or more highly specific agent will take its place. That such an agent may be discovered is, of course, quite possible. The studies of Avery and his co-workers on the effect of certain bacterial enzymes on pneumococci open up a new and very promising field for the control of pneumococcal infections, but thus far the only enzyme which has been discovered is that which affects Type III pneumococcus. Others may eventually be isolated which will control both Type I and Type II infections, and even some of the less prevalent types. These further developments, however, may be far in the future. For the present we must be content with anti-pneumococcus serum for the treatment of both Type I and Type II infections. We have seen that concentrated serum has a striking clinical effect on Type I pneumonia, especially when it is administered early in the disease, and we have shown that by prompt and adequate administration of serum the death rate in early Type I infections can be reduced from 25 to 30 per cent. to approximately 10 per cent. When we remember that Type I pneumonia constitutes one-third of all pneumococcal infections, it must be acknowledged that this is quite an achievement in itself. In Type II pneumonia the results are not so impressive, but even in this difficult group definite clinical effects appear to be obtained when the serum is administered early in the disease.

Modern bacteriology, then, has one more victory to its credit. It has proven the existence of many specific biological types of pneumococci, and through recognition of these specific types immunologists are working out a specific serum treatment which promises a sharp curtailment in the death rate of pneumococcal pneumonia.

CONCLUSIONS

1. The three dominant types of pneumococci are responsible (in America) for two-thirds of all pneumococcal pneumonias.

2. Type I pneumococcus is the most highly parasitic of the types, causing one-third of all pneumococcal pneumonias. Type II ranks second, producing one-fourth of the total.

3. Both Type I and Type II pneumococcal infections of the lung are amenable to serum treatment. In Type I pneumonia the results of serum treatment are excellent. In Type II pneumonia the effect of serum, while not so striking as in Type I cases, is nevertheless definite.

4. The development of a refined, concentrated, and polyvalent anti-pneumococcus serum has reduced the serum therapy of pneumonia to a simple, practical, and valuable therapeutic measure.

REFERENCES

- ¹ Griffith, F.: *Journ. Hygiene*, 1928, xxvii, 113.
- ² Cecil, R. L., and Plummer, N.: *Journ. Amer. Med. Assoc.*, 1932, xcvi, 779.
- ³ Cooper, G., Edwards, M., and Rosenstein, C.: *Journ. Exper. Med.*, 1929, xlix, 461.
- ⁴ Stryker, L. M.: *Ibid.*, 1916, xxiv, 49.
- ⁵ Heidelberger, M., and Avery, O. T.: *Ibid.*, 1923, xxxviii, 73.
- ⁶ Dochez, A. R.: *Ibid.*, 1912, xvi, 665.
- ⁷ Neufeld, F., and Handel, L.: *Arb. a. d. k. Gesundheitsamte*, 1910, xxxiv, 293.
- ⁸ Cole, R.: *Journ. Amer. Med. Assoc.*, 1913, lxi, 663.
- ⁹ Idem: *Ibid.*, 1929, xciii, 741.
- ¹⁰ Blake, F. G., and Cecil, R. L.: *Journ. Exper. Med.*, 1920, xxxii, 1.
- ¹¹ Goodner, K.: *Ibid.*, 1928, xlvi, 413.
- ¹² Gay, F. P., and Chickering, H. T.: *Ibid.*, 1915, xxi, 389.
- ¹³ Huntoon, F. M., Masucci, P., and Hannum, E.: *Journ. Immunol.*, 1921, vi, 185.
- ¹⁴ Cecil, R. L., and Larsen, N. P.: *Journ. Amer. Med. Assoc.*, 1922, lxxix, 343; Cecil, R. L., Baldwin, H. S., and Larsen, N. P.: *Arch. Int. Med.*, 1927, xl, 253.
- ¹⁵ Conner, L. A.: *Amer. Journ. Med. Sci.*, 1922, clxiv, 832.
- ¹⁶ Felton, L. D.: *Boston Med. and Surg. Journ.*, 1924, cxc, 819.
- ¹⁷ Idem: *Journ. Infect. Dis.*, 1928, xliii, 534.
- ¹⁸ Idem: *Journ. Amer. Med. Assoc.*, 1930, xciv, 1893.
- ¹⁹ Cecil, R. L., and Sutliff, W. D.: *Ibid.*, 1928, xci, 2035; Cecil, R. L., and Plummer, N.: *Ibid.*, 1930, xcvi, 1547.
- ²⁰ Krumwiede, C., jun., and Noble, W. C.: *Journ. Immunol.*, 1918, iii, 1.
- ²¹ Sabin, A. B.: *Journ. Infect. Dis.*, 1930, xlv, 469.
- ²² Park, W. H., Bullowa, J. G. M., and Rosenbluth, M. B.: *Journ. Amer. Med. Assoc.*, 1928, xci, 1503.
- ²³ Finland, M.: *New England Journ. Med.*, 1930, ccii, 1244.
- ²⁴ Sutliff, W. D., and Finland, M.: *Journ. Amer. Med. Assoc.*, 1931, xcvi, 1465.

