later on. Partial correction by the first tenotomy, an interval with regulated exercise, and then a similar tenotomy on the fellow eye in case of need, are better practice. Confirmed strabismus often diminishes in degree as time goes on; hence the too common idea that time alone will often cure a squint, and the advice not seldom given to "wait and see." For the squinting eye this too often means waiting and not seeing. Time alone may lessen the disfigurement but will not remove the disability. Binocular vision is not recovered in this way.

THE CROONIAN LECTURES:

A CONTRIBUTION TO THE STUDY OF THE BLOOD AND THE CIRCULATION.

Delivered before the Royal College of Physicians of London.

By GEORGE OLIVER, M.D., F.R.C.P.

LECTURE IV.

DURING recent years observers have found that the percentage of the hæmocytes is considerably affected by altitude, baths, massage, and by surgical interference, such as opening the abdomen and section of the cord. Certain theories have been suggested in explanation of these variations; and it will be convenient to refer to them now as a whole.

I. *Theories associated with the Corpuscles.*—1. The formation and destruction of corpuscles. Whenever a marked increase of the number of the corpuscles has been observed, as in high altitudes, the first adopted theory has almost invariably been that of increased formation. 2. Dislodgment of resting corpuscles has been advanced in explanation of the effects of massage. 3. The transference of corpuscles from the arteries to the capillaries and *vice versa* was suggested by Cohnstein and Zuntz,¹ who found that the proportion of the corpuscles to the plasma was definitely varied in the large vessels and in the capillaries by cutting the cord, by electrically stimulating the cut cord, and by other procedures; and they concluded that the capillaries are normally poorer in corpuscles, and therefore richer in plasma, than the larger vessels; that when the arteries leading to the capillary field are contracted the blood in that field becomes still poorer in corpuscles and that elsewhere still richer, and that when the arterioles are dilated the capillary blood contains a larger proportion of corpuscles and the plasma previously present in it in comparative excess is now distributed and dilutes the rest of the blood. According to this theory widening of the arterioles and filling of the capillaries produce the same effect on the blood of the large vessels as resorption of fluid and narrowing of them as increased filtration.

II. *Theories founded on Alterations in the Proportion of Water in the Plasma.*—1. Increased transudation from the capillaries. Regöczy,² Brasols,³ Klikowitsch,⁴ and others refer peripheral changes in the circulation to disturbance of the equilibrium between filtration on the one hand and resorption on the other, and the adjustment of the normal balance to the operation of these forms of transudation. 2. Increased discharge of water from the kidney, skin, and mucous surfaces is an undoubted cause of apoplasma in various physiological and pathological conditions presently to be referred to.

The following observations mainly support the theories founded on fluid transfer from the blood, and do not corroborate those relating to the formation and destruction, or to the dislodgment and transference of corpuscles.

I.—VARIATIONS IN THE BLOOD IN DIFFERENT PARTS.

The blood derived at the same time from different parts of the body does not always afford the same percentages of corpuscles and hæmoglobin. A large number of observations were made on subject A. with the invariable result that the blood furnished by the toes was much poorer than that afforded by the fingers. This disparity does not seem to be the same in all individuals, for in subject B., who possesses a higher arterial pressure, it was less apparent. It does not,

however, follow that the blood present in the vessels of the parts in question is actually different in quality, for it has been repeatedly found that when the toe, which yielded a sample of very inferior quality, was well rubbed it furnished another quite comparable with that derived from the finger. Probably, therefore, a larger amount of lymph is normally present in the tissues of the feet than obtains in other parts, in consequence of gravity increasing the intracapillary pressure and thus augmenting exudation, and at the same time retarding the onflow of lymph. It would therefore seem that massage applied to the toe merely disperses this excess of tissue lymph, and enables the observer to ascertain the quality of the blood as it actually exists in the vessels. Exactly the same thing is not infrequently observed in anæmia, the percentage of the corpuscles and hæmoglobin rising very considerably after the application of massage for a few minutes to the finger. Probably therefore there is often, if not generally, an excess of tissue fluid even in the finger in anæmia, and consequently in this condition the sample of blood obtained in the ordinary way without previous massage does not always afford a true reading of the actual state of the blood. The existence of this diminutive degree of œdema in the insufficiently nourished tissues of the anæmic is moreover rendered probable by the experiments of Lazarus-Barlow.

II.—POSTURE.

