BREGMANN'S TABLE SHOWING RELATIVE FREQUENCY OF ARTERIOSCLEROSIS IN DIFFERENT ARTERIES. THE FIGURES REPRESENT PERCENTAGES.

Normal.		Slight degree.		Medium degree.		Severe degree.		Without distinction in degree.	
Brachial	45	Radial	56	Carotid, internal	48	Aorta, abdominal	16	Ulnar	94
Iliac, external	42	Carotid, external	56	Subclavian	47	Cerebral	15	Tibial, anterior	92
Aorta, abdominal	36	Cerebral	54	Ulnar	39	Carotid, internal	13	Subclavian	88
Aorta, ascending	33	Ulnar	52	Tibial, anterior	37	Aorta, ascending	13	Cerebral	87
Carotid, common	32	Splenic	46	Axillary	36	Subclavian	12	Carotid, internal	87
Femoral, superficial	31	Tibial, anterior	45	Splenic	29	Tibial, anterior	11	Radial	86
Axillary	29	Femoral	44	Carotid, common	28	Popliteal	10	Splenic	82
Carotid, external	22	Popliteal	44	Radial	27	Carotid, common	9	Popliteal	79
Popliteal	21	Aorta, ascending	41	Popliteal	25	Femoral	18	Carotid, external	78
Splenic	18	Brachial	40	Aorta, abdominal	24	Splenic	7	Axillary	71
Radial	14	Iliac, external	38	Iliac, external	19	Carotid, external	6	Femoral	69
Carotid, internal	13	Axillary	34	Cerebral	18	Radial	3	Carotid, common	68
Cerebral	13	Carotid, common	31	Femoral	17	Ulnar	3	Aorta, ascending	67
Subclavian	12	Subclavian	29	Carotid, external	16	Axillary	1	Aorta, abdominal	64
Tibial, anterior	7	Carotid, internal	26	Brachial	15	Iliac, external	1	Iliac, external	58
Ulnar	6	Aorta, abdominal	24	Aorta, ascending	13	Brachial	0	Brachial	55

In this table no distinction is made as regards the kind of arteriosclerosis.

ing of the intima, but by an increased permeability of the vessel walls. With this disease of the vessels there is an increase in the connective tissue and destruction of large numbers of capillaries, still further diminishing the size of the vascular bed, and then comes a disparity between the calibre of the artery and the territory to be supplied, followed by a compensating growth of connective tissue. This endarteritis of distant organs is extended in the same way to the aorta. Councilman would rather take the view that the changes in the aorta and in the minute arteries are due to the same cause; that diffuse endarteritis is a disease primarily due to a degeneration of the muscular fibres of the media. On this the growth of the intima follows, which is due to the same cause acting in two ways: in one, by the well-known law of connective-tissue growth, to supply a defect, in this case the degeneration of the media; and in the other, possibly acting under the law of Thoma, a compensating endarteritis to restore the abnormally dilated vessel to a normal calibre. Thoma's assumption that this secondary arteriosclerosis is due to an increased blood pressure in the aorta from the increased peripheral resistance cannot be proven.

There seems to be good reason for separating the lesions of angiosclerosis from the senile endarteritis and the lesions accompanying it. The senile endarteritis is a disease of advanced life, seldom occurring before the age of fifty. The lesions in the vessels are slow, and there is little reaction to the degeneration. Clinically, there is absence of the high arterial pressure, which constitutes the most obvious clinical manifestation of the disease arteriosclerosis. The diffuse arteriosclerosis is a definite disease; the lesions in the arteries and tissues form a pathological entity, and the primary lesion to which all the changes are due is a degeneration of the tissue of the media of both the large and the smaller arteries.

ORDER OF FREQUENCY OF NODULAR AND DIFFUSE ARTERIOSCLEROSIS IN DIFFERENT ARTERIES. (Bregmann.)

Nodular Form.	*Diffuse Form (in Thoma's Sense).*
Abdominal aorta.	Radial.
Common carotid.	Ulnar.
Descending thoracic aorta.	Anterior tibial.
Internal carotid.	Popliteal.
Ascending aorta.	Splenic.
Arch of the aorta.	Superficial femoral.
Cerebral.	Axillary.
Subclavian.	External iliac.
Common iliac.	Brachial.
Cœliac.	Subclavian.
Superior mesenteric.	External carotid.
Inferior mesenteric.	Cerebral.
Renal.	Internal carotid.
Coronary.	Ascending aorta.
Popliteal.	Common carotid.
External carotid.	Abdominal aorta.
Splenic.	
Axillary.	
Common femoral.	
External iliac.	
Posterior tibial.	
Superficial femoral.	
Deep femoral.	
Internal iliac.	
Brachial.	
Anterior tibial (below).	
Ulnar.	
Anterior tibial (above).	
Radial.	

Nodular Arteriosclerosis.—In the nodular or primary form of arteriosclerosis there are seen flat, button-like, hemispherical, yellowish or yellowish-white projections above the intima, especially about the orifices of the arterial branches. This is generally regarded as the result of the greater strain that this part of the artery is exposed to. The areas consist of new connective tissue and new elastic fibres in the intima, the underlying media being either fibrous, calcareous, or degenerated and necrotic. Thoma showed that the cast after filling the vessel with melted paraffin injected under the same pressure as that of the blood came out smooth, showing that in the tense vessel the intimal nodules fill defects in the media. The stage of weakening in the intima antecedent to the intimal thickening is liable to result in aneurism (Fig. 631). The new tissue soon becomes hyaline, fatty changes take place, and eventually disintegration into fat drops, cholesterin, granular detritus gives rise to softening. The degeneration begins in the outer layers of the sclerotic thickening, but may extend inward until the epithelium lining the vessel is destroyed and a larger or smaller rough area due to loss of substance is formed. Calcareous infiltra-

FIG. 631.—Nodular Sclerosis of Aorta with Beginning Aneurism. Hæmatoxylin and Weigert's elastic-fibre stain. The intima (I) is thickened, contains parallel, wavy, elastic fibres, except at the point of the bulging; the media (M) is thinned, degenerated, the elastic broken up; A, adventitia. × 150.

tion may take place. More or less leucocytic and round-cell infiltrations occur around softened areas. The adventitia may be unchanged, fibrous, or the seat of foci of cell accumulations.

This form is possibly due to local, circumscribed areas of degeneration and weakening in the media produced by strain, by toxic and infectious lesions. Several French investigators have produced apparently similar plaques in the aorta of animals by injection into the circulation of bacteria, bacterial toxins and other substances, such as lead, uric acid, etc., with or without producing traumatic lesions of the vessel wall. In some cases of this kind the lesions seemed to be the result of proliferation in the intima; in others there were mesarterial and periarterial inflammatory foci about the vasa vasorum.