- ²⁵ Physicians to the Royal Infirmary, Edinburgh: *Lancet*, 1930, ii, 1390.
- ²⁶ Armstrong, R. R., and Johnson, R. S.: *British Medical Journal*, 1931, i, 931.
- ²⁷ Baldwin, H. S.: *Amer. Journ. Med. Sci.*, 1931, clxxxi, 788.
- ²⁸ Heidelberger, M., and Avery, O. T.: *Journ. Exper. Med.*, 1925, xlii, 727.
- ²⁹ Cole, R.: *Ibid.*, 1917, xxvi, 453.
- ³⁰ Avery, O. T., and Dubos, R.: *Ibid.*, 1931, liv, 73; Goodner, K., Dubos, R., and Avery, O. T.: *Ibid.*, 1932, lv, 393.
- ³¹ Idem: *Journ. Amer. Med. Assoc.*, 1931, xcvi, 2062.
- ³² Cooper, G., Rosenstein, C., Walter, A., and Peizer, L.: *Journ. Exper. Med.*, 1932, lv, 531.

TREATMENT OF LOBAR PNEUMONIA BY ANTI-PNEUMOCOCCAL SERUM

BY

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The results of a preliminary study of twenty-six cases of lobar pneumonia, treated with concentrated anti-pneumococcal serum during the winter of 1930-1, have been published already,¹ and the account which follows is to be regarded as supplementary to the earlier report. Further trial was made during the winter 1931-2, with the important addition that alternate cases were treated, as nearly as possible, in order of admission to hospital. Thus a control group was established by which results of treatment could be judged.

SCOPE OF THE INQUIRY

One hundred and sixty cases of primary pneumococcal lobar pneumonia in adults, aged 20 to 60, comprising fifty-four cases of Type I infection, forty-eight of Type II, three of Type III, and fifty-five nondescript ("Group IV") formed the clinical basis of the inquiry. Generally speaking, the illness was more severe in Types I, II, and III than in the nondescript infections. Equal numbers of men and women suffered from pneumonias due to unclassified strains; the proportion of males to females in Type I and also in Type II cases was 4 to 1. No case was treated later than the sixth day of illness. The average age of the patients in the treated and control groups was the same, as also the average day of the illness on admission to hospital. Patients dying within twenty-four hours of admission, whether treatment was begun or not, were omitted from the series.

The only satisfactory method of administering anti-pneumococcal serum is by the veins, requiring some dexterity and care when repeated inoculations have to be made. There is constitutional disturbance or shock in some patients after inoculation, and the concentrated serum is costly; for these reasons treatment is not lightly to be undertaken except in Type I and Type II pneumococcal pneumonias—approximately two-thirds of the cases—for which alone therapeutic serums are available. It follows, therefore, that, in the interests of the patient and of economy, the serological type of infecting pneumococcus must be rapidly determined prior to treatment. A simple method has been devised to meet this need.

DIRECT METHOD OF DETERMINING PNEUMOCOCCAL TYPE

It has been found that the type can be determined² in a few minutes by the simple process of mixing on a microscope slide the three standard diagnostic serums, Types I, II, and III, with a fleck of the sputum to be tested. The specimen is then examined with the dry lens (1/6 inch objective) and 4 ocular with substage condenser removed. The pneumococci, which are normally only just visible with this magnification, appear greatly

enlarged in a positive reaction, the characteristic lanceolate pairs equalling in long diameter the size of a red blood cell. This apparent enlargement is the result of association of the pneumococcal capsular substance with the specific antibody contained in the homologous serum, producing a change in the refractive index of the material surrounding the pneumococci which become conspicuous, as first described by Neufeld.³ Ninety-three per cent. of the 160 cases studied were typed by this direct method, which is most successful early in pneumonia at the stage when serum treatment may be best applied. Type was diagnosed in forty-nine of the fifty-one treated cases on the first specimen of sputum examined, and treatment was begun forthwith. In the two remaining cases the appearances were suggestive and serum was given at once, the expected type being confirmed on subsequent sputa.