The remarkable effects of gravity on the composition of the blood are well illustrated by passively elevating a limb (arm or leg) for fifteen minutes. The percentage of the corpuscles is markedly reduced. This result was invariable in both subjects. The alterations in the blood are closely associated with similar differences in the intracapillary pressure, and this is further illustrated by the fact that when a limb is maintained in the vertical position by muscular action, the percentage of the corpuscles is not only not reduced but is actually increased; the intracapillary pressure of the elevated limb is not only prevented from falling, but is increased by the afflux of blood which occurs when the muscles are brought into play. When the muscular action is withdrawn and the vertical limb is passively supported, the intracapillary pressure promptly falls. These observations on the influence of gravity on the composition of the blood and the thwarting of that influence by muscular action illustrate the wisdom of passively supporting a part when in a state of inflammation or inflammatory congestion, for such a procedure tends not merely to reduce the blood pressure, but to diminish the percentage of the corpuscles also.

III.—EXERCISE.

Local exercise may be active (voluntary) or passive (faradism or massage). Muscular action, however induced, causes an immediate, decisive, and proportionate local rise in the percentages of the corpuscles and the hæmoglobin. Though the rise was rapid, it did not subside so quickly, for the disappearance of it generally required from thirty to sixty minutes, and in the case of massage it lasted longer than after voluntary exercise or faradism. Inasmuch as the rise in hæmoglobin is proportionate to that of the corpuscles, this common effect of active and passive exercise of the muscular tissue for short periods is obviously due to an increased proportion of chromocytes to the plasma. Inasmuch as the blood supply of the finger is not immediately connected with that of the muscles, it is difficult to see how muscular exercise can thus affect the blood in the finger. This, however, is not the only explanation available; for it is known that in a state of rest there is no lymph flow at all,⁵ and that muscular contraction is necessary to propel the lymph from the lymph spaces into the lymphatics; therefore when all the muscles of a limb are thrown into action there will be an immediate acceleration of the circulation of lymph from the whole limb, including a considerable area of non-muscular tissue, accompanied by an augmented exchange of fluid from the blood to the tissues (non-muscular as well as muscular). The muscular action of a limb therefore accelerates the circulation of all the fluids in the limb, and the increased intermediary transfer of fluid from the blood through the capillary wall to the lymph spaces and from these to the lymphatic vessels must reduce the volume of the plasma in all the vessels of the limb.

¹ Pflüger's Archiv, 1888.

² Pflüger's Archiv, B. 37.

³ Archiv f. Anat. u. Physiol., 1884.

⁴ Du Bois Reymond's Archiv, 1886.

⁵ Starling, Arris and Gale Lectures, Lancet, May 16th, 1896.

Since making these observations I find that Chéron has observed that massage, dry friction, and electricity will within ten minutes greatly increase the number of the corpuscles—in one case of anæmia raising it from 2,430,000 to 4,080,000 per c.mm. He also attributes the rise to concentration of the blood from increased transudation of fluid which results from augmentation of the blood pressure.⁶ After an hour's massage J. Mitchell noticed an increase of the chromocytes which attained its maximum an hour after the cessation of the process, but without a corresponding rise in the hæmoglobin. It is well to keep in mind that the observed alteration in the blood is merely an indication that the massage-like exercise or faradism has advanced the onflow of tissue fluid, and has increased the transudation of fluid from the blood; so that this for a time is poorer in water, and therefore richer in corpuscles. In anæmia it is highly probable that the repeated stimulation of the intermediary circulation by massage will eventuate in an improvement of the blood; but only because, like other forms of exercise of the muscles, it raises the nutrition of all the tissues.

General Exercise.—In attempting to determine the effects of general exercise on the blood, it is difficult to eliminate the rise in corpuscles due to perspiration. The general results, however, of the observations already made may be stated to be a rise in the corpuscles, which, after a variable period, somewhat subside, but remain above the initial percentage while the exercise lasts, and a similar though diminished rise and reduction of the hæmoglobin percentage. The rise in corpuscles and hæmoglobin produced by an hour's active walk generally subsides after an hour's rest. The immediate effect of general exercise on "the worth" is to reduce it, and the remote effect—observed after the lapse of some hours—is to increase it.⁷ It would seem that in general exercise there is the same increased transfer of fluid from the blood, and the same augmented lymph-flow, as takes place in local exercise; but the concentration of the blood thus induced is after a time somewhat lessened by the return of a portion of that fluid to the blood. Probably the effect of general exercise is modified by the amount of tissue-lymph present when the exercise is taken. In those, for example, who do not take exercise habitually, or in whom the circulation is languid or the blood poor the lowered intermediary circulation favours the storage of tissue-fluid, and exercise may even fail to incite a rise in the corpuscles. On the other hand those accustomed to regular active exercise have a smaller storage of tissue-lymph, good percentage of corpuscles and hæmoglobin, and a permanently high specific gravity of the blood.⁸

IV.—DIGESTION.

