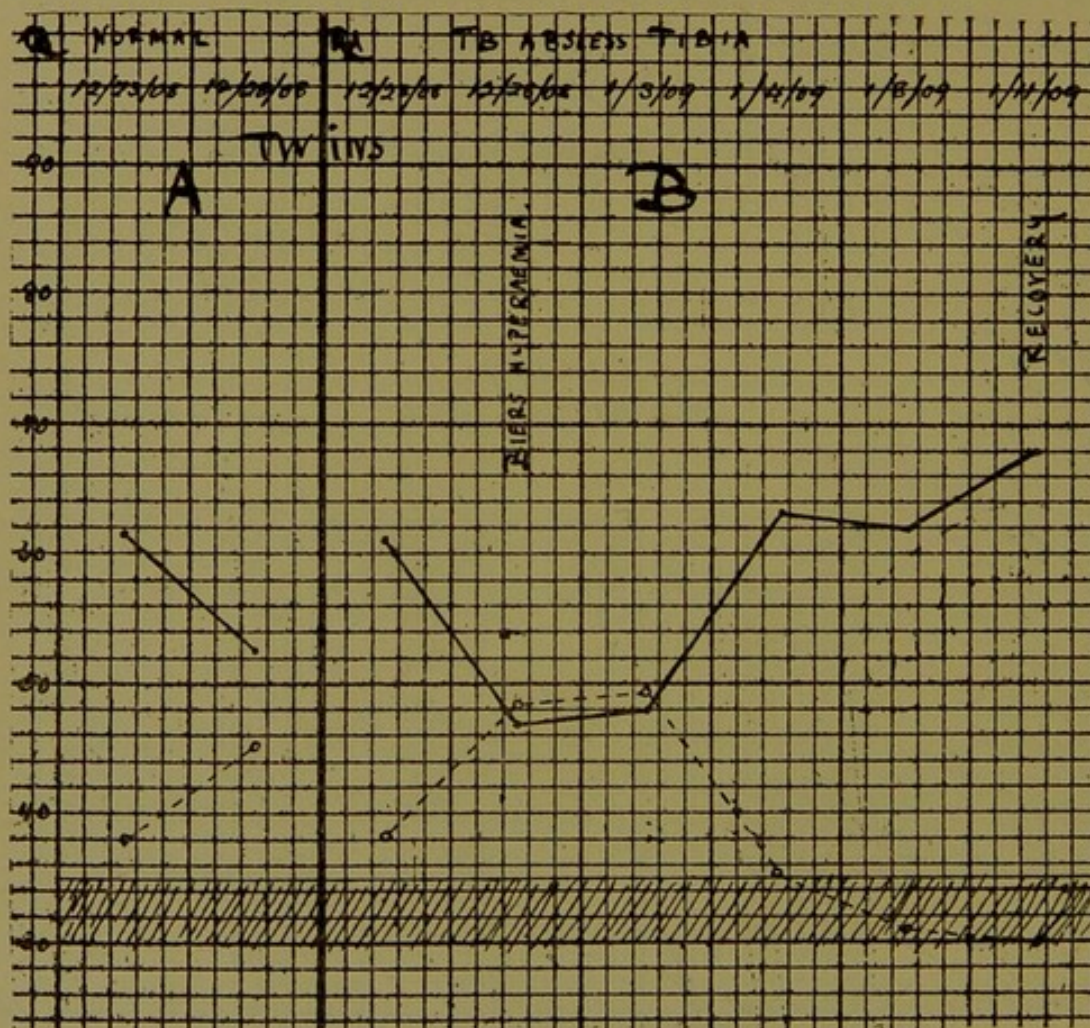


CHART VII

Zuntz⁵ explains the increased numbers of erythrocytes in high altitudes as due to hyperplasia of the bone-marrow, and by his experiments on dogs it would seem conclusively demonstrates this.

By colored plates he pictures the changes in blood-smears due to this increased marrow activity, and in a specimen of blood taken from the marrow

vein of a dog previously almost bled to death, he shows, besides the appearance of nucleated red cells, the presence of large lymphocytes.

In the large number of slides counted we found only one nucleated red corpuscle.

Experiments are now being made to ascertain if marrow hyperplasia can account for the increase in the lymphocyte element we have recorded. It is interesting to observe that the ratio of increase in these cells is approximately 30 per cent., which is about the ratio of erythrocyte increase at this altitude.