It is important to recognize that the clear mucoid bronchial secretion, often mistaken for saliva, expectorated or obtained by swabbing the throat at the very outset of a pneumonia, is the most likely material, when obtained fresh from the patient, to contain the causative pneumococci. The characteristic rusty sputum of pneumonia, consisting mainly of serous exudate from the alveoli, in which pneumococci are often but scantily present, is frequently unobtainable till later in the illness.

The direct method was less satisfactory in testing sputa collected after crisis, this partly accounting for the 7 per cent. of failures. Stryker⁴ has shown that pneumococci cultivated in homologous immunizing serum lose virulence, no longer possess capsules, and are not specifically agglutinable. The pneumococci in post-critical sputa are exposed, in the natural course of events, to the similar influence of the immunizing substances present in the patient's serum and body fluids after crisis. They likewise are changed, for capsule staining by the ordinary methods becomes difficult or impossible, and the characteristic Neufeld reaction fails. Recourse must be had to mouse passage or the older methods of plate culture and agglutination.

In every case a dried film of the sputum was obtained by Gram's method as a necessary preliminary to typing in order to decide the characters and number of the organisms present. As was proper in an experimental inquiry, pneumococcal types diagnosed by the direct method were invariably confirmed by mouse passage, etc.

SERUMS USED

The majority of cases have been treated with the Parke Davis concentrated anti-pneumococcal serum containing antibodies against pneumococcal Types I and II. A gift of serum from Sharp and Dohme, containing Type I and a modicum of Type II antibody, was used in treatment of four cases of Type I infection, and Type I concentrate from the Wellcome Laboratory (as used in 1930-1) was again administered with good results.

The average quantity of Wellcome Type I serum used per case was 75,000 units, as compared with 50,000 units the previous year, the series including some very severe cases. The average quantity of Type II antibody per case was, as before, 70,000 units of Parke Davis serum. Thus three or four doses, each of 20,000 units per case, have usually sufficed both in Type I and in Type II cases. But these doses were inadequate for severe cases, which required 100,000 to 120,000 units before the disease was brought under control. The impression formed in 1930-1 that administration of serum later than the sixth day was of slight avail received confirmation in this series, and the importance of adequate dosage at an early stage in severe cases was emphasized. As before, doses were injected intravenously morning and evening; the initial dose should not exceed 20,000 units, but 40,000 units may be given subsequently and repeated.

SAFEGUARDS AGAINST SHOCK

Excluding one batch of serum found to produce adverse effects, primary shock was noted in one case only, and symptoms were transient. The conventional tests for serum sensitiveness—namely, the instillation of two drops of the serum to be administered, diluted 1 in 10, into the conjunctival sac, or intradermal inoculation of 1/10 c.cm. of this dilution—have proved, in our experience, uninformative. It is the custom in New York to use horse serum diluted 1 in 10 for test. The dermal reaction is there considered too sensitive, and a positive reaction is accepted merely as an indication for slow and cautious therapeutic injection; on the other hand, a positive conjunctival test (reddening of the conjunctiva within twenty minutes of instillation) is accepted as complete contra-indication against serum treatment. Symptoms are occasionally reported in cases in which both tests are negative.

Whatever the nature of anaphylactic shock, it seems improbable that the constitutional disturbances sometimes seen after injection of anti-pneumococcal concentrate are of this nature, for injections of 1 in 1,000 adrenaline are not invariably effective in controlling the adverse symptoms. A mere trace of foreign protein suffices, in the truly anaphylactic patient, to excite an explosive reaction which may be fatal; fortunately the condition is so excessively rare as to be excluded from practical consideration. The symptoms which sometimes follow intravenous injection of anti-pneumococcal concentrate are probably due to the large quantity of foreign substance suddenly introduced, and may be completely overcome if the body be gradually accustomed by a preliminary small dose given by the same route as the main inoculum—namely, by the veins.