Observation of the effects of 96 meals (breakfast, lunch, and dinner), each having an average supply of 17 ounces of fluid, shows that as a rule in from two to three hours the percentages of the corpuscles and hæmoglobin fell in 70 per cent., rose in 23 per cent., and were without change in only 7 per cent. The evidence, therefore, preponderates in favour of a fall of chromocytes⁹ and hæmoglobin during digestion. The average "worth" showed but little alteration, for in 53 per cent. of the observations it slightly fell, while in 47 per cent. it either rose or presented no variation. Two other facts were also very frequently apparent—namely, a preliminary and very transitory rise shortly after the meal, and a rise with slight gain in "worth" subsequent to the lowest point of the fall. These stages of the effect of the digestive process on the blood taken from the systemic periphery are probably the resultants of several causes, of which perhaps the most prominent may be fluid transfer and the hæmolytic and hæmopoietic functions of the organs accessory to primary digestion. The preliminary rise may be due to the copious outpouring of the digestive juices. But this effect is so transitory that it may be easily missed, even though the meal is a solid one; therefore it would seem that it is quickly com-

pensated, either by the absorption of fluid, as from the tissues, or perhaps by a cytolytic process. The digestive fall appears to coincide with an increase in the volume of the blood and with a reduction of the specific gravity, as observed by Lloyd Jones, and the subsequent rise with a reduction of the blood volume through renal elimination, and a corresponding increase of the specific gravity.¹⁰ It has been observed that these variations are not caused by the water taken with the meals, for they are quite as pronounced when it is withheld.

V.—ALTITUDES.

All observers are agreed as to the facts, namely, the presence of a larger number of hæmocytes in the inhabitants of mountainous regions than in the residents of lower altitudes, and a rapidly induced increase of them in those of the latter who resort to the mountains—an increase which, however, as rapidly passes away when they return to the plains. With the view of observing for myself this interesting effect of altitude I spent twenty-three days at Davos Platz (5,200 feet) last month. Exactly the same mode of life was there followed as in London in regard to exercise, etc. The corpuscles began to rise within twenty-four hours, and attained their maximum percentage within the first week. The average increase from the fourth to the fourteenth day was 10 per cent., and the maximum rise 14 per cent. The hæmoglobin increased, but in a less degree than the corpuscles. Consequently the blood decimal fell—from 1.03 to 0.99; when, however, subsequently the consumption of water was increased and the corpuscles were reduced in number it rose to 1.025, and when the ordinary quantity of water was resumed it again fell.

There is another fact strikingly apparent in the Davos observations, namely, the greatly reduced range of the night and morning variations of hæmoglobin and of the corpuscular worth, and particularly the latter. Whereas in London they varied 9 per cent. and 0.05 respectively, at Davos they were reduced to 4.2 per cent. and 0.02. The night and morning variations of the corpuscles were only slightly diminished (from 2.9 to 2.4 per cent.). It therefore follows that though the night and morning worth was reduced the hæmoglobin was more uniformly distributed over the twenty-four hours at Davos than in London, and the worth during the day was approximated to that of the night. After leaving Davos the corpuscles fell much more slowly than after arrival, and the hæmoglobin remained at much the same level as during the visit; hence the blood decimal rose, and indeed advanced beyond the degree present in London before the visit. This after-effect would seem to show that Davos has impressed the blood most favourably notwithstanding the fall of the blood decimal during the immediate influence of the altitude. The question arises: Would this gain in value have taken place at Davos had the visit been prolonged? On return to London the night and morning variations in hæmoglobin and worth again widened as before.

