days she developed frontal headache, and on the day of admission complained for the first time of a stiff neck. On examination she was toxic and ill, with a high fever (104° F.—40° C.) and rapid pulse (148 a minute). She showed gross back and neck stiffness, but no local bone tenderness or signs of cord compression. The C.S.F. was turbid and xanthochromic under markedly reduced pressure, and examination showed 5,000 polymorphs per c.mm., protein 1,950 mg./100 ml., and sugar 35 mg./100 ml. *Staph. pyogenes* was grown from both blood and C.S.F. culture. Treatment was started at once with 10,000 units of penicillin intrathecally, 1 million units intramuscularly, 2 g. of sulphadimidine and 1 g. of streptomycin intramuscularly. Despite this she died suddenly a few hours after admission. Necropsy (Dr. J. S. Faulds) showed multiple staphylococcal lung abscesses, a small splenic abscess, and severe toxic changes in liver and heart muscle. Detailed examination of the vertebrae failed to show any obvious osteomyelitis, and there was no epidural collection of pus. The meningeal changes were marked in the spinal canal, but much less obvious at the base of the brain, and virtually absent over the vertex.

This unexpected death was all the more tragic when it was found that the staphylococcus was fully sensitive to penicillin.

In the other cases the temperature settled in 10–16 days, and the C.S.F. became sterile in three to nine days. In Case 3 relapse occurred at one month, after the temperature had been normal for a fortnight and treatment discontinued for a week. This patient responded well to a second full course of treatment. In Case 1 a small sterile empyema required aspiration, and in Case 3 staphylococcal pneumonia developed with a small left-sided spontaneous pneumothorax. Both these cleared well without residual signs. In Case 5, after one month, the patient still had a polymorphonuclear pleocytosis in the C.S.F. and continued headache, but made slow progress and recovered completely in six weeks. In Case 6 measles developed on the ninth day in hospital, but the patient suffered no more than a temporary setback.

The time in hospital varied from 23 to 60 days, with an average of 40 days. The condition on discharge was excellent and was maintained on routine follow-up.

Discussion

The predominantly spinal localization of the meningitis in this series makes the theory that this form of meningitis is secondary to epidural suppuration attractive. However, Hulme and Dott (1954) state that epidural spinal abscess follows a fairly constant pattern: (1) constant spinal ache; (2) root pain of the affected trunk; (3) impairment of cord function leading to sphincter disturbances and early motor and sensory loss; and (4) complete paralysis.

As no case in this series showed any sign of root irritation, and the one case coming to necropsy, although presenting with obvious C.S.F. loculation, had no evidence of any sizable abscess, there is no clear confirmation of this theory. Four cases did, however, develop sudden neck stiffness after a variable period of severe back pain, and in two of these the initial C.S.F. had been clear. In the absence of any obvious vertebral osteomyelitis, it seems reasonable to postulate spread from the epidural space, perhaps accelerated by lumbar puncture in two cases, as the probable explanation. Therefore it is felt that these cases should be watched closely for the earliest sign of root pain, cord compression, or localized spinal tenderness, when they should be referred to a neurosurgical clinic without delay.

The finding of so many strains of staphylococcus fully sensitive to penicillin may not be usual, and in future wide-spectrum antibiotics may cut out the need for intrathecal injections of penicillin, but the routine followed was so successful that it seems justifiable to treat penicillin-sensitive organisms along these lines in future.

Summary

Seven cases of staphylococcal spinal meningitis are described. One patient died within a few hours of admission; the remaining six made a full recovery.

The predominantly spinal localization of the meningitis is stressed and its relationship to epidural abscess discussed.

My thanks are due to Dr. J. S. Faulds, who carried out the necropsy in Case 7.

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TABLE FOR ASCERTAINING WHETHER DIFFERENCES BETWEEN PERCENTAGES ARE STATISTICALLY SIGNIFICANT

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Smyth and Bainbridge (1957) suggest a scheme of tabulating data and thereby ascertaining whether any two factors concerning a group of patients are related. This they do by calculating the statistical significance of the difference between the percentage incidence (Pa) of one of the factors (a) and of the percentage incidence of both factors combined (Pab/b). The latter percentage is calculated by dividing the actual incidence of the combination of both factors (Nab) by the actual incidence of factor b—that is, Nb.

