The day after admission a full blood count showed: red cells 3,340,000 per c.mm.; haemoglobin, 60%; colour index, 0.9; white cells, 1,900 per c.mm. (polymorphs nil, lymphocytes 65.5%, large mononuclears 33%, eosinophils nil, basophils nil); anisocytosis and poikilocytosis, slight; nucleated red cells, nil; platelets abundant; Türk cells, 1.5%. On the same day sternal marrow aspiration was reported as follows: "Erythroid series normoblastic and less active than normal; myeloid series very considerably reduced in numbers of myelocytes and polymorphonuclear cells; nucleated cell count, 10,600; platelets series, occasional megakaryocytes seen; platelets present in average numbers."

An E.C.G. on July 29 showed auricular fibrillation and left bundle-branch block. July 30: Hb, 64%; white cells, 2,200 (polymorphs 1%). July 31: Hb, 68%; white cells, 3,900 (polymorphs 2.5%). Thrush was noted in the mouth, with encrustations on the hard palate. Gentian violet (1% aqueous solution) was applied for five days. August 1: heart changed to regular rhythm; digitalis stopped. August 4: temperature fell to 98.4° F. (36.9° C.). She was much improved, but still doubly incontinent. August 6: antibiotics stopped; Hb, 70%; white cells, 11,200 (polymorphs 83%, lymphocytes 9.5%, large mononuclears 5%, eosinophils 0.5%, myelocytes 2%). August 7: red cells, 3,960,000; Hb, 70%; C.I., 0.89; white cells, 10,200 (polymorphs 69%, lymphocytes 20%, large mononuclears 8.5%, eosinophils nil, basophils nil, myelocytes 2.5%). Anisocytosis and poikilocytosis slight. August 12: red cells, 3,700,000; Hb, 68%; C.I., 0.91; white cells, 10,200 (polymorphs 71%, lymphocytes 22%, large mononuclears 6%, eosinophils nil, basophils 1%). Nucleated red cells nil.

On August 13 her skin lesions were well healed and the blood pressure had risen to 210/110. She was discharged.

DISCUSSION

Allylthiourea is a drug with marked antithyroid properties, and, like all the members of the thiourea-thiouracil group, has a toxic effect on the bone marrow which is apparently quite distinct from any allergic effects (McGavack and Chevalley, 1954). Morton (1947) has pointed out that in this group of drugs the phenomenon of agranulocytosis does not appear until the drug concerned has been given for a period of one or two weeks. In this case the patient had received medication for about 17 days before any side-effects became obvious.

Schultz (1922), in his original description of the syndrome of agranulocytosis, stressed the importance of faucial inflammation as a diagnostic point in agranulocytosis. This has since been stressed by numerous authorities (Whitby and Britton, 1950; Wintrobe, 1951). An interesting feature of the case reported here is the total absence of faucial inflammation in the acute phase, although treatment was later complicated by a monilial infection of the tongue and palate, after the return of polymorphonuclear leucocytes to the blood. It is now accepted that the pyrexia (which was so prominent a feature in this case) is due to infection, which becomes overwhelming in the absence of a polymorphonuclear response.

The most important step in the treatment of agranulocytosis is withdrawal of the offending drug. Provided this is done early and overwhelming infection by bacteria is avoided by adequate antibacterial therapy, the majority of cases spontaneously recover. Of course, the only absolute proof that the suspected drug is implicated is the demonstration of depression of the marrow for a second time under carefully controlled conditions. This was not considered a justifiable risk.

The antibacterial therapy used in cases of agranulocytosis should be of the bactericidal type preferably, and not of the bacteriostatic type: this really limits therapy to the administration of penicillin and streptomycin. Jawetz and Gunnison (1952) pointed out that chlortetracycline, chloramphenicol, and oxytetracycline are bacteriostatic. Obviously the use of a marrow poison such as chloramphenicol is contraindicated in the presence of marrow depression.