It is undoubtedly dangerous in cases of asthma and elderly arteriosclerotics to inject 20,000 units at a single initial dose. A preliminary dose of 1 c.cm., or at most 2 c.cm., of the serum may safely be given intravenously, and followed twenty to thirty minutes later by the main inoculum, without disturbance of the patient.

SYMPTOMATIC EFFECTS OF TREATMENT

The Parke Davis serum was more concentrated than that used in 1930-1, and therefore contained less of the rigor-producing substances known to be associated with the lower proteins. Rigors were less frequent, occurring in five out of fifty-one cases, as compared with twelve in twenty-six cases in 1930-1. Symptoms of serum sickness were observed in four cases only, and were mild. As before, there was often marked symptomatic improvement after the first dose of serum, and usually following the second dose, with respect to disappearance of cyanosis, improvement in the mental state, and natural sleep; sweating occurred in about half the cases. The general effect of serum treatment on the fever is shown in the following table; there were fifty-one cases treated, and fifty-one control cases.

TABLE I

	Type I				Type II			
	Treatment		Control		Treatment		Control	
	Cases	Average Day	Cases	Average Day	Cases	Average Day	Cases	Average Day
Crisis ...	20	4½	13	7	19	4½	13	6
Lysis ...	3	7	9	9½	3	8	7	8
Death ...	4	—	5	—	2	—	4	—
Total ...	27	—	27	—	24	—	24	—
Convalescence								
Rapid ...	20	—	14	—	20	—	11	—
Slow ...	3	—	8	—	2	—	9	—

Contrasting the outcome in twenty-seven cases of Type I and twenty-four cases of Type II pneumonic infection with similar numbers of controls, the average day of crisis was advanced in Type I by two and a half days, and in Type II by one and a half days; the number of cases ending by lysis was reduced, and convalescence was accelerated.

Although there were fewer deaths among the treated than in the control series, the number of cases studied was too small to permit deductions. It seemed best to judge the efficacy of the serum by symptomatic improvement, as illustrated in the following table of fifty-one treated cases, Types I and II.

TABLE II

Day Treated	No. of Cases	Arrested	Improved	Uninfluenced	Died
1	1	—	1	—	—
2	13	7	4	—	2
3	12	9	2	1	—
4	17	10	6	—	1
5	5	3	2	—	—
6	3	1	—	—	2

Those cases have been classified as arrested in which, coincidentally with the disappearance of pneumonic symptoms, the temperature fell and remained at a normal level within twenty-four to forty-eight hours of first administering serum, at a stage in the illness when a crisis could not otherwise have been anticipated.

The substantial advantages of serum treatment in the first five days of lobar pneumonia are apparent from Tables I and II, but the experience becomes even more informative when the results of the two seasons 1930-1 and 1931-2 are combined—seventy-seven treated cases, Types I and II.

TABLE III

Day Treated	No. of Cases	Arrested	Improved	Uninfluenced	Died
1	1	—	1	—	—
2	19	13	4	—	2
3	23	12	7	1	3
4	19	10	7	—	2
5	9	3	5	—	1
6	6	1	2	2	1

Summarizing the results of treatment in these seventy-seven cases, the ratio of cases "arrested" to cases "improved" (excluding cases "uninfluenced" and "died") was 3.2 when concentrate was given on the second day of illness, 1.7 when given on the third day, 1.4 on the fourth day, 0.6 on the fifth day, and 0.5 on the sixth day. Clear proof of the importance of early treatment is thus afforded. The experience of treatment during the first twenty-four hours of illness was limited to a single case. An estimate of the probable results on this day, based on the foregoing figures, shows a ratio of 5.6, or seventeen cases arrested to three improved.

LIMITATION OF SPREAD OF PNEUMONIA

Analysis was made of the progress of the disease within the lungs in the treated and the untreated case. It is not always easy to say whether an apparent extension of consolidation, on the same side as that on which physical signs were originally detected, is actually a fresh invasion or merely the normal gradual development of classical physical signs of consolidation in an area affected coterminously with the original lesion. This ambiguity may be avoided if observation be limited to the contralateral lung. The inquiry was restricted, there-

fore, to consideration of double pneumonias with frank consolidation on both sides of the chest. Supporting evidence of spread of infection in addition to physical signs is furnished by the patient's general state, the temperature chart, and by recurrence of a more rusty type of sputum, adverse changes occurring on the fifth or sixth day of illness or later.