In goitre of all forms, Jones found degenerative and sclerotic changes in the arteries of the thyroid and its capsule. The changes occurred apart from general arteriosclerosis and were found quite marked in eighteen out of twenty cases examined. The vessels were abnormally friable. The internal elastic coat was granular, broken across, and calcified; in one case it had changed into a calcareous plate; connective-tissue thickening of the intima associated with the formation of new elastic fibres had resulted, followed by hyaline degeneration.

The Distribution of Angiosclerosis.—The relative frequency of angiosclerosis in the different parts of the circulatory system has been studied by Bregmann, Sack, and others. The arteries are more frequently involved than the veins, although the study of phlebosclerosis has been rather insignificant as compared with the amount of attention paid to arteriosclerosis.

Arteriosclerosis in general is more frequent in the vessels of the extremities than in the aorta and its branches of the first and second order; it is most frequent in the arteries of the leg and forearm, beginning first of all in the anterior tibial. This is explained on the score of the general lateral hydrodynamic pressure to which these vessels are exposed on account of posture in addition to the general hydrodynamic pressure.

Arteriosclerosis of the pulmonary artery is exceedingly rare as compared with the frequency of the process in the aorta. In chronic tuberculosis of the lungs, emphysema and other diseases resulting in atrophy and destruction of lung tissue naturally give rise to more or less compensating endarteritis. In Sauné's thesis are collected twelve cases of sclerosis of the pulmonary artery; in seven, emphysema was present. It is suggested by Laache that the carbonic dioxide may tend to prevent the development of arteriosclerosis, although the mode of action is not clear at all; probably the more important factor is the low pressure in the pulmonary artery as compared with that of the aorta (Laache, Frankel, Sauné).

Laache has described an instance of sclerosis with atheroma of the pulmonary artery that clinically presented the symptoms of congenital heart disease ("morbus cœruleus"); there were hypertrophy of the right ventricle, marked nodular condition of the intima, and dilatation of the pulmonary artery. Apparently the sclerosis in this case was due to weakening of the arterial wall. Romberg has described a similar case. He found but one similar case in the literature, a case of Klob's. The striking blueness of the skin in Romberg's and Laache's cases—in both instances it led to diagnosis of congenital heart disease—is difficult to explain.

Huchard and von Schrötter describe each a case of sclerosis in the pulmonary artery associated with pressure upon it by aortic aneurism. Edgren attributes pulmonary sclerosis in one case to patency of the ductus arteriosus.

Phlebosclerosis.—The early observations on sclerosis of the veins were made by Hodgson, Rokitansky, Virchow, and others. Lobstein introduced the term phlebosclerosis. Rokitansky described thickening of the intima and of the adventitia of the veins involved in varicose aneurism; and Virchow called attention to chronic endophlebitis in long-continued passive congestions; in both cases the influence of mechanical causes is quite evident.

According to the careful studies of Sack the localization of phlebosclerosis is determined largely by the same factors as arteriosclerosis, and the tendency is to regard phlebosclerosis in many cases as a systemic disease, analogous to diffuse arteriosclerosis, and due to general nutritional disturbances resulting in weakness of the middle coat. But it may appear as a local disease in consequence of local venous congestions, as, for instance, in the portal system in atrophic cirrhosis of the liver, and in the pulmonary veins in mitral stenosis. As will be seen from the adjoining table of Sack, phlebosclerosis attacks especially those vascular provinces in which the venous pressure varies greatly in different positions of the body, and in which the activity of the voluntary muscles favors the venous flow to relatively but a slight extent. Now every obstruction to the venous flow hinders also the arterial flow, though in a much smaller degree, and undoubtedly phlebosclerosis in some cases precedes arteriosclerosis. Sack showed by the statistical method that the two diseases are closely related. There is need of further study of these questions.

The important relations of phlebosclerosis to varicose dilatations of the veins are discussed under *Varicose Veins.*

SACK'S TABLE SHOWING THE DISTRIBUTION OF PHLEBOSCLEROSIS.

	Number of bodies examined.	Number with phlebosclerosis.	Frequency of disease in percentages.
V. jugular. int.	20	7	35
V. brachialis	55	4	7
V. cephalic.	6	3	50
V. basilar	7	4	57
V. radial	52	0	0
V. ulnar.	58	0	0
V. iliac. ext.	61	23	38
V. femoral	67	51	76
V. popliteal	72	65	90
V. saph. mag.	55	50	91
V. saph. par.	14	13	93
V. tibial. ant.	88	24	27

Sclerotic veins are elongated and of varying calibre. They present constrictions and dilatations, the dilatations amounting in some cases to well-marked pouches filled and distended with blood. In the severer forms of the disease the vessels are curved upon themselves, and if superficial, they can be rolled under the finger like a cord.

The valves are insufficient, either from retraction of their leaflets or from adherence to the side of the vein. When the vein is cut open its walls show differences in thickness, at one point being strong enough, perhaps, to gape open like an artery, at another collapsing as a vein usually does. At times, portions of the veins show calcified plates and ulcerous spots, resembling in each case those so frequently found in arteriosclerosis. The most marked changes take place in the intima and the inner part of the media. The coats are thickened and present points of fatty changes and of coagulation necrosis often infiltrated with lime salts; at other points atheromatous débris may have formed.

SYPHILIS.—Some of the first observations on syphilis of the blood-vessels, as it affects the arteries at the base of the brain, were made by Virchow and Lancereaux. A good anatomical description of syphilitic arteritis was given by Allbutt in 1868. In 1874 Heubner published a study of fifty cases of syphilis of the cerebral vessels, in which he endeavored to establish a primary endothelial proliferation ("arterioma") as the specific form of arterial syphilis, the virus acting directly on the intima. In this he was opposed by Baumgarten, who, while not denying that syphilis causes endarteritis, yet claimed that the only arteritis histologically characteristic of syphilis begins in the lymph spaces of the adventitia and results in a gummatous periarteritis. Köster, Friedländer, and others supported Baumgarten's view, and

Friedländer regarded Heubner's endarterial proliferation as indistinguishable from endarteritis obliterans in general. According to this view the virus acts principally upon the adventitia through the vasa vasorum and the lymph vessels, the inflammatory process extending inward.