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Penicillin V

The excellent annotation in the *British Medical Journal* (1956) on the new oral penicillin V draws attention to what promises to be a most useful, effective, and popular therapeutic weapon. Since its discovery by Brandl, Giovannini, and Margreiter in 1953 much work has been done, largely on the Continent; the only published notes in this country are those by Bowerbank (1955) and Dove (1955). Through the kindness of Dr. W. P. Kennedy supplies of "distaquaine V," the Distillers Company (Biochemicals) brand of phenoxymethyl penicillin, were sent to us some months ago. Cases were placed at random alternately on oral penicillin V and intramuscular crystalline penicillin without any discrimination. Details of the first 24 cases are given in Tables I and II, printed on the next page.

These two tables compare the results of penicillin administration to two groups of 12 patients, 7 suffering from lobar pneumonia and 5 from other respiratory infections. The cases in Table I were treated with courses of oral penicillin (phenoxymethyl penicillin), 120 mg. stat. and 60 mg. four-hourly, except Cases 5 and 12, which were given double this dose. The course was given for five days or until three days had elapsed after the fever had settled, whichever was the longer. The cases in Table II were treated with intramuscular penicillin, between 1,000,000 and 1,200,000 units daily for a similar period. Cases were taken at random on admission, usually alternately, for inclusion in either of the two trial groups.

It will be seen that there is little to choose between the two groups as regards the site of disease, radiological findings, and white-cell response. Similarly, the clinical response of the two groups is roughly identical. Patients unquestionably prefer oral to injection treatment. The only side-effects noted in the group given oral penicillin were soreness of the tongue, lasting two days in two cases. There were no cases of diarrhoea or allergy in either group.

Since then we have treated several further cases of infection of the upper and lower respiratory tract; these have strengthened our impression that there seems little to choose between the oral and the intramuscular forms as regards therapeutic effectiveness. As it turned out, the group treated with intramuscular penicillin contained two more cases of bronchopneumonia than did the penicillin V group, which possibly explains the longer time spent in hospital by the intramuscular group—261 days as against 229 days in the oral group of cases. The total figures for duration of fever on therapy are 36½ days in the intramuscular group and 32½ in the oral, the small difference again being probably due to the two extra cases of bronchopneumonia in the intramuscular group.

The results in this small initial series of routine admissions into the same two wards of this hospital in the last three months makes us hopeful that here we have a useful and practical alternative to parenteral penicillin which should be particularly useful in busy general practice.

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TABLE I

Case No.	Age and Sex	Diagnosis	Initial Temp.		Initial W.B.C.	Predominant Organism Isolated	Initial Chest X-ray	Time Febrile	Days in Hospital	Final W.B.C.	Final Chest X-ray	Side-effects	Comment
			°F.	°C.									
1	41 M	L.L.L. pneumonia	101.8	38.8	Not done	Scanty Gram-neg. cocci and <i>Str. viridans</i>	Moderate consolidation L.L.L.	12 hours	16	7,500	Virtually clear	2 days sore tongue	Mild febrile relapse 3rd day lasting 48 hours. Temp. 100.2 °F. (37.9 °C.)
2	42 M	"	100	37.8	17,600	Heavy <i>Str. viridans</i>	Consolidation L.L.L.	24 "	15	8,600	Improved but not quite clear	Nil	Subsequently relapsed and was treated at home with oxytetracycline
3	60 F	L.U.L. pneumonia	102	38.9	7,600	No sputum	Dense opacity in L.U.L. with slight L.L.L. involvement	5 days	21	6,100	Virtually clear	Nil	This was probably a virus pneumonia
4	37 M	R.U.L. pneumonia	101	38.3	12,000	Pharyngeal organisms	Consolidation of base of R.U.L.	24 hours	11	—	Clear	Nil	—
5	57 F	R.L.L. pneumonia	102.4	39.1	29,600	Pneumococci	Some consolidation of base of R.M.L. and a little in R.L.L.	3½ days	17	9,800	R. base virtually clear	Nil	—
6	34 F	L.U. and L.L. pneumonia	103.8	39.9	12,200	<i>H. influenzae</i>	Consolidation of L.L.L. and base of L.U.L. posteriorly	4½ "	17	10,300	Minimal residual L.L.L. shadowing only	2 days sore tongue	—
7	20 F	L.L.L. pneumonia	100.4	38	16,400	Pneumococci and <i>Str. viridans</i>	Consolidation L.L.L. and part of L.U.L.	4½ "	24	6,700	Virtually clear	Nil	—
8	91 M	Broncho-pneumonia	100.5	38.1	12,200	—	Slight opacity L.L.L.	3 "	39	8,200	Clear	Nil	Long stay because of original admission for hemiplegia
9	70 M	"	102	38.9	5,900	—	Lung fields clear	3 "	24	—	—	Nil	Admitted also with obstructive jaundice due to stones
10	22 F	Acute bronchitis	100	37.8	8,800	Scanty pneumococci	Chronic bronchitic changes only	3 "	12	—	—	Nil	Mild febrile relapse 6th day for 48 hours
11	59 M	"	100.2	37.9	8,000	Pneumococci	Mild basal hyperaemia; left greater than right	3 "	12	6,900	—	Nil	—
12	48 F	"	99	37.2	5,400	Scanty haemolytic strep.	Nil abnormal	12 hours	21	—	—	Nil	—

