effect over capillary permeability and salt balance of the body. Because of this its use has been strongly advocated in shock with a view to increasing the capillary permeability. It is, however, evident that it cannot be expected to be efficacious in every type of shock. A few successful experiments have been published by Wilson and his co-workers, but here again there is urgent need for extensive investigation.

Conclusion

At the present stage of our knowledge we must conclude that shock is a clinical state that may be produced by several processes which are initially quite different and which may act separately or in conjunction. It is, however, quite unnecessary to assume that all shock is produced in the same way. It would therefore be quite wrong to dogmatize regarding treatment; much less should we attempt to apply the same treatment to all. We must know more accurately what factors are concerned in the particular case we are attempting to treat. To obtain this knowledge detailed investigation of large numbers of cases must be studied. To make all the necessary observations a great deal of labour is needed, and I suggest that at the present time those responsible for our medical services should consider the possibility of organizing on a wide scale the study of this subject, which may soon become a primary consideration of many of these doctors.

BIBLIOGRAPHY

Owing to the vast number of references involved the following three volumes are given as containing the majority:

- McDowall, R. J. S. (1938). *The Control of the Circulation of the Blood*, Longmans, London.
Moon, V. H. (1938). *Shock and Allied Conditions*, Oxford University Press.
Seudder, J. (1940). *Shock: Blood Studies as a Guide to Therapy*, Lippincott, Philadelphia and London.

NOTES ON RUBELLA WITH SPECIAL REFERENCE TO CERTAIN RHEUMATIC SEQUELAE

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During the epidemic of rubella in February and March, 1940, more than 300 cases were observed. It was noticed that in a large number of these the onset and course did not follow the lines usually considered to be normal in this disease. It is thought, therefore, that these notes may be of interest in view of the fact that, as rubella does not ordinarily attract much attention and no observations have to our knowledge been published regarding it for some time, its course may have changed in some respects. Our observations may be divided into three parts: (1) differences in its onset and course; (2) differences in the complications from those described in most textbooks; (3) the question of relapses.

Onset and Course

In four cases the onset of rubella had been very acute. There had been a period of malaise lasting from twenty-four to forty-eight hours, during which a swelling of the

mucous membranes of the nose, palate, and gums, without catarrh, was noticed, giving rise to considerable trouble. After that the patients experienced a sudden rigor with high temperature, and had stiff necks and occipital headache. They also complained of considerable muscular pain at this time, and one stated that the right wrist had swelled up. A diagnosis of meningitis was made in two of these cases, and appeared to be confirmed in the morning by the appearance of a rash of the type seen in cerebrospinal fever. Within a few hours, however, these symptoms had passed off, and the correct diagnosis was made. Another such case was diagnosed as "encephalitis," while the fourth was labelled "influenza." It is worthy of remark that all the cases seen during 1939 and also the first two weeks of the present epidemic were of an exceptionally mild type.

A progressive increase in the severity of the cases as the epidemic proceeded was noted, however. We had particular facilities for observing this fact as one of our hospitals was made the clearing-station for the British Expeditionary Force, and from the beginning of February until the end of March two batches of patients were admitted each week. The severer cases all occurred towards the end of the epidemic.

Rheumatic Sequelae

Osler (1939) states that there are no special complications of rubella, but mentions that in rare instances certain symptoms may occur, among which is arthritis. Ker (1934) states that rubella differs from other infectious diseases in that it shows a remarkable freedom from complications.

During the course of the epidemic described we have been much impressed with the occurrence of various "rheumatic" symptoms. Their grades of severity range from transient muscular pains that disappeared after twenty-four to forty-eight hours (15 per cent.) to cases that were indistinguishable clinically from severe rheumatic fever, one of which is described in detail below. The muscular pains appeared on the third day of the disease (taking the average of ten unselected cases), although two patients complained for the first time on the ninth day. These pains affected the shoulder-girdle in a majority of cases, and were most noticeable on movement of the arms or on turning in bed. In some cases, however, the onset was in the gluteal and thigh muscles. Occasionally, where the patient gave a history of having suffered from fibrositis in the past, it was the site of this old trouble which became reactivated. In one case fibrositis of the lumbar region had been experienced two years previously, and on the ninth day of rubella this returned and spread down the leg as "sciatica," which did not improve in spite of treatment. On account of this the patient was ultimately transferred to England. The patients who showed rheumatic complications were not always those who had had the septic throats referred to later, although in some cases this was so.