Syphilis of the Smaller Vessels.—At the present time the general teaching is that syphilis of the smaller vessels occurs either as an independent process or as part and parcel of a local syphilitic infiltration; von Zeissel and other syphilologists state that primary vascular syphilis is one of the rare localizations of the disease. In the primary form the vessels involved usually present yellowish-white or grayish thickening of the adventitia and the intima. A smaller vessel, such as a cerebral artery for example, may be studded with translucent or whitish, circumscribed patches, more or less cartilaginous in consistency and non-calcified; or a certain length of the vessel may be transformed into a whitish cord. The tendency to fibrous obliteration of the lumen is pronounced, but in the earlier stages the proliferation in the intima is richly cellular and vascular. This is the syphilitic endarteritis of Heubner. It is now generally held that this form cannot be distinguished either microscopically or macroscopically from certain thickenings of non-syphilitic origin. The occurrence of obliterating endarteritis in circumscribed form in youthful persons is regarded, however—and as unquestionably so when associated with gummous nodules—as in the majority of cases the result of syphilis. The new tissue in the intima may contain vascular spaces. The elastic layer is greatly thickened and folded. Bands of elastic fibres appear in the thickening, and their development is ascribed by Abramow and Haga as due to a splitting up of the old membrane by the growth of fibrous tissue between its layers. But it is also probable that new elastic fibres form; at all events, that is not impossible. A reduplication of the elastic layer is regarded by Wendeler as marking each standstill of the process. The elastic elements do not appear to differ in their behavior from that seen in endarteritis obliterans in general.

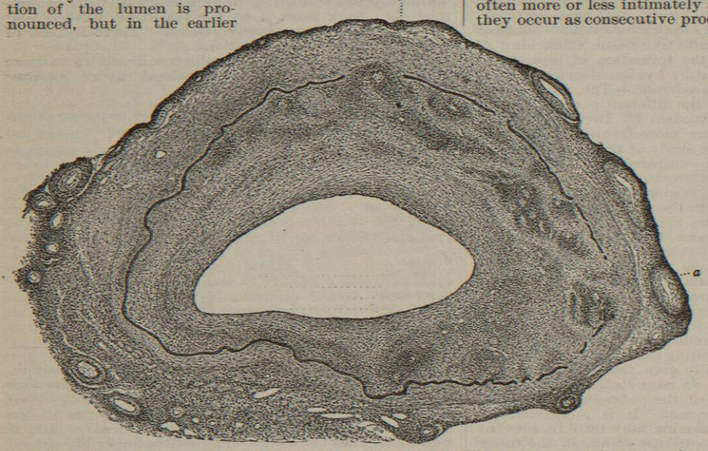

FIG. 632.—Gummous Arteritis. Great intimal thickening with small cellular areas—gummata. At *a*, perivascular infiltration of intima. (From Nothnagel's "Specielle Pathologie und Therapie," 1899, xv., p. 147.)

At other times the vessels are surrounded either with nodular, cellular infiltrations or dense cicatricial tissue. In the primary syphilitic lesion there is marked periarterial infiltration, which is surrounded by an external ring of elastic elements, probably part of the walls of the perivascular lymph spaces in which the cellular proliferation takes place. In later syphilitic foci, when the granulation-tissue formation is in the recent stage, there is cellular infiltration in the adventitia, media, and intima. Distinct gummous nodules, either purely cellular (lymphoid and epithelioid cells) or with a granular, necrotic centre and a cellulo-fibrous periphery with giant cells, may be found in the vessel wall (Baumgarten's gummous arteritis), most frequently in the adventitia. This is the only form of syphilitic arteritis that is histologically specific (Fig. 632).

The gummata develop especially in the adventitia, more rarely in the media and the intima. Occasionally a single cross section may show a series of nodules in the various layers of the wall. Later, when fibrous transformation takes place, all the coats become fibroid, the media atrophic.

Gummous periarteritis and productive endarteritis are often more or less intimately associated, especially when they occur as consecutive processes in the midst of syphilitic foci. The different appearances so often observed are explainable in a measure by the degree and the duration of the disease. Syphilitic arteritis differs from arteriosclerosis by its circumscribed occurrence and by the tendency to organization and obliteration; fatty changes and calcification are not characteristic of syphilis.

Most of the investigations on syphilis of the smaller arteries concern the cerebral. The apparent frequency with which the cerebral vessels, especially at the base, are affected by these processes is explained as in part the outcome of the great interest that clinicians take in all the phases of cerebral syphilis, and perhaps also because the basal vessels are constantly bathed in cerebro-spinal lymph. The anterior cerebral arteries—the cerebral branches of the internal carotid—are the ones especially involved. But syphilitic vasculitis as an independent process occurs elsewhere. In the spinal cord both arteries (Marinesco, Pick) and veins (Lamy, Orlowsky) may be involved. The coronary arteries, the arteries of the extremities, the splenic, the retinal, the mesenteric, and the adrenal (Weichselbaum) may be diseased more or less extensively as well. According to Urlich, Palma, and Birch-Hirschfeld, syphilitic changes in the coronary arteries may be primary or consecutive, the left coronary artery being affected more frequently than the right.

In Abramow's cases there were circumscribed nodules in the walls of the arteries of the extremities and of the intimal organs, the cerebral being spared. In some the appearances described by Heubner predominated; in others, a more diffuse cellular infiltration with gummous nodules, especially in the adventitia, the muscular coat showing a granular disintegration. The destruction of the media by cell proliferation beginning either in the adventitia or the intima had resulted in places in aneurismal dilatations. Some of the appearances presented resemble not a little those of periarteritis nodosa.

Von Zeissl, Lomokowsky, and Haga describe syphilitic arteritis of the extremities. In Haga's case the vascular

disease resulted in spontaneous gangrene; this form of spontaneous gangrene seems quite frequent in Japan. Haga reports thirteen cases, in all of which the vessels of the affected extremities presented the same changes. The vascular lumen was obliterated either as the result of successive intimal thickenings, due to the production of a vascular new tissue solely, or from thrombosis. The media was thickened. In nine of the thirteen cases there were focal accumulations of round cells about the vasa vasorum, and in some instances cellular nodules were present in the media and the intima (gummous arteritis). Quite similar changes were observed in the veins. Scriba suggests that in some cases this arteritis is the result of congenital syphilis.

Von Zeissl and Langenbeck describe syphilitic arteritis of the brachial artery that was healed by antiluetic treatment.

Syphilis of the Aorta and Larger Vessels.—Isolated instances of gumma in the walls of the larger arteries, especially the pulmonary, have been described by Weber, Wagner, Virchow, and others. Weber describes a gumma as large as a bean in the pulmonary artery, beginning in the media under the intact intima and causing great narrowing of the lumen.