The question of differences in observations on the blood of men and women emphasized by Kjer-Petersen² caused us to separate our results as depicted in the following table:

POLY-MORPHO-NU-CLEARS	MONONUCLEARS						EOSINO-PHILES	MAST-CELLS
	Small Lymphocyte			Large Lymphocyte, Large Mono-nuclear; Transitionals				
	Average	Mean	Extremes	Average	Mean	Extremes		
	CLASS I—NORMAL ADULTS							
	57 MEN; 112 COUNTS							
52.9	21.5	21	4-42	23.4	23	4-40	1.9	0.3
	34 WOMEN; 43 COUNTS							
55.2	21.6	18	0-41	20.9	22	4-47	1.7	0.6
	CLASS II—CURED CASES							
	34 MEN; 53 COUNTS							
53.8	20	19	0.5-39.5	24	22	4-56	1.7	0.5
	23 WOMEN; 50 COUNTS							
58	18.5	18	4-38	20.7	21	6.5-32	2.3	0.5
	CLASS III—IMPROVING CASES							
	20 MEN; 56 COUNTS							
63.6	13.9	14	3.5-33	20.5	20	4-43	1.6	0.4
	23 WOMEN; 59 COUNTS							
54.9	20	19	0.5-33	22.8	22	9.5-44	1.9	0.4
	CLASS IV—STATIONARY CASES							
	32 MEN; 85 COUNTS							
65.8	15.4	15	2-20.5	16.7	16	2.5-37.5	1.6	0.5
	18 WOMEN; 46 COUNTS							
64.7	15.8	15	5.5-33	17.7	18	3-29	1.5	0.3
	CLASS V—ADVANCING CASES							
	25 MEN; 90 COUNTS							
70.7	11.2	9	2-29.5	16.2	14	2.5-34	1.4	0.5
	20 WOMEN; 71 COUNTS							
73.6	10.5	10	1.5-22.5	14.7	15	0.5-27	0.9	0.3

By this table can also be seen the lymphocytes separated into two groups, showing the average, mean, and extremes in each group.

In the next table the results of all the counts are arranged together, to show the average, mean, and extremes of the small and large lymphocytes.

POLY-MORPHO-NU-CLEARS	MONONUCLEARS						EOSINO-PHILES	MAST-CELLS
	Small Lymphocyte			Large Lymphocyte, Large Mono-nuclear; Transitional				
	Average	Mean	Extremes	Average	Mean	Extremes		
	CLASS I—NORMAL 90 CASES; 154 COUNTS							
54.1	19.3	20	0-42	24.2	23	4-47	2	0.4
	CLASS II 55 CASES; 101 COUNTS							
56.4	17.5	17	0.5-39.5	23.3	22	4-56	2.3	0.5
	CLASS III 40 CASES; 102 COUNTS							
59.7	16	17	0.5-33	22.2	20	4-44	1.7	0.4
	CLASS IV 50 CASES; 108 COUNTS							
65.5	15	15	2-33	17.5	17	5.5-37.5	1.6	0.4
	CLASS V 45 CASES; 128 COUNTS							
71.3	11	10	1.5-29.5	16	16	0.5-34	1.3	0.4

The time of day and the consequences of digestion and exercise also were considered, and our observations, as indicated by the following results on a healthy male adult, confirm those of Kjer-Petersen,² that great variations were not encountered from these causes.

C. W. L.	TOTAL LEUCOCYTES PER C.MM.	MONONUCLEARS
10.30 A. M.	4764	43.5
2 P. M.	5544	46.5
6.30 A. M.	5652	53.5
12.30 P. M.	5486	46.5
6 P. M.	5040	57.5

However, most bloods were taken at hours when such possible factors in inducing changes might be avoided. For instance, the blood-smears from the Colorado college students were collected on a day when no exercise had been taken and one hour before the evening meal.

The specimens in Charts V and VI were first obtained within fifteen minutes

of arrival by train, 2.30 P. M., and the subsequent observations were made at breakfast time, 8 A. M.

Discussion on the Possible Bearing of These Observations.—For many years it has been presumed that dwellers at an altitude possessed a high degree of immunity to tuberculosis.