The following cases are chosen as being typical of the mild type of temporary muscular pains encountered.

Miss A., aged 29.—Admitted 3/3/40; discharged 14/3/40. Rash appeared 3/3/40. Throat and gums normal; swelling of occipital glands. Pains in joints began 4/3/40 in wrists, knees, and ankles. No swelling of joints. Rash disappeared in three days and pains in joints improved on disappearance of rash. Temperature 99° on admission; normal since.

Miss B., aged 24.—Admitted 8/3/40; discharged 17/3/40. Rash appeared 8/3/40, with severe pains in gums. Throat normal; occipital glands enlarged; gums appeared normal. Pains in joints 10/3/40—in wrists and ankles—which kept

her awake. No swelling. Rash lasted about four days. Joint pains and pains in gums disappeared when rash faded. Temperature 100.2° on admission. Next day 99°. Normal subsequently.

Miss C., aged 27.—Admitted 10/3/40; discharged 19/3/40. Rash appeared, with swelling of occipital glands, 9/3/40. Throat sore 11/3/40. Throat inflamed. No pain in gums. Rash lasted three days, then patient complained of pains in small joints of both hands. First interphalangeal joint of middle finger of left hand and both metacarpo-phalangeal joints of thumbs considerably swollen. This swelling lasted until about two or three days before discharge. Temperature 101.4° on admission; next day 101.6°–101.4°; following day 99.2°–99.8°. Normal subsequently.

Miss D., aged 39.—Admitted 18/3/40; discharged 4/4/40. Rash appeared 18/3/40, lasting four to five days. Pain in gums on admission, lasting three to four days. Throat normal; occipital glands much swollen and slightly tender; gums appeared normal. Pain in joints started 17/3/40 in wrists, shoulders, and knees, lasting six days and keeping her awake at nights. No swelling. Has been very "run down" since.

In other patients these muscular pains did not disappear so rapidly. Effusion into one or more joints also occurred, and this lasted for a considerable period. The following case is typical:

Sister E., aged 37.—Admitted 3/3/40; discharged 2/4/40. No rheumatism previously and always in good health. She had been in hospital with "flu" and had returned to duty for four days, when she developed rubella. She had a typical rash, and in addition to the posterior cervical glands those of the groin were considerably swollen. She had a slight sore throat, for which she was given a gargle. She did not at any time feel very ill. She was worried by the fact that her nose seemed congested, however, and she could not breathe easily through it. There was no coryza. On the third day all her gums became very painful and the teeth sore. She thought the palate was also swollen, but the nose cleared. The eyes, which had been very sore for several days, also cleared. Aspirin had no effect on the "toothache." On the fourth day she complained of low lumbar pain and, later in the day, aching of the ankles, hips, and wrists. On the fifth day the outer two fingers were swollen (metacarpal joints) and became more painful throughout the day. The next day the pain was less, and on the seventh day pain had disappeared from all the joints. Slight swelling, however, was still present in the two fingers when seen a fortnight later.

As an example of the most severe type of rheumatic complication the following case will be of interest. The patient was eventually evacuated to England with what appeared to be true rheumatic fever and a loud cardiac murmur, which had developed during the illness.

Driver F., aged 22.—Admitted on February 14, 1940, with a rubella rash of three days' standing and an enlargement of cervical glands; also complained of slight sore throat and cough. On the 19th his left tonsil and glands were swollen, and he was given sulphanilamide 3 grammes daily for five days. Appetite was very poor. Next day he complained of severe headache for the first time, which aspirin relieved. On the 24th he felt very much better and appetite returned; and on the 26th he sat up in a chair for two hours. That night he was restless and his temperature rose to 99°. Tonsils were still large. Sulphanilamide was resumed in the same dosage on the 28th, when his temperature was 101° F. He started to complain of aching pain in both shoulders, which became acute on movement. Lin. methyl. salicyl relieved this. The patient remained more or less in this state until March 7, the temperature gradually coming down from 103° (March 2) to 99.8° F. The pulse was raised; there was a loss of appetite; colour was poor, with cyanosis often at night; and he had a slight headache continuously. He used to feel rather better in the early evenings, although pain in the

shoulders became worse between 8 and 9 p.m. He used to experience profuse sweats twice in the twenty-four hours—at 2 a.m. and 2 p.m. These did not seem to bear any relation to the aspirin which he was taking. He was seen by the ear, nose, and throat specialist, who reported that there was no active inflammation of the tonsil, although the tonsillar glands were enlarged and some muco-pus was seen.

