the examination of human serum have indicated the presence of complement-fixing antibodies of significant level in some cases. In a group of 20 samples of normal individuals taken at random, 35 percent showed the presence of antibodies. In a group of 35 samples from patients with nonbacterial respiratory disease, the reaction level was 3 percent. In similar examination of 63 canine samples, where the reaction rate would be expected to be higher, a positive percentage of 45 was obtained.

There is no doubt that serologic methods for identification of Carré's virus antibodies require further improvement. An antigen giving specific reactions in greater serum dilution would be very advantageous. Perhaps more highly purified preparations would be more efficient. Adaptation of the virus to tissue culture may help solve some of these problems. With the realization of probable public health significance of the virus, the need for further immunologic and serologic studies is reemphasized.

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Observations at an Ancient Smelting Site in Negev

Prospecting for copper and other metals in Timnah area, Negev, is leading us to a closer study of some ancient mining and smelting sites. A reconstruction of ancient prospecting, mining, and smelting practices may prove to be of use in our current exploration. The present advance note (*1*) deals with some of our findings at a smelting acropolis (*2*) in the central part of Wadi Timnah (Meneiyeh Um Adak). A more detailed account is to be submitted elsewhere for publication (*3*).

Table 1. Chemical analysis of ores found in the Timnah acropolis (percentage of original sample). ND, not detected; P, Ti, HCl-soluble S, SO_4, and water-soluble Cl were not detected in any of the ores.

No.	CuO	MnO	Fe_2O_3	Al_2O_3	CaO	MgO	SiO_2	CO_2	Cl	Loss at 1100°C
348/55	19.3	0.09	23.9	1.3	1.4	0.4	43.2	3.9	0.8	12.5
349/55	23.4	ND	2.0	1.1	0.6	0.1	62.2	5.8	0.3	10.8
350/55	20.1	ND	3.3	0.9	7.8	0.2	52.1	10.6	0.3	16.0
351/55	24.2	ND	0.8	1.0	0.8	0.3	61.4	5.8	0.7	11.7
352/55	29.3	ND	0.6	1.1	0.7	0.3	54.8	7.8	0.1	14.9

Table 2. Some chemical data on concretionary copper ores containing chalcocite (percentage of original sample).

No.	Cu	S	SiO_2	CO_2	Cl	Loss at 1000°C
1416/55	38.5	2.4	35.4	8.9	1.95	18.4
1417/55	62.8	10.8	6.3	6.2	4.77	23.7
1029/55	58.7	6.9				
78/52	67.3	14.1		8.3		

The composition of the ancient ores and slags here reported poses more problems than it solves. Our success in following the ancient trails to the apparent sources of the ores found in the acropolis is in need of further evaluation. The quality of ancient slags and their remarkably high melting ranges (*4*) need to be reconciled with current views of ancient metallurgy. Finally, the out-of-place materials, other than artifacts, found in the acropolis cannot be accounted for in the present state of our knowledge. However, a preliminary report is not devoid of interest, in view of the cultural-historical importance of the area and the insufficiency of contemporary archeological knowledge.

Notwithstanding the opinion of such scholars as Glueck (*2*, pp. 77–79), mining in Timnah could not have been arduous at any time. Outcrops and tunnels utilized by our predecessors in mining required more skill than manpower in their discovery and development (*5*). Smelting of the ancient copper ores required far more skill than brawn, judging by the quality of the slags and of the finished products. Fuels and flux materials were procurable apparently within a short distance of the smelting site. The climate was pleasant in winter and easily tolerable in summer, even as it is now. All the operations for the production of copper in the ancient times could be accomplished by a handful of laborers, a few skilled technicians, and the military guard—essential then as it is today.

The acropolis containing ash and slag heaps is situated on a flat top of an isolated hill of white sandstone in the central part of the wadi. The hill is a rectangle, about 1000 by 400 feet, with vertical slopes about 100 feet high above the surface of the wadi. The hill can be ascended by one of the two paths cut or worn in the rock or by a talus slope from the south, by the side of a sand-filled cave now concealed by boulders and poorly accessible. The acropolis was visited by us five times in 1954–55. Collections of suitable materials were made for subsequent studies, and the largest slag heap was excavated in two places, to the sandstone floor of the hilltop.