TABLE IV

Lesion	Type I		Type II		Non-descript
	Treated	Control	Treated	Control	
Initial:					
Right lung ...	12	10	7	10	28
Left lung ...	13	14	13	13	22
Both lungs ...	2	3	4	1	5
Subsequent:					
Spread to contralateral lung	1	7	4	6	7
Spread per cent. ...	4	29	20	26	14

There appears evidence that treatment lessens the liability to spread of infection in the lungs, particularly in the case of Type I pneumonias. It will be noted that the total incidence of double pneumonia in cases due to nondescript pneumococcal strains—22 per cent.—is less than in untreated cases of type infection—33 per cent.—corresponding to a generally milder type of illness, and in accord with the clinical fact that the greater the number of lobes involved the more severe the pneumonia. Support is, thus, afforded to the work of Sutliff and Finland,⁵ and to our own observations in an earlier paper.⁶

INFLUENCE ON COMPLICATIONS

There is general agreement that the incidence of complications is unaltered by serum treatment, and this is borne out by the evidence in the following table—fifty-one cases treated and fifty-one control cases.

TABLE V

	Type I		Type II	
	Treated	Control	Treated	Control
Serum sickness ...	3	—	1	—
Late dry pleurisy ...	2	2	4	0
Simple effusion ...	2	2	3	4
Empyema ...	3	1	0	2
Pericarditis ...	0	2	0	0
Meningitis ...	2	1	0	0

FATAL CASES

A study of the evidence furnished in the preceding tables leaves little doubt that the serum treatment exercises a favourable influence on the course of the average case of lobar pneumonia; this alone might justify extensive application of the remedy. It is admitted, however, that concentrated anti-pneumococcal serum has had, in our experience, comparatively little influence on the severest type of case, even when treatment was begun early and pressed throughout the illness. A characteristic of the severe cases was early spread of infection to the pleura with development of a synpneumonic effusion, often swarming with pneumococci but almost devoid of lymphocytes. There was an associated leucopenia in the circulating blood. Positive blood cultures were the rule in this type of case. Serum treatment was found effective in clearing the blood stream and bringing about a temporary symptomatic improvement on the fifth day of

illness. It would appear, however, that the normal immunity response of the body failed to reinforce passive immunization, since circulating antibodies were not found in a particular case tested on the seventh day of illness. These patients collapsed and died from the shock of the disease or from meningitis; their vital response was, in fact, overwhelmed at an early stage by the severity of the infection. Similarly, in a rabbit to which an excessive dose of killed pneumococcal vaccine was given experimentally, response was delayed ten days from the third, the normal day of appearance of immunity, till the thirteenth day after inoculation.⁷ Further experience is required in the application of serum treatment to severest cases of pneumonia.

GENERAL METHODS OF TREATMENT

It is important to realize that treatment by concentrated anti-pneumococcal serum does not replace general measures, of which the most essential are: (1) a minimum of disturbance of the patient, (2) early digitalization to conserve cardiac energy, (3) sedatives to procure sleep, (4) glucose, with alcohol as required, to furnish a readily assimilable food, and (5) oxygen—less often necessary in the treated than in the untreated case owing to the favourable effect of serum on the cyanosis and toxæmia.

SUMMARY

1. Serological type of the responsible pneumococcus in lobar pneumonia can be decided in a few minutes, early in the illness, by simple direct test on the patient's sputum. No special apparatus or skill is required; animal inoculation is abolished.

2. Approximately two-thirds of cases of lobar pneumonia in winter are due to infection by pneumococcal Types I and II, and are therefore suitable for serum treatment.

3. At the beginning of treatment an initial desensitizing dose of 1 c.cm. of serum should be injected intravenously, to be followed, twenty to thirty minutes later, by the main inoculum.

4. Serum treatment shortens the duration of fever and favours termination by crisis, particularly in Type I infections.

5. There is marked symptomatic improvement following serum treatment. The earlier serum is administered the more frequently is the illness aborted, the favourable effects observed being inversely proportional to the time elapsed from onset of illness till serum treatment.