If the difference between Pa and Pab/b exceeds 1.96 times its standard error, then the difference is significant at the 5% level, and thus there are 19 chances out of 20 that the two factors are related. The standard error (S.E.) of the difference is given by:

$$S.E. = \sqrt{Pa(100 - Pa) (1/Nb - 1/N)}$$

where N = total number of patients (Yule and Kendall, 1950). It is therefore possible to tabulate values of 1.96 times the S.E. for various values of Pa and of (1/Nb - 1/N). This has been done in the accompanying table. By using this table it is possible to find whether the difference between Pa and Pab/b is significant without having to work out the S.E. When there are many such differences the table should save a considerable amount of time.

Method of Use

To use the table, the percentage incidence of each factor (Pa, etc.) should first be calculated. These are the diagonal percentages in Smyth and Bainbridge's diagram. Then (1/Nb - 1/N) = n should be calculated for each factor. This

Table of D Significant at 5% Level-Percentages

$P_a =$ or $n = 0.100$	0.5 99.5	1.0 99.0	1.5 98.5	2.0 98.0	3 97	4 96	5 95	6 94	7 93	8 92	9 91	10 90	12 88	14 86	16 84	18 82	20 80	25 75	30 70	35 65	40 60	45 55	50% 50%
	4.38	6.17	7.54	8.68	10.6	12.2	13.6	14.8	15.9	16.9	17.8	18.6	20.2	21.6	22.8	23.9	24.8	26.9	28.5	29.6	30.4	30.9	31.0
0.095	4.27	6.02	7.35	8.46	10.4	11.9	13.2	14.4	15.5	16.4	17.3	18.2	19.7	21.0	22.2	23.3	24.2	26.2	27.7	28.9	29.6	30.1	30.3
0.090	4.15	5.86	7.15	8.24	10.1	11.6	12.9	14.0	15.1	16.0	16.9	17.7	19.2	20.5	21.6	22.6	23.6	25.5	27.0	28.1	28.9	29.3	29.5
0.085	4.04	5.69	6.95	8.01	9.75	11.2	12.5	13.6	14.6	15.6	16.4	17.2	18.6	19.9	21.0	22.0	22.9	24.8	26.2	27.3	28.0	28.5	28.6
0.080	3.91	5.52	6.74	7.77	9.46	10.9	12.1	13.2	14.2	15.1	15.9	16.7	18.1	19.3	20.4	21.3	22.2	24.1	25.5	26.5	27.2	27.6	27.8
0.075	3.79	5.35	6.53	7.52	9.16	10.6	11.7	12.8	13.7	14.6	15.4	16.2	17.5	18.7	19.7	20.7	21.5	23.3	24.6	25.7	26.3	26.7	26.9
0.070	3.67	5.16	6.31	7.27	8.85	10.2	11.4	12.4	13.3	14.1	14.9	15.6	16.9	18.0	19.1	20.0	20.8	22.5	23.8	24.8	25.5	25.8	26.0
0.065	3.53	4.98	6.08	7.00	8.53	9.80	10.9	11.9	12.8	13.6	14.4	15.0	16.3	17.4	18.4	19.2	20.0	21.7	22.9	23.9	24.5	24.9	25.0
0.060	3.39	4.78	5.84	6.73	8.20	9.41	10.5	11.5	12.3	13.1	13.8	14.5	15.7	16.7	17.7	18.5	19.3	20.8	22.1	22.9	23.6	23.9	24.1