In 1853 Alexander Spengler⁶ noticed such protection among the inhabitants

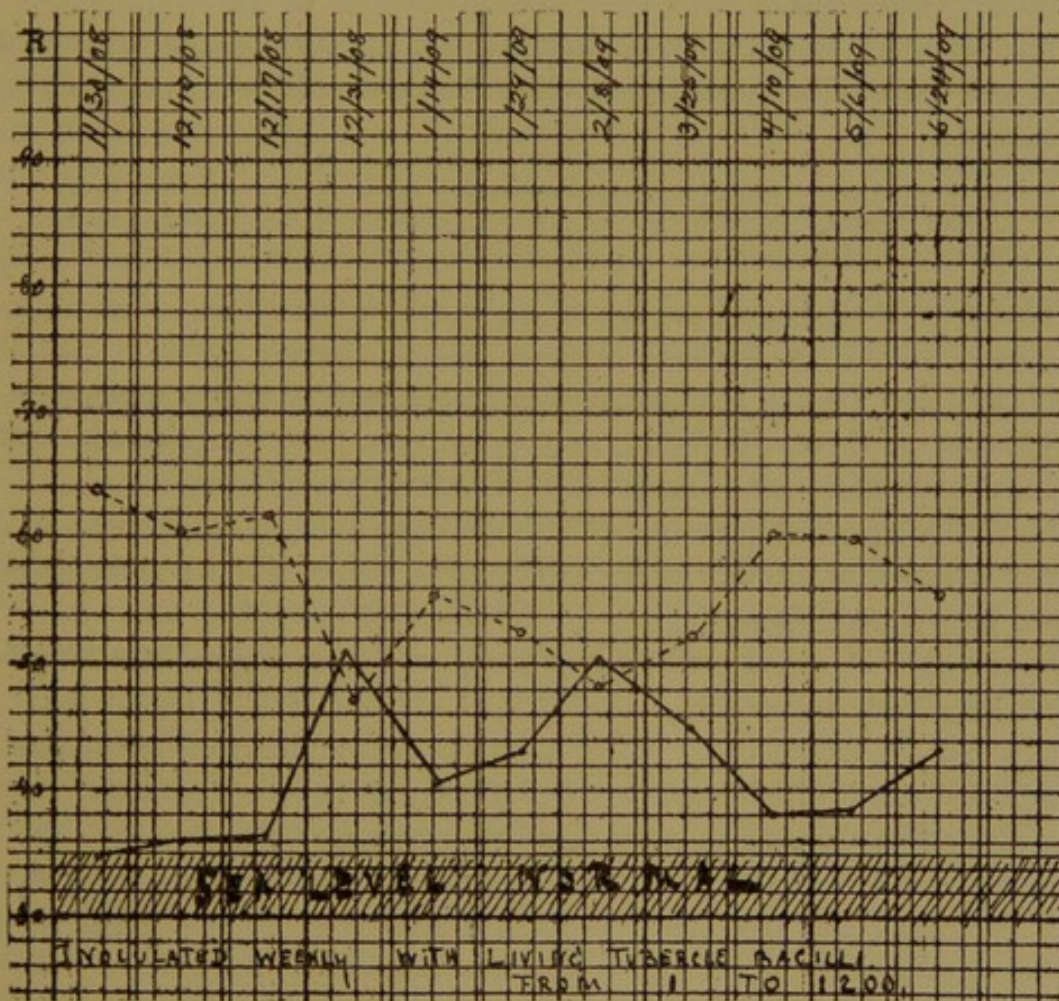


CHART VIII

at Davos, Switzerland, in spite of the poor housing of the people. He also called attention to the fact that natives of Davos who went to the lowlands as waiters and indoor workers developed tuberculosis, but by returning to their native town regained their health.

We in Colorado have seen many similar occurrences, especially among the children of tuberculous parents. Many of these have returned from eastern

schools and colleges with open tuberculous lesions, to rapidly recover in this altitude.

The rarity of an outbreak of tuberculosis here, in spite of the large numbers of tuberculous invalids and their children, is proverbial.

However, according to Latham⁷ tuberculous disease has been found to be rife among the watchmakers in the high Alps, and he quotes Dettweiler as saying that the idea that at a certain altitude there exists a zone free from tubercle bacilli is erroneous.

The statistics⁸ compared regarding sanatorium plus climatic cures of the Swiss and German sanatoria, corroborate the experiences of old practitioners in Colorado.

German sanatoria, after four years, permanent cures.....	20 per cent.
Turban (Davos)	48 per cent.
Basle Sanitorium (Davos).....	64 per cent.

That fever disappears from the tuberculous invalids coming to an altitude more surely than in the lowlands is shown by the following figures:⁸

Volland and Turban (Davos), in over 60 per cent. fever disappeared.

Schröder, at Hohen-Honnef, in only 37 per cent. fever disappeared.