6. Serum treatment appears to restrict the spread of pneumonia from one side of the chest to the other, particularly in Type I infections.

7. Complications and sequelæ are apparently uninfluenced by serum treatment.

8. The results of serum treatment in the severest type of case have been, on the whole, unsatisfactory. Further research is needed in this direction.

ACKNOWLEDGEMENTS

The observation and treatment of cases has been carried on at St. Bartholomew's and the following London County Council Hospitals: Hackney Hospital, St. Olave's, St. Andrew's, Mile End Hospital, St. Peter's, and Bethnal Green Hospital; a few cases were studied at the Victoria Park Hospital. Thanks are due to the staffs of these institutions for unremitting encouragement and help. The serum used in the London County Council hospitals was provided by the Council, and particular acknowledgement is made to the Medical Officer for this provision and for permission to work in the several hospitals named. The Medical Research Council provided the serum used at St. Bartholomew's, and defrayed the general expenses of the inquiry, to which the Cattlin Fund contributed an important share.

REFERENCES

- ¹ Armstrong and Johnson: *British Medical Journal*, 1931, i, 931.
- ² Armstrong: *Ibid.*, 1932, i, 187.
- ³ Neufeld, F.: *Zeit. f. Hyg. u. Infektionsk.*, 1902, xl, 54.
- ⁴ Stryker, L. M.: *Journ. Exper. Med.*, 1916, xxiv, 49.
- ⁵ Sutliff and Finland: *Journ. Amer. Med. Assoc.*, 1931, xcvi, 1465.
- ⁶ Armstrong and Johnson: *Med. Supp., Rep. Hosp. Services*, London County Council, 1932, iv, Part 3.
- ⁷ Armstrong: *Proc. Roy. Soc., B.*, 1925, xcvi, 539.

TREATMENT OF INFLAMMATORY CONDITIONS BY RADIATIONS *

BY

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ACUTE INFLAMMATORY DISEASE

The acute inflammatory affections range in severity from the most trivial furunculosis to pyæmic states complicating osteomyelitis, endocarditis, or other severe infection. Many isolated reports in the early literature suggested that radiotherapy might be of assistance in combating the progress of local sepsis resistant to the usual surgical measures, but it was the work of a surgeon, Heidenhain, and his assistant Fried, in Worms, which instituted a systematic clinical research into this field, and the publication of their nine years' results in 1924, on 243 cases, has aroused much interest in this little-known sphere of radiotherapy. Holzkecht has said, from several hundred cases of his own, that "we have to do with a great roentgenotherapeutic advance in the x-ray treatment of the coccal inflammations."

X-ray treatment has been found most useful when given in 15 to 20 per cent. doses (surface doses) in furunculosis, carbuncle, whitlow, erysipelas, and a considerable number of deeper-lying inflammatory states.

* Read in opening a discussion in the Section of Radiology at the Centenary Meeting of the British Medical Association, London, 1932.

The results are best when no previous surgical treatment has been given: should fluctuation appear, a simple aspiration or stab-incision drainage should be carried out. Sterile pus has frequently been found, and some experiments show that in addition the pus may have a high bactericidal power. Seeman, in 171 cases, had very similar results to those of Heidenhain and Fried: thus in axillary sweat-gland abscess he had, out of twenty-seven cases, 91 per cent. good results. Of the deeper infections, he treated six chronic appendix abscess cases, two-thirds of which responded well; while two kidney abscess patients, with renal pain and swinging temperatures, who were passing blood and pus, showed a prompt improvement—loss of pain in a few hours, and rapid subsidence of all infective signs—following a single radiation. Seven acute mastitis cases and fourteen patients with pneumonia were treated: to the first he gave 40 per cent. doses with 100 per cent. good results; to the pneumonia cases he began with 5 to 10 per cent. doses, and in just over half the patients there was rapid lysis and resolution. Holfelder reports rapid response in post-operative hypostatic pneumonia and in acute gonococcal arthritis: he warns against roentgenotherapy in acute infections where the process cannot be easily observed clinically. Thus it is not suitable treatment for acute osteomyelitis, acute abdominal infections, or acute otitis media.

It is evident that further study of these acute coccal inflammations is desirable, as much of this region is still largely unexplored.