0.055	3.25	4.58	5.59	6.44	7.85	9.01	10.1	11.0	11.8	12.5	13.2	13.8	15.0	16.0	16.9	17.7	18.4	20.0	21.1	22.0	22.6	22.9	23.0
0.050	3.10	4.37	5.33	6.14	7.48	8.59	9.56	10.5	11.2	11.9	12.6	13.2	14.3	15.3	16.1	16.9	17.6	19.0	20.1	21.0	21.5	21.9	22.0
0.045	2.94	4.14	5.06	5.83	7.10	8.15	9.07	9.88	10.7	11.3	11.9	12.5	13.6	14.5	15.3	16.0	16.7	18.1	19.1	19.9	20.4	20.7	20.8
0.040	2.77	3.91	4.77	5.49	6.69	7.69	8.55	9.31	10.1	10.7	11.3	11.8	12.8	13.7	14.4	15.1	15.7	17.0	18.0	18.7	19.3	19.6	19.7
0.035	2.59	3.65	4.46	5.14	6.26	7.19	8.00	8.71	9.36	9.95	10.5	11.1	12.0	12.8	13.5	14.1	14.7	15.9	16.9	17.5	18.0	18.3	18.4
0.030	2.40	3.38	4.13	4.76	5.80	6.66	7.40	8.07	8.67	9.22	9.72	10.2	11.1	11.8	12.5	13.1	13.6	14.8	15.6	16.2	16.7	16.9	17.0
0.025	2.19	3.09	3.77	4.34	5.29	6.08	6.76	7.36	7.91	8.41	8.87	9.30	10.1	10.8	11.4	12.0	12.4	13.5	14.3	14.8	15.2	15.5	15.5
0.020	1.96	2.76	3.37	3.89	4.73	5.44	6.05	6.59	7.08	7.52	7.94	8.32	9.01	9.62	10.2	10.7	11.1	12.1	12.8	13.3	13.6	13.8	13.9
0.015	1.70	2.39	2.92	3.37	4.10	4.71	5.24	5.71	6.13	6.52	6.87	7.21	7.81	8.33	8.81	9.23	9.61	10.4	11.1	11.5	11.8	12.0	12.1
0.010	1.39	1.96	2.39	2.75	3.35	3.85	4.28	4.66	5.01	5.32	5.61	5.89	6.37	6.81	7.19	7.54	7.85	8.49	8.99	9.35	9.61	9.76	9.81
0.008	1.24	1.75	2.14	2.46	3.00	3.44	3.83	4.17	4.48	4.76	5.02	5.26	5.70	6.09	6.43	6.74	7.02	7.60	8.04	8.37	8.59	8.73	8.77
0.006	1.08	1.52	1.85	2.13	2.59	2.98	3.31	3.61	3.88	4.12	4.35	4.56	4.94	5.27	5.57	5.84	6.08	6.58	6.96	7.25	7.44	7.56	7.60
0.004	0.875	1.24	1.51	1.74	2.12	2.43	2.71	2.95	3.17	3.37	3.55	3.72	4.03	4.31	4.55	4.77	4.96	5.37	5.69	5.92	6.08	6.17	6.20
0.002	0.619	0.873	1.07	1.23	1.50	1.72	1.92	2.09	2.24	2.38	2.51	2.63	2.85	3.05	3.22	3.37	3.51	3.80	4.02	4.19	4.30	4.37	4.39
0.001	0.438	0.617	0.754	0.868	1.06	1.22	1.36	1.48	1.59	1.69	1.78	1.86	2.02	2.16	2.28	2.39	2.48	2.69	2.85	2.96	3.04	3.09	3.10
0.0005	0.310	0.437	0.533	0.614	0.748	0.859	0.956	1.05	1.12	1.19	1.26	1.32	1.43	1.53	1.61	1.69	1.76	1.90	2.01	2.10	2.15	2.19	2.20
0.0001	0.139	0.196	0.239	0.275	0.335	0.385	0.428	0.466	0.501	0.532	0.561	0.589	0.637	0.681	0.719	0.754	0.785	0.849	0.899	0.935	0.961	0.976	0.981
0.00001	0.044	0.062	0.076	0.087	0.106	0.122	0.136	0.148	0.159	0.169	0.178	0.186	0.202	0.216	0.228	0.239	0.248	0.269	0.285	0.296	0.304	0.309	0.310
0.000001	0.014	0.020	0.024	0.028	0.034	0.039	0.043	0.047	0.051	0.054	0.057	0.059	0.064	0.069	0.072	0.076	0.079	0.085	0.090	0.094	0.097	0.098	0.099