TABLE II

No.	Age and Sex	Diagnosis	Initial Temp.		Initial W.B.C.	Predominant Organism Isolated	Initial Chest X-ray	Time Febrile	Days in Hospital	Final W.B.C.	Final Chest X-ray	Side-effects	Comment
			°F.	°C.									
A	16 M	L.L.L. pneumonia	102.8	39.3	15,900	<i>Str. viridans</i> with pharyngeal organisms	Pneumonic shadowing in the apical segment of L.L.L.	24 hours	21	—	Normal	Nil	—
B	65 M	R.U.L. pneumonia	102	38.9	13,300	Pharyngeal organisms only	Consolidation of posterior half of R.U.L.	3½ days	16	8,100	Improved but not quite full resolution	Nil	—
C	57 M	Lobar pneumonia (M.L.)	101	38.3	7,500	Pneumococci	Opacity R.M.L.	24 hours	15	—	Clear	Nil	—
D	43 F	R.L.L. pneumonia	100.2	37.9	15,800	<i>Str. viridans</i>	Consolidation R.L.L.	5½ days	22	6,400	"	Nil	Slight febrile relapse 10th day. Treated with oxytetracycline
E	79 M	Massive pneumonia	103	39.4	7,300	Pneumococci	Consolidation R.U.L. and R.L.L.	2 "	31	9,200	R.U.L. clear. Slight shadowing R.L.L.	Nil	—
F	53 M	R.U.L. pneumonia	99.6	37.6	8,000	<i>H. influenzae</i>	Consolidation of most of R.U.L.	2 "	16	—	Resolution not quite complete	Nil	—
G	15 F	L.L.L. pneumonia	100.4	38	16,000	<i>H. influenzae</i> and pneumococci	Slight opacity left lower zone	12 hours	16	9,700	Clear	Nil	—
H	67 M	Broncho-pneumonia	102.6	38.1	10,900	<i>H. influenzae</i>	Acute on chronic infection base of L.L.L.	7 days	17	—	Clearing of the acute infection	Nil	—
I	53 F	"	102.5	38.1	18,000	Pneumococci	Bilateral basal infection in the lower lobe	3 "	26	7,000	Much improved but not quite clear	Nil	—
J	80 M	"	100.8	38.2	9,600	<i>H. influenzae</i>	Acute on chronic basal infection. Left greater than right	3 "	11	—	Improved	Nil	Relapsed 2 days after discharge
K	74 F	"	100.4	38	25,600	Coliforms with pharyngeal organisms	Acute on chronic infection. Right greater than left	5 "	42	6,400	Bases nearly clear	Nil	Long stay for social reasons
L	74 M	Acute bronchitis	102	38.9	9,200	Monilia and pharyngeal organisms	Chronic infective changes only	3 "	28	—	—	Nil	—