In explanation of the facts, all observers regard the increase of the chromocytes as due to rapid constriction incited by lessened supply of oxygen from the reduced pressure; and they believe that it compensates for the deprivation of oxygen. Recently, Grawitz has criticised this position, and has shown it to be untenable.¹¹

He refers the solution of the problem to increased loss of water from the blood through the skin and respiratory tract, in consequence of the great diminution of humidity in the atmosphere. At the same time, also, we should not overlook the fact that high altitudes may, perhaps, favour polycythæmia in another way. In the first lecture it was shown that deep breathing raises arterial tension. The rarified air of mountain climates is known to induce deeper breathing, and in consequence to increase the circumference of the chest from 1 to 3 inches.¹² Shortly after arriving at Davos it was observed that my arterial tension was raised, and continued to be raised, throughout the visit; for the radial pressure and calibre were increased, the former being from 20 to 30 mm. of Hg., and the latter from 2 to 3 points higher, than in London; and, moreover, the postural variation was reduced from 1 to 3 points. All these signs of increased arterial tension gradually subsided after leaving Davos. It may be concluded that the physiological effect of altitude on the blood is to raise the percentage of the corpuscles more than that of the hæmoglobin, and thus to reduce the blood decimal, and that this reduction may be counteracted by the increased consumption of water.

Dr. Theodore Williams¹³ regards high altitude climates as contra-indicated in anæmia, diseases of the heart and great

⁶ *Comp. rend. de l'Acad. des Sciences*, 1895, vol. ii, No. 6.

⁷ Though the data obtained support these positions, I do not present them just now, because observation in this direction should be extended.

⁸ Lloyd Jones, *Journ. of Physiology*, vol. xii, p. 318.

⁹ Hayem states that his pupils Duparie and Cadet found a diminution of from 200,000 to 300,000 corpuscles per c.mm. during digestion. *Du Sang et de ses Altérations Anatomiques*. Paris, 1889.

¹⁰ *Op. cit.*

¹¹ *Berliner klinische Wochenschr.*, 1895, pp. 713 and 740.

¹² *Aëro-therapeutics*, by C. Theodore Williams, M.D., p. 100.

¹³ *Op. cit.*

vessels, chronic renal disease, and in all forms of albuminuria. This physiological study so far seems to support this clinical experience. In anæmia, perhaps the ingestion of more fluid will prevent the fall of the blood decimal. It is easy to understand how cases of cardiac incompetency may be severely tried by the rarefied and dry air of high altitudes, for the friction-coefficient of the blood will be increased by the polycythæmia, and the deeper breathing will tend to maintain heart hurry and over-incitement of the weakened heart may be maintained by the increased respiration. But inasmuch as the breathing of rarefied air seems to lead to filling of the arteries and reduction of the veins, it is quite conceivable that if applied *gradatim* in suitable cardiac cases, it might prove to be of considerable therapeutic value. Physiology and pathology likewise join hands in regarding cases of chronic interstitial nephritis as unsuitable for treatment by the mountain cure, for in that disease polycythæmia and high arterial tension are prominent pathological conditions.

Undoubtedly this physiological mode of treatment by mountain air is very decisive in character. It is certainly of the highest value in phthisis.

VI.—BATHS.

Hot and cold baths, whether local (as hand baths) or general, produce contrary effects on the blood, the former lowering the percentage of the corpuscles and hæmoglobin, and the latter raising them. The fall from a warm bath of 15 minutes' duration may be 7 per cent., and the rise from a short immersion (3 minutes) in cold water may be 4 per cent. The alteration is merely a disturbance of the relation between the corpuscles and the plasma, for the blood decimal remains unaffected. It would, therefore, seem that temperature, which is the predominant influence in bathing, alters the composition of the blood by retarding or accelerating the rapidity of fluid transfer through the capillary wall, warmth slackening it and probably favouring the lodgment of tissue lymph, and cold stimulating it. In all probability this influence is mainly exerted through the effect of warmth and cold on the intracapillary pressure.

VII.—OXYGEN INHALATION AND ETHER ANÆSTHESIA.

The inhalation of oxygen in rabbits produces, as a rule, a concurrent rise in the corpuscles and hæmoglobin. Probably this result arises from the increased arterial and consequent intracapillary pressure caused by oxygen.

It having been stated during the past year that ether anæsthesia, particularly in anæmic subjects, produces a rapid and marked diminution of the hæmoglobin,¹⁴ it seemed desirable to make some observations on animals in order to ascertain if the normal red corpuscle is affected by ether, especially as observations on the effects of anæsthetics on the blood made before, during, and after operations are unreliable, because these themselves, whether producing loss of blood or not, profoundly disturb the composition of the blood.