may easily be done by using a slide rule or a table of reciprocals. Then any calculated difference—for example, $|Pa - Pab/b|$ —may be immediately compared with the appropriate value in the table. If the calculated difference (D) is equal to or exceeds the appropriate tabulated D, then the calculated D is significant.

The actual values of Pa and of n will not usually coincide with the tabulated values of Pa and n respectively, but the actual values will each lie between two adjacent tabulated values. When this is the case, four values of D will be obtained from the table, corresponding to the two adjacent tabulated values of both Pa and n. If the calculated D is greater than or equal to the largest of these four tabulated Ds, then the difference is significant. If the calculated D is less than the smallest of the four tabulated Ds, then the difference is not significant. In practice the calculated D will seldom fall within the range of the four tabulated Ds. But when this does occur it will be necessary to interpolate. An example will make the appropriate procedure clear.

Let $Pa = 33.1\%$, $Nb = 21$, and $N = 504$. Thus $1/Nb - 1/N = n = 0.0476 - 0.0020 = 0.0456$. Now Pa lies between 30 and 35 and n lies between 0.045 and 0.050. The four values of D corresponding to these values of Pa and n are as follows: 19.1, 19.9, 20.1, and 21.0. Thus if the calculated D is equal to or greater than 21.0, then it is significant, but if D is less than 19.1, then it is not significant. But if the calculated D is 19.3, for example, then we must interpolate. To do this, take $n = 0.045$ and note that for $Pa = 30\%$, D is 19.1, and for $Pa = 35\%$, D is 19.9. Thus for $n = 0.045$ and $Pa = 33.1\%$, $D = 19.1 + \frac{33.1 - 30.0}{35.0 - 30.0} (19.9 - 19.1) = 19.1 + \frac{3.1 \times 0.8}{5} = 19.1 + 0.5 = 19.6$.

Now take $n = 0.050$. For $Pa = 30\%$, D is now 20.1 and for $Pa = 35\%$, D is 21.0. For $n = 0.050$ and $Pa = 33.1\%$, D therefore $= 20.1 + \frac{33.1 - 30.0}{35.0 - 30.0} (21.0 - 20.1) = 20.1 + \frac{3.1 \times 0.9}{5} = 20.1 + 0.6 = 20.7$. Thus for $n = 0.0456$ and $Pa = 33.1\%$, $D = 19.6 + \frac{0.0456 - 0.0450}{0.0500 - 0.0450} (20.7 - 19.6) = 19.6 + \frac{0.0006 \times 1.1}{0.0050} = 19.6 + \frac{0.66}{5} = 19.6 + 0.1 = 19.7$. Thus if the calculated D is equal to or greater than 19.7 it is significant at the 5% level. The figure 19.7 is the same as is obtained if the S.E. is worked out in the usual way and multiplied by 1.96.

The table should not be used if Pa or $(100 - Pa)$, whichever is smaller, multiplied by Nb or $(N - Nb)$, whichever is smaller, is less than 500. This figure seems large, but it is really a percentage. It corresponds to an actual number of only 5. If the smallest product is less than 500, then a more accurate method of testing significance should be used (see Fisher and Yates, 1948).

I should like to thank Professor Martin Roth, professor of psychological medicine, University of Durham, for bringing this matter to my attention.

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A new feature of the Royal Society of Health's annual congress is to be a section devoted to Radiation. This will be introduced at Harrogate next April. The existing Tropical Hygiene Section will be amalgamated with the World Health Section under the new title "World Health including Tropical Hygiene." Provision has also been made for a Conference of Health Visitors in addition to a separate Conference of Domiciliary Nurses and Midwives.

HAEMOGLOBIN O (BUGINESE X) IN SULAWESI

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In 1956 the finding of what might be a new haemoglobin in the Buginese in Sulawesi (formerly Celebes) was reported (Lie-Injo, 1956). This report, however, did not attract any attention as it was written in the Indonesian language. In the meantime the haemoglobin has been studied more extensively by laboratories in other parts of the world, and we all agree that it is not identical with any other known haemoglobin. In this paper we record the results of further study.

Physico-chemical Properties

In 1956 the electrophoretic mobility of this haemoglobin at pH 8.6 was described as being between that of Hb S and Hb E (see Fig.). In phosphate buffer pH 6.5 it was slightly slower than Hb S and Hb C. It was not alkali-resistant, and the erythrocytes containing it gave negative sickling tests on repeated examinations. It occurred in addition to normal haemoglobin in the blood and was always present in a low concentration.

After repeated examinations it was not so easy to establish the exact electrophoretic mobility of the abnormal component. It was thought to be partly due to the low concentration (Lie-Injo, 1957). Study of this haemoglobin, which had provisionally been called Hb Buginese X, by three different well-known experts in three different countries did not make the problem easier, as all three had a different opinion regarding its electrophoretic mobility.

Recently a large amount of blood containing Hb Buginese X was obtained from the blood bank in Djakarta (Java), and large samples were again sent to different laboratories. Dr. H. Lehmann, of London, found that Hb Buginese X at pH 8.6 had a mobility between that of the Hb S and Hb E just as originally published by one of us in 1956 (Lie-Injo, 1956). He is of the opinion that our haemoglobin is indeed a new haemoglobin.

Dr. T. H. J. Huisman, of Holland, examined our haemoglobin by different methods and came to the conclusion that it was not identical with any other known haemoglobin. On examining Buginese X chromatographically with "amberlite IRC-50" he found that it moved faster than Hb L but was slightly slower than Hb S. Also, with his newly developed chromatographic method using carboxymethyl cellulose, he again found that our haemoglobin differed from other known haemoglobins. Dr. H. A. Itano, of Bethesda, Maryland, examined it in the Tiselius apparatus

Paper electrophoresis showing Hb O compared with Hb A, E, and S at pH 8.6.