Syphilitic Mesarteritis.—Wagner, Hertz, Backhaus, Doehle, Heller, and others describe a primary syphilitic mesaortitis. Macroscopically the intima presents circumscribed fissured and furrowed areas and depressions, which occur in groups especially at the beginning of the aorta and near the origin of the larger vessels. Elsewhere the intima may be smooth and normal or the seat of sclerotic changes. The media in such areas may be wholly absent or replaced by a thin layer of scar tissue. Microscopically there is proliferation about the vasa vasorum which may show obliterating changes, and there may be more or less distinct gummata with necrotic centres (Heller, Backhaus) as well as cicatricial areas with thickening of the intima and retractions, giving it the peculiar linear and irregular pit-like depressions that are regarded as characteristic of specific mesaortitis. Foci of small-celled infiltration, as well as diffuse fibrous changes, are present in the adventitia. These changes may be combined with ordinary arteriosclerosis. Backhaus states that of ninety-nine syphilitics examined at the Kiel Institute, seventeen showed mesarteritis. Doehle describes a typical case in a syphilitic woman, aged twenty-five. Belfanti describes beginning gummous nodules in the aorta with marked circumscribed thickenings in the intima. Irregular ulcerations in the aorta with callous margins are also recorded as of syphilitic origin. Bollinger has also described a gummous form of endarteritis. All seem to agree that the presence of circumscribed areas of fibrous attenuation of the aortic wall, associated with more or less dilatation, may be regarded as the result of syphilitic mesaortitis; the changes are observed not rarely in rather young persons; there are often distinct syphilitic lesions in other organs, and the changes in the aorta certainly do not correspond to those of ordinary arteriosclerosis. It is upon the basis of such lesions that aneurisms in young syphilitics probably develop. I have seen two cases of multiple, small sacculated aneurisms in the beginning of the aorta that originated in fibrous mesaortitis; in both cases were areas of marked fibrous attenuation without much compensating fibrous thickening in the intima.

Syphilis is also regarded as playing an etiological rôle of a more general nature but of great importance in the vulgar form of arteriosclerosis. The occurrence of arteriosclerosis and of arteriosclerotic aneurism in young syphilitics is rather frequent and is generally known. On account of the many complex factors that enter into consideration in arteriosclerosis the exact rôle of syphilis is hard to define.

Syphilitic Phlebitis.—Much that has been said of syphilis of the arteries is applicable to syphilis of the veins, and especially as regards the secondary changes that occur in smaller veins in the midst of larger syphilitic foci. Dowse briefly refers to obliterative changes in the posterior cerebral sinuses in a gummous pachymeningitis.

Oedmanson, Winckel, and Birch-Hirschfeld described diffuse and circumscribed endophlebitis of the umbilical veins of congenital syphilitics. Schüppel has described a gummous pylephlebitis in congenital syphilis, and Bowman attributes certain cases of thrombosis of the stem of the portal vein to syphilitic periphlebitic changes. Huber found intimal thickening with petrification in the veins of the extremities of a syphilitic girl twenty-two years old.

In *congenital syphilis* there frequently occurs an obliterative vasculitis of the umbilical vessels which was first described by Oedmanson. Schüppel has described peripylephlebitis in a syphilitic infant, and in 1864 Virchow observed an ossifying endaortic process in a girl of eighteen with congenital syphilis. The vascular changes of the lesions of congenital syphilis in the internal organs resemble those of the acquired disease. Reference has been made to Scriba's view that spontaneous gangrene may be caused by an arteritis of congenitally syphilitic origin.

TUBERCULOSIS.—The older pathologists, such as Rokitansky and Virchow, regarded the blood-vessels as immune to tuberculosis. The demonstration by Weigert in 1877 that acute general miliary tuberculosis results from the tuberculous invasion of either a blood-vessel or the thoracic duct put an end to this theory. So thoroughly did Weigert demonstrate this course of events that when the tubercle germ was discovered a few years later he could say truthfully that it was necessary only to substitute bacillus for poison in order to make the report of his investigations conform fully to the new requirements.

Tuberculosis of the walls of blood-vessels may result from the extension of the process from adjacent tuberculous foci. This may occur in the arteries and veins. In case the lumen is not closed by productive endovasculitis and thrombosis, the infiltration in the vessel wall on caseation and disintegration may give off tuberculous material and bacilli to the circulating blood. This leads to embolic or miliary tuberculosis of the corresponding capillary district. In the case of the pulmonary vein, the general circulation becomes infected; in the case of a systemic vein, miliary tuberculosis of the lungs results; and if it concerns an artery, miliary tubercles may spring up in its capillary district. Tuberculous and suppurative destruction from without of the branches of the pulmonary artery exposed in tuberculous pulmonary cavities may so weaken the wall that aneurismal dilatations develop ("erosion aneurism"). Many of the copious hemorrhages in advanced pulmonary phthisis result from the rupture of aneurisms of this nature.

Dittrich, Kamen, and Sigg have described tuberculosis of the wall of the aorta due to direct extension. In Dittrich's case an adherent lymph gland communicated the disease to the thoracic aorta, the intima of which presented an oval defect with elevated ridges, a continuous tuberculous process traversing the aortic wall. Kamen's case was of similar origin, the vessel presenting a dilatation with rupture of the wall. In Sigg's case a tuberculous lung was adherent to the aorta, which presented a bulging corresponding to the caseous replacement of its wall, the caseous area being covered internally by a thrombus.

When tubercle bacilli reach the circulating blood they sometimes become implanted upon the intima of larger vessels such as the aorta. Weigert, Flexner, Hanot and Levy, Stroebe and Blumer have described pinhead-sized intimal, aortic tuberculous masses. Blumer describes two instances of intimal tuberculosis of the abdominal aorta; in one of the cases there were several minute nodules of characteristic structure. The sclerosis of the aorta present in both cases did not play any part in determining this localization. In all of these cases the infection took place directly upon the intima and not through the vasa vasorum or the lymphatics of the walls of the artery. The tuberculous masses appeared as if

they had been fastened upon the intima. The surface of such areas may contain tubercle bacilli in large numbers.

According to Cadéac tuberculous aortitis is not uncommon in cattle. I have recently studied a tuberculosis of the aorta in a dog. A large nodule developed in the wall of the aorta near the heart, producing such weakening that a small bulging had resulted.

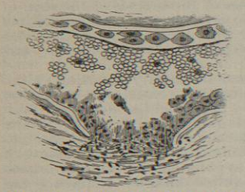

FIG. 633.—Perforation of the Elastic Layer by Caseous Intimal Focus, Infiltration into Media and Adventitia, and Beginning Aneurismal Bulging. Note beginning subendothelial proliferation in opposite wall from tuberculous leptomeningitis. (Hektoen, *The Journal of Experimental Medicine*, vol. 1.)