On March 11 the temperature, after being down for two days, rose to 100.4°, and pain occurred behind the knees as well as in the shoulders. The pulse rate increased to 100, and a systolic murmur became audible which was loudest at the apex and was conducted towards the axilla. There was some visible throbbing of the carotids. The patient looked very pale. On March 13 he was still in this condition, and complained in addition of lumbar pain and slight swelling in the left wrist with pain running up the forearm. He was seen in consultation by Major-General R. Priest on this day. His B.S.R. (Westergren) was 56 mm. By March 17 he felt considerably better and had very little pain. The swelling had left the wrist, but his evening temperature was 99°. The cardiac murmur was still present. On the next day he was evacuated to England. This patient was on sulphanilamide 3 grammes daily from February 28 to March 1 inclusive, with no apparent effect. He received temporary relief from aspirin throughout, however. His case appeared to be rheumatic fever arising during the course of rubella. A follow-up note was received from him on April 9 from another hospital stating that for some days after arrival pains had been very severe in his wrists, and he had not been able to feed himself. Subsequently he improved and felt fairly well, and after the first week his temperature was normal. His case was diagnosed as subacute rheumatism and carditis, and he was told he must remain in bed for two months longer.

Other Complications

Other unusual complications of rubella were also observed:

The Temperature.—We noticed a secondary rise of temperature in about 10 per cent. of our cases, following an apyrexial period of forty-eight hours or more. This secondary rise generally reached about 101°, and was accompanied by malaise and by increased swelling with some pain in the enlarged lymphatic glands. Ker states that the temperature in rubella is usually only slightly elevated, in adults often only to 99°, and is seldom maintained for more than one or two days.

The Throat.—We were much struck with the fact that while most of our patients complained of some degree of sore throat a large number of these throats when examined appeared to be very much worse than would have been expected. Yellow follicles were present, and often a considerable amount of pus in addition. Of the first 133 patients seen forty-five had apparently very bad follicular tonsillitis and were put under the care of the throat specialist, although they had themselves complained very little of their throats. Ker states that the majority of rubella patients complain of slight sore throat and there is some mild congestion of the fauces; while Tidy (1938) states that the fauces may show "dryness and slight redness."

The Gums.—A large number of our patients complained of a complication to which we have been unable to find any reference in the books consulted. This was described by many patients as "toothache." On further investigation, however, it appeared that it was in reality an intense aching of the gums. This lasted for forty-eight hours and was severe enough in some cases to keep the patient awake at night. It started on the second day in most cases. In certain others, however, it was a feature of the onset. It was noted by one of us that in those cases

the patient's temperature was higher than is considered normal for rubella, sometimes rising to over 101° F.

Glandular Enlargement.—Generalized glandular enlargement was another prominent feature of this epidemic, as opposed to enlargement merely of the posterior cervical region, which ordinarily subsides on the third or fourth day after the appearance of the eruption. A small group of cases were admitted with "fever," fairly severe sore throat, and generalized enlargement of the lymphatic glands. Neither liver nor spleen was palpable in these cases. The clinical picture, apart from the rash, was very suggestive of glandular fever. A white blood count was done in these cases, and in the majority this showed a leucopenia with a relative lymphocytosis, lymphoblasts being present in some cases. The glandular enlargement, seldom with tenderness, remained for ten days or more, and a further blood count in some of the cases before discharge from hospital showed a return to normal.

Case	Day of Disease	Total White Cells	Polymorpho-nuclears %	Lympho-cytes %	
I	4th	5,300	53	41	Transitional 4%
II	5th	6,700	51	42	Lymphoblasts 4%
	10th	7,200	70	27	
III	2nd	5,900	42	46	Lymphoblasts 4%
IV	7th	3,700	25	71	
	2nd	4,700	46	50	
V	9th	8,350	32	37	Large mono's 22%
					Lymphoblasts 2%
					Eosinophils 4%
VI	2nd	8,800	55	32	Large mono's 6%
	9th	8,500	64	32	Lymphoblasts 4%
					Large mono's 1%
					Lymphoblasts 7%
VII	4th	2,850	54	33	Eosinophils 4%
	10th	7,850	52	35	Large mono's 2%
					Eosinophils 2%
					Large mono's 11%

A further peculiarity which was much commented upon by the sisters in charge of the wards was the fact that desquamation of the skin occurred in a large number of cases as soon as the rash had faded. This was often as intense as that seen after severe scarlet fever, and affected the hands particularly.