Three types of materials were especially interesting in the earlier exploration: (i) fragments of copper ore on the surface of the ground and in the heaps, all of a uniform size but of five different kinds, morphologically; (ii) fragments of slag of two different kinds but of a rather small and uniform size, in contrast with other slag heaps in the area; and (iii) the out-of-place materials (*6*), notably fragments and masses of red sandstone and conglomerate containing small amounts of gold, as well as some other kinds of materials, including large crystals of calcite the sources of which are still undiscovered.

Fragments of the copper ores found in the acropolis were grouped into five categories, on the basis of their appearance and of the associated rock. The chemical analysis (*7*) of these ores is given in Table 1.

Outcrops of copper ore resembling the five kinds found in the acropolis were located by us within a short distance of the site, after a detailed search, involving utilization of ancient trails (along which sparse fragments of ores, calcite, and other materials were scattered), the normal dispersion trains, and other prospecting leads. Significantly, no chalcocite copper was found in the acropolis and it is possible that none was taken by the ancients of the acropolis from the outcrops or the wadis, despite its high copper content (Table 2) and its fairly common presence in some alluviums.

Table 3. Comparison between some chemical constituents of slags and copper ores (percentage of original sample); cobalt and lead were not detected in the slags.

No.	Material	Cu	Fe	Mn	Cl	P_2O_5	CaO	MgO
136/55	Porous slag	1.74	35.6	2.71	0.1	0.72	4.17	1.04
137/55	Massive slag	1.55	35.3	2.74	0.06	1.05	4.68	1.11
348/55 through 352/55	Copper ores	15–23	0.4–17	0–0.07	0.1–0.8		0.8–7.8	0.1–0.4

Two kinds of black slag are found in the ash heaps of the acropolis, massive and porous. They are found in relatively small fragments, as a rule, in contrast to the large and irregular pieces of slag found at the foot of the acropolis, within an enclosure, and elsewhere in the area. It is not clear whether the slag in the acropolis was fragmented by man or by the natural agencies. If it was fragmented by man, the purpose of the operation is obscure. Melting points of both kinds of slag are the same, about 1250°C and higher—a remarkably high temperature. Their chemical composition is nearly the same (Table 3).

The discrepancy between the manganese content of the slags and of the copper ores is significant enough to make one doubt any relationship between the two materials, to doubt possibly the very supposition that it was copper that was melted in the acropolis, unless one could prove that manganiferous materials were used in the smelting flux (*8*). No such materials were found by us there, except a few rounded fragments of a manganese-quartz conglomerate. Studies now in progress may help clarify this and other problems posed by our preliminary findings.

Archeological-historical understanding of the ancient metallurgical skills is not possible without detailed chemical analysis and experiments in the laboratory and a full accounting in the field for all materials in the acropolis—that is, for the sources of ores, fluxes, and the out-of-place rock. Our interest is not in the scale of the operations but in their quality and kind, the more so since the acropolis seems to be unique among the smelting sites of southern Negev in regard to the materials it contains and the kind of operations their presence implies.