The relation of tuberculosis of the blood-vessels to general miliary tuberculosis is discussed elsewhere. At this time it is sufficient to say that tuberculosis of the intima of blood-vessels or of the thoracic duct or tuberculous endocarditis constitutes an essential, intermediate stage in the development of acute general miliary tuberculosis. It is in the tuberculous areas that result from infection of the intima and of the endocardium that the germs multiply so freely that masses are thrown into the general circulation and produce on lodgment in the internal organs the numberless nodules characteristic of general miliary tuberculosis. There is no satisfactory evidence that tubercle bacilli multiply in the blood; hence miliary tuberculosis means the setting free into the circulation at one time of large numbers of bacilli (Weigert, Benda, Gaylord).

The vascular changes in tuberculous leptomeningitis are interesting and well marked. There is a tuberculous endarteritis characterized by the formation of intimal tubercles and a diffuse subendothelial intimal proliferation (Figs. 633 and 634), probably induced by the implantation of tubercle bacilli from the blood. From the intima the infiltration may spread into the muscular coat and the adventitia and the whole wall may undergo caseous and hyaline degeneration. Occasionally, though rarely, the intimal process so weakens the wall that small, local dilatations take place—a species of mycotic aneurism. Proliferation in the adventitia may invade the media and the intima and the whole wall of the arterial segment may undergo degeneration. In tuberculous leptomeningitis the muscularis often presents the hyaline degeneration described by Guarnieri and others. The epithelioid cells that constitute such a prominent feature of the intimal proliferation undoubtedly originate from the subepithelial connective tissue rather than from the epithelial lining, which appears to remain intact until caseation takes place. Plasma cells and phagocytic cells are also present.

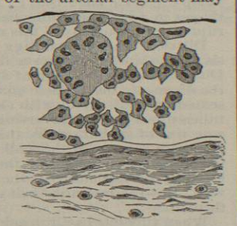

FIG. 634.—Subendothelial Intimal Proliferation with Multinuclear Giant Cell. From tuberculous leptomeningitis. (Hektoen, *The Journal of Experimental Medicine*, vol. 1.)

In this form of tuberculosis adjacent extravascular and arterial foci frequently extend to the veins (Fig. 635).

Banti describes a case of general tuberculosis in which nearly the whole length of the superior vena cava was completely filled by a mass of neoplastic tuberculous tissue which projected into the right auricle.*

* Mügge: Virchow's Archiv, Bd. 76.

ACTINOMYCOSIS.—As actinomycosis spreads through the tissues by direct extension, no anatomical structure is absolutely secure from invasion, not even the blood-vessels. In metastatic actinomycosis the fungus gains entrance into the circulation by the direct involvement of the walls of the blood-vessels in the vicinity of a local process. In the cases in which the point of invasion of the vascular system has been directly demonstrated it concerns some of the larger veins and cerebral sinuses.

The meningeal sinuses and veins are frequently attacked in cranio-cerebral actinomycosis. In many cases of actinomycotic phlebitis the generalization of the process is undoubtedly prevented or delayed by consecutive thrombosis.

Ponfick describes an actinomycotic proliferation which projected button-like into the lumen of the internal jugular vein; this invasion became the direct or indirect source of secondary foci in the heart, lungs, spleen, and brain.

In a case of primary pulmonary actinomycosis with extension through the diaphragm and into the spleen, Arnold Paltauf found the splenic vein infiltrated and thrombosed, the thrombosis extending into the portal vein; there were metastatic foci in the liver and in the brain. Lüning and Hanau describe perforation in the hepatic vein in a secondary actinomycosis of the liver. In pulmonary actinomycosis with extension to the pleura and pericardium Habel found the base of the heart and the larger vessels surrounded by a spongy tissue; just above the entrance into the auricle the superior vena cava presented a circumscribed area in which the normal wall was substituted by a nodular mass of pale yellow color; the jugular veins were thrombotic. Abée describes an actinomycotic perforation of the inferior vena cava. Beginning in the œsophagus the process spread out in the prevertebral, mediastinal, and peripleural tissue, and invaded the diaphragm and the spinal column. The infiltration between the right lung and the diaphragm surrounded the inferior vena cava in the form of a layer, 3 to 4 cm. thick, of a reddish, soft tissue riddled with confluent abscesses. At the point where the vein enters the auricle its lumen was materially narrowed, the intima roughened, covered by parietal thrombi and perforated by numerous yellowish suppurative foci; below, the vein was partially filled with a large softened thrombus. There were numerous metastatic actinomycotic abscesses in various parts of the body.

FIG. 635.—Focal Tuberculous Infiltration with Giant Cell, Extending through Wall of Vein with Secondary Thrombosis, Caused by Extension in Tuberculous Leptomeningitis. (Hektoen, *The Journal of Experimental Medicine*, vol. 1.)

LEPROSY.—Leprous nodules sometimes occur in the walls of the veins in leprosy of the extremities.

PERIARTERITIS NODOSA.—This remarkable disease was described by Kussmaul and Maier in 1866. Cases had been observed previously by Pelletan in 1810 and by Rokitansky, but their descriptions were confined to the macroscopic appearances. Since Kussmaul and Maier fastened the attention upon the disease additional instances have been recorded, so that the total number of cases now is thirteen (von Schrötter). All of the cases have occurred in Central and Southern Germany except one—a Russian instance (Freund). The disease appears to attack young persons mostly between twenty and thirty; it occurs also in children. The male sex has so far furnished more cases. The symptoms are, generally speaking, those of a more or less severe toxic polyneuritis and polymyositis with constitutional and digestive disturbances, abdominal pain, renal symptoms, etc. In nearly all cases a peculiar anæmia and general weakness have been recorded. The whole course of the disease takes from six to twelve weeks, the termination as far as known being always fatal. In Kussmaul and Maier's instance minute nodules were present in the skin of the face, neck, and upper extremity. It is quite likely that in the future the disease will be diagnosed during life, especially in instances with subcutaneous nodules which might be excised and examined microscopically. Clinical observation has not brought out any common or striking etiological conditions. Syphilis has been present in some cases and definitely excluded in others.

The vascular lesions consist of nodular, eccentric, and more diffuse thickenings of arteries of the general size of the coronaries and hepatic and smaller; the swellings are grayish and grayish white in color, vary in size from pinhead to pea and larger, occur especially at the branchings, but also in the course of the arteries both when free and intraparenchymatous. The distribution and number of the swellings, usually present in great numbers, vary somewhat in different cases (Weichselbaum and Thompson); the favorite locations are the mesenteric (including the intraparietal branches of the gastro-intestinal tract), and the coronary, then the muscular, intraneural, renal, hepatic, splenic, bronchial, and subcutaneous. Nodules have also been described at the origins of the intercostal branches of the aorta and of branches of the crural and popliteal arteries. It is noteworthy that up to this time the veins have not been involved (Fig. 636).