In a series of 6 experiments on rabbits, in which 18 observations were made during the profound ether anæsthesia of one hour, the average blood decimal was 1.01 before and 0.98 during the administration. The corpuscles examined during the anæsthesia were normal in appearance. No obvious after-effects were observed.

From this too limited number of observations it would seem that ether anæsthesia does not produce a very pronounced effect on the normal red corpuscles. But it should not be inferred that it will be equally harmless when the corpuscle is abnormal, as in anæmia. There is some ground for believing that the stroma varies in its resistance to the same chemical agent: for example, it has been observed that the corpuscles of different subjects vanish at different rates when mixed with the same solution of sodium chloride in the same proportion and exposed to the same temperature.¹⁵

VIII.—VARIATIONS IN THE PLASMA AND THE CIRCULATION OF WATER.

The concurrent variations in the percentages of the corpuscles and hæmoglobin which have been so repeatedly pointed out are indeed volumetric indications of the circula-

tion of water into or from the blood—into it from the digestive tract and the tissues, and from it by the kidneys, skin, and lungs, and probably into the muscles during exercise. The blood is continually tending to balance its income and output of water, but variations in the proportion of water present in the plasma are constantly taking place within certain physiological limits. When, for example, the output of water, whether by the kidneys, skin, or bowels, temporarily exceeds the income, the volume of the plasma is for the time reduced and there is a proportionate rise in the corpuscles. All such transitory phases of concentration of the corpuscles can only be due to the shrinking of the plasma from loss of water.

Clinical observation during last summer also indicated that persistent deviations are to be met with on one or the other side of the physiological mean percentage of the hæmocytes. For example, polycythæmia was frequently observed in chronic interstitial nephritis with high arterial tension, in diabetes mellitus, in chronic gout with increased arterial tension, and in those disposed to hæmorrhage (epistaxis, etc.). At present I refer to this matter merely in general terms, for further observation is necessary in order to test these preliminary conclusions.

When the arterial tension is raised by any means, such as by small doses of suprarenal extract, by tonics generally, and even by mere change of air and scene and by recreation, the corpuscles will, as a rule, rise considerably; but it does not follow that the rise is necessarily and entirely due to the formation of chromocytes, for the major part of it probably arises from accelerated transfer of water from the blood as the result of increased intracapillary pressure. Even in anæmia the blood may become apoplasmic. The pathogenic cause is not always obvious; it may, however, be frequently traced to a reduced ingestion of water and occasionally to the increased elimination of it, probably under neurotic influence. In such cases the volume of the blood is obviously reduced, the percentage of the corpuscles is absolutely either normal or in excess, and that of the hæmoglobin—though it may be absolutely in excess—is always relatively subnormal, and improvement is indicated by a fall in the absolute percentages and a rise in the blood decimal. On the other hand, the reduced elimination of water, as when the blood pressure is much diminished, tends to lower the percentages of the corpuscles and hæmoglobin.

CONCLUSION.

In conclusion, it is perhaps superfluous to point out that, according to the data which have been advanced in these lectures, it would seem that in health the composition of the blood varies quite as much as the calibre of the arteries, and that the variations in the former are largely influenced by the forces of the circulation; in a word, that the physiological relationship that subsists between the blood and the circulatory apparatus is as intimate as is the anatomical.

A GOÏTROUS CRETIN UNDER THYROID EXTRACT.

By WILLIAM RUSHTON PARKER, M.A., M.D.(CANTAB.),
Kendal.

In the English Lake district lies a valley, running from west to east, and open only on the eastern side. At the bottom of the valley runs a stream in a fairly straight course from west to east, and widening out in one spot into a tarn, 340 feet above sea level. The valley is bounded both north and south by hills upwards of 1,000 feet high, and south-west, west, and north-west by a range upwards of 2,000 feet in height. The valley and adjacent hills are formed out of Borrowdale volcanic rocks, the only other neighbouring formation being an overlying narrow belt of Conistone limestone nearer the eastern outlet of the valley. Both parents of our patient had lived since birth in this valley, the father at the bottom, close to the tarn, the mother 80 or 100 feet higher up the southern slope.

The patient, Lizzie P., was born on November 20th, 1877, in the bottom of the valley, near the tarn; two years afterwards the family migrated to a house on a level with that of the

¹⁴ The Blood Alterations in Ether Anæsthesia. By J. Chalmers de Costa. Philadelphia Medical News, 1895, vol. i. p. 225.

¹⁵ The effects of chloroform on the red corpuscle have not been sufficiently observed to warrant any statement of results.