This observation, too, is agreed to by Colorado physicians.

No physiological change due to altitude has yet been settled upon to explain the benefit of altitude to the tuberculous, and it may be probable that several factors participate.

In the light of recent work, autoinoculation due to deeper breathing has been a suggested explanation.

However, in following the latter work on the immunity investigations in tuberculosis, one is struck with the growing importance placed upon the lymphocyte element as the chief machinery of the organism's defence.

Bartel⁹ states that the behavior of tubercle bacilli that have entered the body through natural channels indicates a protective action on the part of the cells of organs, and especially of lymphocytes, against infection.

Recent researches by Opie¹⁰ show that the epithelioid cells in tuberculous tissue contain an enzyme exactly similar to that possessed by the large mononuclear leucocytes of the circulating blood.

His work indicates that these epithelioid cells may in reality be emigrated large mononuclear leucocytes, which they very closely resemble.

Nichols¹¹ has shown in the histological study of the lesions of immunized rabbits that the reaction to infection on the part of the lung of the vaccinated animals is much more rapid and intense than in the control or non-vaccinated animals.

He intimates that the tissue-cells could hardly multiply quickly enough to account for the excess of epithelioid cells, and that more probably most of these are leucocytes from the blood.

The participation of the lymphoid * cells in tubercle formation has long been known, and Metchnikoff has claimed the giant-cells to be accumulated macrophages.

In experimental tuberculosis the response of tissue to a beginning infection is accompanied by an accumulation of polymorphonuclear leucocytes, but these are soon replaced by epithelioid and lymphoid cells.

Claude and Zaky¹³ in 1902 showed in animals which best resisted tuberculous infection the presence of many large mononuclears. Halbron in 1903¹⁴ also emphasized the importance of these cells. In 1905 Ullom and Craig,¹⁵ in summarizing their investigations on blood studies in pulmonary tuberculosis, stated that they had received the impression, that the actual increase in the lymphocytes, corresponded to increased resistance of the patient to tuberculosis. It is also an interesting fact that the age-period of greatest outbreak of pulmonary tuberculosis, is not that of childhood, when the percentage of lymphocytes is greatest.

It would seem, therefore, that the increased numbers of lymphoid cells we have observed, as probably due to our altitude, may at least be one factor in the explanation of the benefit derived by the tuberculous invalids who come to Colorado, and in the relative tuberculosis immunity supposedly enjoyed by our inhabitants.

Our grateful thanks are due to Clarence W. Lieb, M.A., who assisted us with many of our blood-counts.

Dr. G. W. Holden, of the Agnes Memorial Sanatorium, Denver, and Dr. Saling Simon, of the National Jewish Hospital, Denver, kindly sent us a number of differential counts made in their institutions. Their results agreed very well with ours, but as the classification of their patients differed, we have not been able to group the results in the classes we divided our cases into.†

* The power of the lymphoid blood-cells to split wax has been shown by MM. Noël Fiessinger et Pierre-Louis Marie.¹² This is especially interesting in view of the wax content of the tubercle bacillus. Berghel found a similar lipolytic function in the mononuclears. The early demonstrations of Metchnikoff, and more recently by Metalnikoff, on the larva of the bee moth, corroborate this finding. Metalnikoff found in the blood of this insect, which feeds on bee's wax, a very active lipase, and these insects can destroy large quantities of tubercle bacilli, when injected, with remarkable facility.

† The writers wish to thank Mr. G. B. Bosworth, of Denver, and Mr. F. H. Morley, of Colorado Springs, and others, for their generosity in contributing to the expenses incidental to the work.

REFERENCES

1. Barach: "Morphology of the Blood in Pertussis," *Archives of Internal Medicine*, July, 1908.
2. Kjer-Petersen: "Ueber die numerische Verhältnisse der Leukocyten bei der Lungentuberkulose," Würzburg, 1906.
3. Huggard: "Handbook of Climatic Treatment," Macmillan, 1906.
4. Tissier: "System of Physiologic Therapeutics," Cohen, vol. x, 1903.
5. Zuntz: "Hohenklime und Bergwanderungen," 1906.
6. Hauri: "Davos as Health Resort," 1906.
7. Latham: "Pulmonary Consumption," 1907.
8. Nienhaus: "Davos as Health Resort," 1906.
9. Bartel: "Experiments in Immunization Against Tuberculosis," International Congress on Tuberculosis, 1908.
10. Opie: "The Part of Enzymes in Tuberculous Lesions," International Congress on Tuberculosis, 1908.
11. Nichols: "Studies on Immunity in Tuberculosis," *Medical News*, September 30, 1905.
12. *La Presse Medicale*, June 2, 1909.
13. Claude and Zaky: *Revue de la Tuberkulose*, July, 1902.
14. Halbron: *Revue de la Tuberkulose*, October, 1903.
15. Ullom and Craig: "Examinations of the Blood in Pulmonary Tuberculosis," *American Journal of the Medical Sciences*, September, 1905.