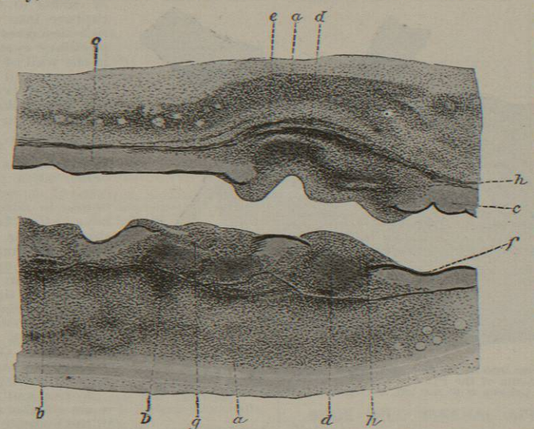

FIG. 636.—Periarteritis Nodosa. Longitudinal section of a small muscular branch. (After Freund.) *a*, Adventitia, greatly infiltrated with cells; *b*, foci of especially dense cell accumulations in adventitia; *c*, normal media; *d*, degenerated media; *e*, external elastic lamina, bulging outward; *f*, internal elastic layer; *g*, remnants of internal elastic layer; *h*, proliferating intima.

The histogenesis of the arterial lesions, which are of an inflammatory nature associated at times with aneurismal dilatations, fibrous tissue formation and thrombosis, is not agreed upon. Fletcher, von Kahlden, and Freund regard the process as primarily inflammatory, due to the action of some unknown substance, which reaches the adventitia by way of the vasa vasorum. This view is supported by the presence, in Fletcher's case, of nodules upon the vasa vasorum and by the microscopic appearances in the early stages of the process (Freund). Accordingly, the inflammatory round-cell infiltration, which appears to be of a non-specific type, begins in the adventitia and extends through the media to the intima, producing in the last marked cellular accumulations between it and the media. As a result of the inflammation the muscular coat undergoes a circumscribed hyaline degeneration, and hyaline material, probably of exudative origin, also appears in the subepithelial layers. There are not many polymorphonuclear cells in the cellular infiltration, which consists largely of spindle-shaped cells with large nuclei. Freund did not find proliferation in the intima when the media was normal. Eventually the internal elastic coat and the media are so thinned and destroyed that circumscribed aneurismal bulgings of the vessel wall may occur, but the formation of aneurisms is not constant because the development of fibrous tissue may prevent dilatation.

Others, like Weichselbaum and Chvostek, hold that the process is primarily an endarteritis, which extends to the outer coats. In the case of smaller arteries and of vasa vasorum this would seem to be the fact probably.

It has been suggested that periarteritis nodosa is a primarily multiple tumor of the nature of lymphoma, beginning in the adventitia. Circumscribed accumulations of cells occur in the adventitia that resemble lymphomata; but the singular fact that the process is confined to arteries speaks against this view. The subsequent formation of fibrous tissue is also inconsistent with this theory.

Meyer regarded tears in the media as the essential cause, and Eppinger has elaborated the theory that periarteritis nodosa is the result of the formation of multiple aneurisms on account of ruptures of the elastic elements, which are congenitally weak and imperfect. Eppinger proposes to call the disease congenital aneurism. The proliferation observed, in the adventitia and intima, which constitutes such a striking feature of the lesions, is regarded by Eppinger and the supporters of the aneurismal theory (von Schrötter) as secondary; and the thrombi and hard fibrous masses sometimes observed are similarly explained. Aneurisms are not observed in every instance of periarteritis nodosa; in Pelletan's, Rokitansky's, Eppinger's, Weichselbaum's, and Meyer's cases they were marked. In Pelletan's case sixty-three aneurisms were present. The development of aneurisms is consistently explained on the score of more marked inflammatory and degenerative weakening of the arterial wall in some nodules than in others in which these processes were not so rapid. Any evidence of a histological nature of a congenital structural imperfection of the arteries in periarteritis nodosa has not been furnished. Eppinger's theory does not satisfactorily explain the relative infrequency of involvement of the cerebral arteries, which would seem to be as liable to aneurismal dilatations as other arteries, if not more so. The clinical course of the disease is also against this view.

The histological appearances and the genesis of the changes as explained by Freund and others rather favor the view that periarteritis nodosa is a primarily inflammatory process in the further course of which aneurisms frequently develop; but further studies are essential before the question of the nature of this disease can be definitely established. Micro-organisms have not been found in the lesions. Syphilis has been suggested as the underlying condition. Graf finds histologically periarteritis nodosa resembles not a little Heubner's endarteritis syphilitica; and the appearances described by Abramow in two cases of syphilitic arteritis involving many of the smaller arteries, except the cerebral, are also decidedly suggestive of periarteritis nodosa, the clinical symptoms of which were absent, however. The absence, in some cases of periarteritis nodosa, of all history of syphilis and the freedom of other organs from syphilitic lesions and

their consequences are also against the specific theory; and it does not appear that the vascular lesions of periarteritis nodosa ever present nodular foci of cell accumulations with central necrosis such as occur in the gummous form of syphilitic arteritis. Periarteritis nodosa must be regarded, for the present, as a distinct disease, histologically and clinically. Syphilitic periarteritis should not be included under periarteritis nodosa, as is done by some writers like Mott in Allbutt's "System."

Many of the clinical symptoms are evidently due to secondary lesions in the internal organs. Although the intramyocardial branches of the coronary arteries are generally involved, the myocardium itself usually presents but slight changes. Whether bronchitis and other inflammatory changes in the lungs are directly secondary to changes in the bronchial arteries, the pulmonary being usually free (von Schrötter), cannot be stated. The mucous membrane of the gastro-intestinal tract has been found to be the seat of multiple ulcers and hemorrhages; the ulcers in the stomach being more of the nature of erosions while those in the intestines may resemble typhoid ulcers. These changes are regarded as the result of circulatory disturbances in the areas nourished by the affected branches, many of which become entirely occluded by thrombosis. Enlargement of the mesenteric glands is usually present. The spleen may be the seat of infarcts, in various stages of absorption, caused again by the occlusion of terminal arteries. Pressure of the nodules in the intrahepatic branches of the hepatic artery on the bile ducts may cause jaundice (von Schrötter). Severe changes are produced in the kidneys. Multiple ischæmic necrosis results from thrombosis of the affected arteries. Degeneration of the glomeruli, hemorrhages, parenchymatous and interstitial changes develop, due either to extension of the vascular changes or to the action of toxic substances in the blood. The changes in the peripheral nerves and in the skeletal muscles explain well the nervous and muscular phenomena observed clinically. The pressure of changed arteries upon adjacent nerves may cause degenerations, and in Freund's case foci of degeneration in the nerves were found to correspond to nodules upon intraneural arterial branches. The development of nodules upon the intramuscular arteries gives rise to granular and fatty disintegration of the muscle fibres and to waxy changes.