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References and Notes

1. Published by permission of the director, Machzavei Israel (Israel Mining and Industries).
2. A superficial description of this site is given by N. Glueck, in *The Other Side of Jordan* (American Schools of Oriental Studies, New Haven, Conn., 1940), p. 79.
3. The district may have been worked repeatedly, both before and after the reign of King Solomon.
4. The incipient white range; we are indebted to M. Chvalov of the Technion, Haifa, for these measurements.
5. According to Glueck, (*2*, p. 77) "Cupriferous sandstone protrudes all over the surface of the entire wadi." This is far from being the case. Outcrops of mineralized rock were not easy to find in Timnah, after extensive studies by a sequence of geologists. Some outcrops were found only recently and others remain inferred rather than proved. The wadi floors are chiefly alluvium, with only occasional fragments of concretionary copper ore of the kind that *was not* smelted by the ancients, despite its high copper content. The protrusions of cuprite and malachite mentioned by Glueck still remain to be found.
6. Not including the artifacts: a few blades of flint of a highly skilled workmanship; potsherds of different kinds, thicknesses, and modes of tempering and firing; grinding stones; mortar slabs; egg tray-like slabs of obscure origin or use; and so forth. Weathered fragments of large marine shells and bones of desert animals were found in bonfire residues, among other things.
7. We are indebted to A. Alon and Y. Mashal for the chemical data in this report, and to Nevies for analysis No. 78/52.
8. A. Dor and Y. Cohen, of the Machzavei Israel, succeeded in smelting a chrysocolla ore from Timnah using a charcoal, calcium carbonate flux.

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Cocarcinogens and Minimal Carcinogenic Doses

The concept of cocarcinogenesis originated in 1938, when it was reported that a coal tar distillate, the basic fraction of a creosote oil, was capable of enhancing the activity of 3,4-benzopyrene on mice even though alone it did not give rise to tumors after skin painting or subcutaneous injection (*1*). Since the fraction did not appear to be carcinogenic, it was termed a "cocarcinogen." Subsequent studies with croton oil, croton resin, ultraviolet light, ionizing radiation, trauma, heat, and burns established those agents as experimental cocarcinogens for the mouse and led to acceptance of the term to apply to physical or chemical agents that are noncarcinogenic but which enhance the effect of a carcinogen, especially when the carcinogen is weak or applied at too low a level to produce tumors (*2, 3*).

Recognized tumor-inducing agents also have been used experimentally as cocarcinogens on the assumption that they were applied at so-called "minimal" or "subminimal" levels. It was supposed that they could not both "initiate" and "promote" neoplastic changes at low dosages in normal cells; their action was interpreted to be only that of "promoting" the growth potential of cells already rendered neoplastic by some preceding mechanism.

With the recent demonstrations that almost all heretofore identified cocarcinogens are capable of both initiating and promoting the growth of tumors (*4*), it would appear that, with the possible exception of trauma, what have been termed cocarcinogens are probably tumor-inducing agents tested under conditions that did not disclose their potency as tumor initiators. It appears timely therefore to question what is meant by "minimal," "subminimal," "initiating," and "promoting" doses when a known tumor-inducing agent is involved.

A technique frequently employed in experiments on cocarcinogenicity involves the application of a single subminimal carcinogenic stimulus to a selected site of the experimental animal to initiate a neoplastic change; this is followed by repeated applications of a cocarcinogen to promote the development of a grossly visible tumor from the initiated, but latent neoplastic cells. An experiment (*5*) to study the individual effects of the initiating and promoting dose with the carcinogen 3,4-benzopyrene is illustrated in Table 1. In that experiment, one group of mice received on the shaved interscapular skin a 0.01-ml drop of 1.25-percent benzopyrene in benzene. This provided approximately 125 μg of the carcinogen as a single subminimal dose. To a second group of mice, an estimated total of 120 μg was applied as a promoting agent in a dosage form of approximately 1 μg of 3,4-benzopyrene in benzene three times weekly for 40 weeks. The absence of any interscapular tumors in the first group is in sharp contrast with tumor induction in 9 of 42 mice in the second group by the 40th week of the experiment. Thus, depending on dosage and duration of exposure, the total amount involved in a subminimal acute exposure was more than adequate for tumor induction when exposures involved fractions of the total dose administered repeatedly. These results, obtained with a percutaneously applied carcinogen, parallel the observation that repeated oral doses of CCl_4 produced hepatomas in mice, whereas an equal total amount given in one dose did not (*6*). The factors of dosage and

Table 1. Tumor induction following single and repeated exposures to equal amounts of 3,4-benzopyrene in benzene.

3,4-Benzopyrene (μg per application)	Applications (No.)	Tumors after 40 wk (%)
125	1	None
1	120*	20 (9/42)

* Applied three times per week to interscapular skin of C57/B1 male mice.