DISCUSSION ON DOCTOR WEBB'S PAPER

Dr. T. W. Hastings, New York: Dr. Webb has called attention to an interesting fact which has not been noted before, that there is a change in the relations between the different types of leucocytes at certain high altitudes which consists of an increase in the mononuclear elements in the blood from healthy and tuberculous individuals. It has been known for long that the lymphocytes are relatively and absolutely increased to a slight degree in the more chronic tuberculous conditions provided that the case is uncomplicated with a secondary infection, yet the changes are not so marked as noted in Dr. Webb's cases.

The authors have not made it perfectly clear in what type of cell was found this increase at high altitudes. They refer to all the mononuclear cells as lymphocytes, and, according to the charts shown in connection with the paper, all the large forms of cells are increased in number. This large mononuclear element is the one cell in the blood regarding the origin of which we are in doubt. We cannot prove that the large mononuclear type comes from any one cell. If we accept Pappenheim's idea that it is a transitional type, Dr. Webb might conclude that the high altitude stimulated the bone-marrow. On the other hand, according to other views, he would have to recognize this as the result of stimulation of the spleen or endothelial tissues.

The type of mononuclear cell which apparently monopolizes the increment is the large mononuclear—judging from the drawings—the cell which is

relatively and absolutely increased in pertussis and variola, and not the small lymphocyte, which is increased in chronic tuberculosis. This is interesting in the light of results obtained by Opie and Buxton from experiments upon the question of phagocytosis in immunity, yet it would be rash for one to draw conclusions from such observations, and from these variations in blood-counts, until some definite relation between the mononuclear phagocytic cells and the large mononuclear of the blood is proved.

The reference made to the statements of Kjer-Petersen and Cabot, that the differential leucocyte counts of women are so variable under normal conditions that one may not consider lymphocytosis and mononucleosis of significance in disease, does not apply to Dr. Webb's results, for the variations found by him are beyond the limits of any found under normal conditions except in infants.

Dr. Lawrason Brown, Saranac Lake, N. Y.: I think Drs. Webb and Williams are to be congratulated upon their excellent paper, giving the results of their hematological studies in tuberculosis. I would like to ask what proportion of the subjects of their experiments were males and females, both of the children and adults, and also whether the experiments were made at the same hour of the day.

Dr. Duncan A. L. Graham, Pittsburg: The increase in the number of red cells following residence in high altitudes is a compensatory phenomenon. This increase in number merely represents the effort on the part of the body to maintain the normal oxidation of the tissues. Chronic carbon monoxid poisoning closely simulates the condition found in patients living in high altitudes. From experimental studies in this subject in guinea-pigs by Dr. Nasmith and myself we were able to increase the number of red blood-cells of the pig from 5,500,000 per c.mm. to 11,000,000 per c.mm. This increase in number of 50 per cent. exactly corresponds with the percentage saturation with CO.

Boycott and Douglas have shown that the total oxygen capacity of the blood in polycythemia is only normal, and is not increased with the increase in the number of red cells.

The increase in white blood-cells, especially the large mononuclear cells found by Dr. Webb in people living or coming to high altitudes, I think is a part of the same phenomenon. We do get a moderate leucocytosis with an absolute increase of the large mononuclear cells in chronic monoxid poisoning. These changes found in the white blood-cells by Dr. Webb I think are wholly due to altitude, and are a part of the body process necessary to maintain normal oxidation at altitude.

Dr. Gerald Bertram Webb, Colorado Springs (closing the discussion): I think the chart referring to the Harvard and Colorado college students will answer Dr. Brown's question. The percentages of men and women on whom observations were made are also charted.

In reply to Dr. Hastings we think it is more than probable that the increased activity of the bone-marrow which is responsible for the increased erythrocytes is probably responsible for the increase in lymphocytes.

The increase in lymphocytes in whooping-cough has been explained by some as due to the violent muscular efforts. The muscular effort of breathing is probably also increased by altitude.