In Weichselbaum's case the rupture of an aneurism, 2 cm. in diameter (the largest so far recorded in periarteritis nodosa), upon the arteria profunda cerebri gave rise to hemorrhage.

TUMORS.—The primary tumors composed of blood-vessels—the various forms of angioma—are described in the article on *Tumors*. Here is described also the part that blood-vessels play in the general dissemination of the malignant tumors. Primary tumors rarely develop in the walls of blood-vessels. Brodowski has described a primary sarcoma of the thoracic aorta, which started in the adventitia and extended through the muscular coat and into the intima; the sarcomatous infiltration of the intima produced a marked thickening of the latter.

I have described an interesting pedunculated outgrowth of the intima of the basilar artery, which at that time was regarded as a fibroma. It is possible, however, that the outgrowth in reality was the result of an endarteritic proliferation of inflammatory nature.

Several instances of myoma, fibroma, and sarcoma have been described as primary in veins (Orth).

Secondary tumors occasionally occur in the walls of the blood-vessels. Quincke, in "Ziemssen's Encyclopedia," cites an instance, described by Broca, of cancer at the root of the aorta with rupture into the pericardium. Friedrich describes metastatic nodules of a papillary cystocarcinoma of the ovary in the wall of the thoracic and abdominal aorta and the renal artery; here the metastases evidently occurred through the vasa vasorum. The nodule in the thoracic aorta ruptured into the lumen of the vessel.

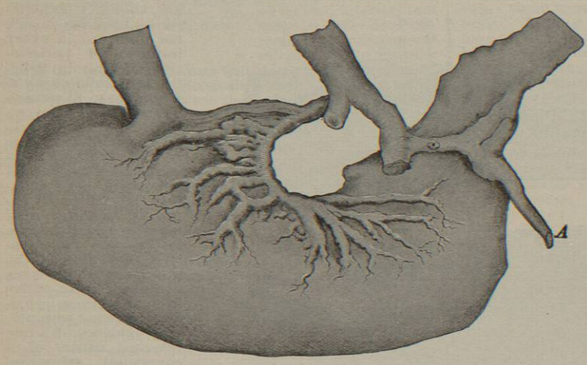

FIG. 637.—Growth of Carcinoma into the Gastric and Portal Veins and the Radicles of the Latter, Secondary to Carcinoma of the Pylorus. The posterior surface of the stomach, which is turned so that the pylorus is to the left, is exposed. *A*, Cut end of gastro-duodenal vein.

Extensive intravascular growth of malignant tumors, especially in the veins, takes place in the case of sarcoma of various kinds, especially of the bones, in adrenal tumors of the kidneys, etc. Intravascular growth of this kind has extended from the renal vein, for instance, to the heart.

In carcinoma of the stomach I have observed an extensive intravenous growth of the tumor resulting in a kind of carcinomatous injection of all the veins about the lesser curvature of the stomach and of the portal vein (Fig. 637). Orth observed the entire venous plexus of the dorsum of the foot filled with sarcomatous masses.

Norĭca and Haret* describe a carcinoma of the stomach with metastases in the mesenteric, mediastinal, and deep cervical glands, followed by carcinomatous invasion and thrombosis of the superior vena cava, the two brachiocephalic, subclavian, and internal jugular veins. In 1885 Oulmont collected nineteen cases of obliteration of the superior vena cava. He distinguished two groups, namely, obliteration by pressure and obliteration by concretion. The first group comprised five cases due to cancer of the mediastinum or of the lung, two cases due to tuberculous lymph glands, and four cases due to aortic aneurism. The second group included five cases of thrombosis and three cases of cancerous invasion. Comby and Rendu each report a clinical case in which aneurism of the aorta was thought to be the cause. I have examined post mortem a case of this kind, in which an aneurism of the ascending aorta compressed the superior vena cava, which was wholly obliterated by the formation of fibrous tissue in the intima. The occlusion took place gradually and resulted in a great dilatation of the subcutaneous thoracic and abdominal veins which for years furnished routes for collateral circulation. Letulle lays stress on occlusion of the large veins of the neck and mediastinum on account of propagation of carcinomata of the glands, the thyroid, and the thymus.

*Bulletins et mémoires de la Société Anatomique de Paris, 1899, lxxiv., 861.

Gallavardin reports thrombosis of the large cervical veins in mitral stenosis. The extensive occlusion described by Norĭca and Haret has been equalled by the case of Reid only, which is included in Oulmont's series. There was in Norĭca and Haret's case dilatation of subcutaneous veins of the right side of the chest and abdomen, showing that the blood in the superior vena cava was diverted into the inferior by way of the azygos vein. This diversion furnished a sufficient collateral circulation. The condition of the thoracic duct was not examined.

Ludvig Hektoen.

LITERATURE.

General.

Allbutt: A System of Medicine, 1899, vii.
Orth: Lehrbuch d. path. Anatomie, 1887.
Von Schrötter: Nothnagel's Specielle Path. u. Therapie, 1899, xv.

Abnormities.

Brooks: Journal of Anat. and Physiol., 1886, xx.
Dowse: Transactions London Path. Society, xxvii., 11.
Lancereaux: Traité d'anatomie path., 1881, ii., 948.
Peacock: Malformations of the Heart, 1866.
Rauchfuss: Virch. Arch., 1859, xvii., 376.
Shaw, D. Lee: Aorta with Double Arch. Journal of American Medical Association, 1897.

Retrogressive Changes.

Mallory, F. B.: A Contribution to the Study of Calcareous Concretions in the Brain. The Journal of Pathology and Bacteriology, 1896, iii., 110.

Angeitis.

Borchard: Beiträge zur primären Endarteritis obliterans. Deutsche Zeitschrift f. Chirurgie, xliv.
Bollinger: Endophlebitis verrucosa im Pfortader eines Pferdes. Virchow's Archiv, 1872, lv., 279.
Boinet et Romary: Recherches expérimentales sur les aortites. Arch. d'Anat. Path., 1897, ix., 902.
Chiari: Ueber die selbstandige Phlebitis obliterans der Hauptstamme der Venae Hepaticæ als Todesursache. Ziegler's Beiträge, 1899, xxvi., 1.
Fenger, Christian: Stenose af Ostium pulmonale og Arteria pulmonalis, forårsaget ved Vegetationer pa Pulmonalklapperne og i Arterien, oplyst ved et Sygdomstilfælde. Nordisk Medicinskt Arkiv, Band v., No. 4.
Flexner, Simon: Perforation of the Inferior Vena Cava in Amœbic Abscess of the Liver. The American Journal of the Medical Sciences, May, 1897.
Haga: Ueber Spontane Gangrän. Virchow's Archiv, 1898, cliii., 26.
Hunter, John: Transactions of a Society for the Improvement of Medical and Surgical Knowledge, 1793.
Jones: Ueber die Neubildung elastischer Fasern in der Intima bei Endarteritis. Ziegler's Beiträge, 1898, xxiv., 458.