Relapses

Box, writing in Price's *Medicine* (1937) on rubella, states that "second attacks are known, but not common, and relapse is very rare." In the present epidemic relapses have occurred in about 8 per cent. of all our cases. Some of these were very mild, but in three cases it was acute and was mistaken at first for the onset of meningitis, which it was believed to be for twenty-four hours. The relapses in these three cases were similar to the cases of acute onset described above. The following is an account of one of them:

Private G., aged 21 (see Chart).—He was admitted on March 6 with rubella; the rash had appeared on March 3 and had

Temperature chart of Private G.

already faded on admission. His cervical glands were much enlarged and slightly tender and his throat was rather red; he had also complained that his nose was "choked up," and

douching and inhalations were begun. He appeared to be convalescing normally until 3 a.m. on March 15, when he awakened and vomited two ounces of watery fluid. He then slept for an hour, when he awoke again complaining of intense headache behind the eyes and in the occipital region. He also complained of severe thirst and blocking of his nose. His temperature was 101.2°, pulse 130, and respirations 30. Aspirin was given with slight relief. He dozed at intervals until 6 a.m., when his temperature was 103.2°, pulse 130, and respirations 30, and photophobia was marked. At 7.40 a.m. no rash was present.

At 9.30 a.m. his condition was similar, and there was some tenderness over the region of the frontal sinuses and slight nasal discharge. There was increase of pain in bending his neck forward, but otherwise no neurological abnormality. He felt better towards the evening, and on the next day his temperature was 99.5°, the headache had gone, as had the frontal tenderness, and the rash was typically rubelliform. He made an uneventful recovery from this point, and was discharged ten days later.

Two cases were observed in which patients developed true measles within ten days of recovery from rubella. These were at first believed to be relapses of rubella, but the subsequent course of the disease showed it in each case to be morbilli.

Summary

In a recent epidemic of rubella certain deviations from the normal were observed. These are described, and concern the onset, course, and complications of the disease. Certain cases of relapse are also described and commented upon.

The most important complication described is the occurrence of "rheumatic" conditions of varying degrees of severity. These ranged from transient joint and muscle pains to severe lumbago and sciatica, for which the sufferers had to be hospitalized. Three cases also occurred that were clinically indistinguishable from rheumatic fever. One of these is described in detail.

Other unusual complications observed frequently were severe pains in the gums; tonsillitis, which appeared to be severe but of which the victim seemed to be almost unaware; and an intense degree of desquamation, occurring within a few hours of the rash having faded. Generalized adenitis with a temporarily abnormal blood count showing leucopenia with relative lymphocytosis was not infrequent, whilst a secondary rise of temperature forty-eight hours after deferescence with a recurrence of constitutional symptoms was also noticed in a considerable number of cases.

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REFERENCES

- Ker, C. B. (1934). *Manual of Fevers*, 3rd ed., revised by C. Rundle, p. 53, London.
 Osler, Sir W. (1939). *Principles and Practice of Medicine*, 13th ed., revised by H. A. Christian, p. 280, New York.
 Price, F. W. (1937). *Text Book of Medicine*, 5th ed., p. 263, London.
 Tidy, H. L. (1938). *Synopsis of Medicine*, 7th ed., p. 265, Bristol.

I. Dogramaci, *Annal. Paediat.*, 1940, **154**, 357, made a study of ninety cases of erythema nodosum which occurred among 53,000 Turkish children examined between March, 1934, and December, 1939. The ages ranged from 2 to 16 years, the maximal incidence being between 8 and 10 years: forty-four were boys and forty-six girls. The incidence was highest in the winter (October to February, thirty-seven) and lowest in the summer (June to August, thirteen). Of thirty-nine tested with tuberculin four were negative and thirty-five positive. In one of the negative cases erythema nodosum followed typhoid fever.