Angiosclerosis.

Councilman, William T.: On the Relations between Arterial Disease and Tissue Changes. Trans. Assn. of American Physicians, 1891, vi., 179.
Dmitrijeff: Die Veranderung der elastischen Gewebes der Arterienwände bei Arteriosklerose. Ziegler's Beiträge, 1897, xxii., 207.
Durante: Athérome congenital de l'aorta et de l'arterie pulmonaire. Bull. et Mém. de la Soc. Anat. de Paris, 1899.
Eberhardt, Alexander: Ueber den sogenannten körnigen Zerfall und Querzerfall der elastischen Fasern und Platten in ihrer Beziehung zu den Erkrankungen des Arteriensystems, 1892.
Epstein: Ueber die Struktur normaler und ectatischer Venen. Virchow's Archiv, 1887, cviii.
Gazert: Ueber den Fett und Kalkgehalt der Arterienwand bei Atheromatose und Arteriosclerose. Deut. Arch. f. kl. Med., 1899, lxii., 389.
Laache, S.: Om Sklerose af arteria pulmonalis og erhvervet "morbus cœruleus." Norsk Magasin fer Lägevidenskaben, 1900, lx., 51.
Malkoff: Ueber die Bedeutung der traumatischen Verletzungen ven Arterien für die Entwicklung der wahren Aneurysmen und der Arteriosklerose. Ziegler's Beiträge, 1899, lxxv., 431.
Peabody, George L.: Relations between Arterial Disease and Visceral Changes. Trans. Assn. of American Physicians, 1891, vi., 154.
Sack: Ueber Phlebosklerosis und ihre Beziehungen zur Arteriosclerosis. Dissertation, 1887.
Sauné: De l'athérome et de l'artère pulmonaire. Thèse de doctorat, 1877.
Thoma: Virchow's Archiv, vols. xciii., xcv., civ., cv., cvi., cxi., cxii., cxiii.

Syphilis.

Abramow: Ueber die Veränderungen der Blutgefasse bei der Syphilis. Ziegler's Beiträge, 1899, xxvi., 202.
Birch-Hirschfeld: Beitr. zur pathol. Anatomie der heredit. Syphilis. Arch. f. Heilk., 1875, xvi., 106.
Bowman: Beiträge zur Thrombose des Pfortader-stammes. Deut. Arch. f. kl. Med., 1889, lix., 283.
Huebner: Die leutische Erkrankungen der Gehirnarterien, 1874.
Huber: Ueber syphilitische Gefässerkrankung. Virchow's Archiv, 1880, lxxix., 573.

Tuberculosis.

Blumer, George: Tuberculosis of the Aorta. The American Journal of the Medical Sciences, January, 1899.
Gaylord, Harvey R.: Critical Summary of Literature on Tuberculosis of the Walls of the Blood-Vessels and the Production of Miliary Tuberculosis. The American Journal of the Medical Sciences, July, 1899.
Hektoen, L.: The Vascular Changes in Tuberculous Leptomeningitis, Especially the Tuberculous Endarteritis. The Journal of Experimental Medicine, 1896, i.

Periarteritis Nodosa.

Fletcher: Ziegler's Beiträge, 1892, xi.
Freund: Deutsche Arch. f. kl. Med., 1899, lxii.
Graf: Ziegler's Beiträge, 1896, xix.
Von Schrötter: Nothnagel's Specielle Pathologie u. Therapie, 1899, xv., 35.

BLOUNT SPRINGS.—Blount County, Alabama.

POST-OFFICE.—Blount Springs. Hotel.

ACCESS.—Viâ Alabama and Chattanooga Railroad, also viâ Louisville and Nashville Railroad to Elyton.

The springs are about thirty miles northwest from this station. The waters of Blount Springs may be classed as saline sulphureted. The springs are six in number, and are located in a triangular valley 1,580 feet above the sea level.

ONE UNITED STATES GALLON CONTAINS:

Solids.	No. 1 Red Spring. R. T. Brumby.	Sweet Spring. Brumby.	Spring No. 4. Summers.
	Grains.	Grains.	Grains.
Magnesium carbonate	4.40	3.60	9.40
Calcium carbonate	6.80	4.48	5.72
Barium carbonate	....	....	.91
Iron carbonate	1.92	1.12	3.19
Sodium carbonate	....	....	....
Magnesium sulphate	1.60	2.40	....
Calcium sulphate	....	....	1.27
Calcium phosphate	....	....	Trace.
Potassium chloride	....	....	7.07
Sodium chloride	32.32	30.88	23.21
Magnesium chloride	6.00	....	2.04
Iodides	....	....	....
Magnesium iodide	....	....	.14
Magnesium bromide	....	....	.16
Lithium	....	....	Trace.
Alumina	....	....	Trace.
Silica	....	....	2.44
Sulphur	....	....	....
Total	53.04	42.48	55.55
Gases.	Cu. in.	Cu. in.	Cu. in.
Carbonic acid	6.00	6.00	4.72
Sulphureted hydrogen	14.96	12.56	30.67
Oxygen	....	....	7.08
Nitrogen	....	....	

J. K. Crook.

BLUE HILL MINERAL SPRING.—Hancock County, Maine.

POST-OFFICE.—Blue Hill. Hotels.

ACCESS.—Viâ steamer from Portland, also by stage from Ellsworth, fourteen miles distant.

The Blue Hill Mineral Spring is located two and one-half miles northwest of Blue Hill village, and about six hundred feet in perpendicular height above the base of Blue Hill Mountain. Its situation assures freedom from all surface impurities. The existence of the spring was noticed by Dr. Charles T. Jackson in his second report of the geology of the State of Maine, published in 1838. It was not until recently, however, that improvements were made. A handsome and commodious building has been erected for the comfort of tourists and visitors at the springs, and a large bottling plant established. An analysis by Prof. S. P. Sharples, of Boston, resulted as follows:

ONE UNITED STATES GALLON CONTAINS:

Solids.	Grains.
Sodium chloride	0.29
Sodium sulphate	.81
Sodium carbonate	.15
Calcium carbonate	1.87
Iron carbonate	.59
Silica	1.07
Organic matter	Traces.
Total	4.78